**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

**For the fiscal year ended December 31, 2024**

**OR**

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

**For the transition period from _to_**

**Commission File Number 001-36352**

# AKEBIA THERAPEUTICS, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **20-8756903** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| **245 First Street, Cambridge, MA** | **02142** |
| (Address of principal executive offices) | (Zip Code) |

**Registrant's telephone number, including area code: (617) 871-2098**

**Securities registered pursuant to Section 12(b) of the Act:**

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| **Common Stock, $0.00001 par value per share** | **AKBA** | **The Nasdaq Capital Market** |

**Securities registered pursuant to Section 12(g) of the Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☒ |
| Non-accelerated filer | ☐ | Smaller reporting company | ☒ |
| | | Emerging growth company | ☐ |

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the registrant's Common Stock on The Nasdaq Capital Market on June 28, 2024, was $210,916,948.

The number of shares of registrant's Common Stock outstanding as of March 10, 2025 was 236,231,057.

**DOCUMENTS INCORPORATED BY REFERENCE**

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2025 Annual Meeting of Stockholders within 120 days after the end of the registrant's fiscal year ended December 31, 2024. Portions of the proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

**Akebia Therapeutics, Inc.**
**Form 10-K**
**For the Year Ended December 31, 2024**

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In this Annual Report on Form 10-K, or Form 10-K, unless otherwise stated or the context otherwise requires, references to "Akebia," "we," "us," "our," "the Company," "our Company" and similar references refer to Akebia Therapeutics, Inc. and, where appropriate, its consolidated subsidiaries. On December 12, 2018, in connection with the consummation of the merger, or Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, Keryx became a wholly owned subsidiary of the Company.

**CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This Annual Report on Form 10-K, or Form 10-K, contains forward-looking statements that are being made pursuant to the provisions of the U.S. Private Securities Litigation Reform Act of 1995 with the intention of obtaining the benefits of the "safe harbor" provisions of that Act. All statements contained in this Form 10-K other than statements of historical fact are forward-looking statements. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "build," "can," "contemplate," "continue," "could," "should," "designed," "estimate," "project," "expect," "forecast," "future," "goal," "intend," "likely," "may," "plan," "possible," "potential," "predict," "strategy," "seek," "target," "will," "would," and other words and terms of similar meaning, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements about:

- our plans with respect to commercializing Vafseo® (vadadustat) and label expansion opportunities currently under evaluation for Vafseo;
- our ability to maintain contracts with dialysis organizations for the sale of Auryxia® (ferric citrate) and Vafseo in the U.S.;
- the potential therapeutic benefits, safety profile, and effectiveness of Vafseo;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- the timing, investment and associated activities involved in continued commercialization of Auryxia, its growth opportunities and our ability to execute thereon;
- the potential indications, demand and market opportunity, potential and acceptance of Auryxia and Vafseo, including the size of eligible patient populations;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our capital requirements, need for additional capital, financing our future cash needs, costs, expenses, revenues, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations and the period of time our cash resources will fund our current operating plan, estimates with respect to our ability to operate as a going concern, our internal control over financial reporting and disclosure controls and procedures, and any future deficiencies or material weaknesses in our internal controls and procedures;
- delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for stockholders;
- the direct or indirect impacts of the COVID-19 pandemic on our business, operations and the markets and communities in which we and our partners, collaborators, vendors, and customers operate;
- our manufacturing, supply and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences;
- estimates, beliefs and judgments related to the valuation of goodwill, debt and other assets and liabilities, including classification of expenses, assets and liabilities, our impairment analyses and our methodology and assumptions regarding fair value measurements;
- the timing of the availability and disclosure of clinical trial data and results;
- the designs of our studies, and the type of information and data expected from our studies and the expected benefits thereof;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, supply, commercialization, launch, marketing and sale of Auryxia and Vafseo and the associated timing thereof;
- our ability to maintain any marketing authorizations we currently hold or will obtain, including our marketing authorizations for Auryxia and our ability to complete post-marketing requirements with respect thereto;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Auryxia and Vafseo;
- the timing of initiation of our clinical trials and plans to conduct preclinical studies and clinical trials in the future;
- the timing and amounts of payments from or to our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements, including with respect to milestones and royalties;

- our intellectual property position, including obtaining and maintaining patents, and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights, patent infringement suits that we have filed or may file, or other actions that we may take against companies, and the timing and resolution thereof;
- expected ongoing reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of Auryxia and Vafseo;
- accounting standards and estimates, their impact, and their expected timing of completion;
- estimated periods of performance of key contracts;
- our facilities, lease commitments, and future availability of facilities;
- cybersecurity;
- insurance coverage;
- management of personnel, including our management team, and our employees, including employee compensation, employee relations, and our ability to attract, train and retain high quality employees;
- the implementation of our business model, current operating plan, and strategic plans for our business, product candidates and technology, and business development opportunities including potential collaborations, alliances, mergers, acquisitions or licensing of assets;
- additional costs we may incur due to events associated with or resulting from our prior workforce reductions or other operating expenses, including additional costs related to vadadustat and selling, general and administrative expenses; and
- the timing, outcome and impact of current and any future legal proceedings.

Any or all of these forward-looking statements in this Form 10-K may turn out to be inaccurate. These forward-looking statements involve risks and uncertainties, including those that are discussed below under the heading "Risk Factors Summary", and the risk factors identified further in Part I, Item 1A. "Risk Factors" included in this Form 10-K and elsewhere in this Form 10-K and in our Securities and Exchange Commission reports filed after this report, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date of this Form 10-K. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason. Unless otherwise stated, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

This Form 10-K also contains estimates and other information concerning our industry and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

**RISK FACTORS SUMMARY**

Investing in our common stock involves numerous risks, including the risks summarized below and described in further detail in "Part I, Item 1A. Risk Factors" of this Form 10-K, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects. These risks include, but are not limited to, the following.

- We have incurred significant losses since our inception, and anticipate that we will continue to incur losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.
- We may require substantial additional financing to fund our business. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our products and product candidates on unfavorable terms to us.
- We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.
- We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.
- Our obligations in connection with the BlackRock Credit Agreement and requirements and restrictions in the BlackRock Credit Agreement could adversely affect our financial condition and restrict our operations.
- Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.
- Our business is substantially dependent on the commercial success of Auryxia and Vafseo. If we are unable to continue to successfully commercialize Auryxia and Vafseo, our results of operations and financial condition will be materially harmed.
- If we are unable to maintain or expand sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, Vafseo or any other product candidates that may be approved.
- Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, Vafseo or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.
- The commercialization of ferric citrate, branded as Riona in Japan, Vafseo in Europe, Japan and other territories where it is approved, and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the United States, or U.S., subject us to a variety of risks associated with international operations, which could materially adversely affect our business.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development of any of our product candidates.
- Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.
- We may not be able to obtain marketing approval for any label expansion for Vafseo or any current or future product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.
- If we are unable to obtain or maintain marketing approval in jurisdictions outside the United States, we and our partners will not be able to market any product or product candidates outside of the United States.
- Products approved for marketing are subject to extensive post-marketing regulatory requirements, including post-approval pediatric studies for Auryxia and Vafseo, and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if approved.

- We are subject to complex regulatory schemes that require significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.
- We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia, Vafseo or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.
- Policy changes or disruptions at the U.S. Food and Drug Administration, Centers for Medicare & Medicaid Services, regulatory authorities outside the U.S. and other government agencies caused by funding shortages, global health concerns or other events could prevent products, product candidates and services from being developed or commercialized in a timely manner, with expected terms or at all, which could negatively impact our business.
- Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the U.S. or foreign jurisdictions.
- We depend on collaborations with third parties for the development and commercialization of Auryxia, including an authorized generic version of Auryxia, Riona and Vafseo and, if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona and Vafseo, and our business could be materially harmed.
- We rely upon third parties to conduct all aspects of our product manufacturing and commercial distribution, and in many instances only have a single supplier or distributor, and the loss of these manufacturers or distributors, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.
- We rely upon third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, Vafseo or any of our product candidates, and our business could be substantially harmed.
- If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.
- Changes in U.S. and international trade policies, particularly with respect to China and Canada, may adversely impact our business and operating results.
- If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.
- We may not be able to protect our intellectual property rights throughout the world.
- The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia, Vafseo or other future products.
- The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia and Vafseo sales and have an adverse impact on our business and results of operation.
- Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.
- We have identified a material weakness in our internal control over financial reporting as of December 31, 2024 relating to our accounting for inventory and inventory related transactions. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in our internal control over financial reporting in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately or timely report our financial results or prevent fraud, and we may conclude that our internal control over financial reporting is not effective, which may adversely affect our business.
- Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors and could result in substantial costs and divert management's attention.

**PART I**

**Item 1. Business**

***Overview***

We are a fully integrated biopharmaceutical company with two commercial products for patients impacted by kidney disease. We have built a business focused on developing and commercializing innovative therapeutics that we believe serve as a foundation for future growth. Our team has significant expertise in hypoxia-inducible factor, or HIF, science having developed and commercialized Vafseo® (vadadustat), an oral HIF prolyl hydroxylase, or HIF-PH, inhibitor and have selected two additional HIF-based molecules for preclinical development.

We have established the company as a leader in the kidney community, and we believe our cross-organizational expertise in renal disease positions us for success. Chronic kidney disease, or CKD, is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient's blood, leading to other health problems, including anemia, cardiovascular disease and bone disease. CKD significantly impacts the United States, or U.S., healthcare system, potentially affecting approximately 37 million patients and costing Medicare nearly $125 billion annually for treating Medicare beneficiaries with CKD or end-stage renal disease, or ESRD, according to the Centers for Disease Control and Prevention. Our two commercial products address certain complications of kidney disease.

Our current portfolio includes:

**Vafseo** was approved by the U.S. Food and Drug Administration, or the FDA, in March 2024 for the treatment of anemia due to CKD in adult patients on dialysis for at least three months. Shipment of Vafseo commenced in January 2025. We have commercial supply agreements for the purchase of Vafseo in place with dialysis organizations caring for nearly 100% of dialysis patients in the U.S. The current U.S. market opportunity for the treatment of anemia due to CKD in patients with dialysis is approximately $1 billion based on current erythropoiesis-stimulating agent, or ESA, pricing, and Vafseo is the only oral HIF-based treatment available in the U.S.

In the European Union, or EU, the United Kingdom, or UK, Switzerland and Australia, Vafseo is approved for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. Our partner MEDICE Arzneimittel Pütter GmbH & Co. KG, or Medice, has an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in defined territories and launched Vafseo in Germany, Austria, Switzerland, the Netherlands and certain other countries in Europe in 2024.

In Japan, Vafseo is approved as a treatment for anemia due to CKD in both dialysis dependent and non-dialysis dependent patients and is marketed and sold by our collaborator Mitsubishi Tanabe Pharma Corporation, or MTPC. In Taiwan, Vafseo is approved for the treatment of symptomatic anemia due to CKD in adult patients on chronic maintenance dialysis and was launched in October 2024 by Tai Tien Pharmaceutical Company, an affiliate of MTPC. In Korea, Vafseo is approved as an anemia treatment for patients with CKD on hemodialysis.

**Auryxia® (ferric citrate)** is an orally administered medicine approved and marketed in the U.S. for two indications: (1) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis-dependent chronic kidney disease, or NDD-CKD.

Today, we market Auryxia in the U.S. Auryxia became part of our portfolio in 2018 and has historically contributed meaningful revenue to the business. In March 2025, Auryxia will lose exclusivity, or LoE. We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B could result in slower revenue decline after the LoE date than in other LoE situations, but the impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

Ferric citrate hydrate has also been approved in Japan, and is marketed and sold by our Japanese sublicensee, Japan Tobacco, Inc., and its subsidiary, Torii Pharmaceutical Co., Ltd., collectively, JT and Torii, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA under the trade name Riona in Japan. Averoa SAS, or Averoa, has an exclusive license to develop and commercialize ferric citrate in the European Economic Area, or EEA, Turkey, Switzerland, the UK, the Balkans and certain countries in Eastern Europe and the Middle East. Averoa applied for marketing authorization for ferric citrate in Europe in April 2024.

**Our HIF-based product candidates and other pipeline assets** are being evaluated to target areas of unmet needs. The discovery of HIF laid the foundation to explore the central role of oxygen sensing in many diseases. As we have

seen through the development of Vafseo as a treatment for anemia due to CKD, when stabilized, HIF triggers wide-ranging adaptive, protective responses during hypoxic or ischemic conditions. We have selected two additional HIF molecules for preclinical development: AKB-9090, potentially for cardiac surgery-related acute kidney injury, or CS-AKI, or acute respiratory distress syndrome, or ARDS, and AKB-10108 for retinopathy of prematurity, or ROP, in neonates.

In June 2021, we acquired from Cyclerion Therapeutics, Inc., or Cyclerion, an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator. We believe there is potential to explore the use of praliciguat for indications within kidney disease.

We continue to explore additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation to leverage our fully integrated team.

***Strategy***

Our deep understanding of kidney disease helps us serve the unmet needs of kidney patients and others impacted by chronic and debilitating illness. Our commitment to patients informs our business decisions and short and long-term planning. There is a clear need to improve quality of life outcomes for people living with kidney disease. The prevalence and incidence of CKD is increasing in the U.S. population. The progression of CKD towards renal failure is complicated by multiple conditions which further deteriorate kidney function and the general health of patients if left untreated. Typically, the prevalence of these conditions increases as CKD progresses.

With two revenue-generating products and the research and development capabilities to discover, advance and commercialize new therapies, our intention is to both fulfill our purpose to better the lives of those impacted by kidney disease as well as leverage our internally developed innovations and explore therapies in other disease areas with high unmet needs.

Our strategic imperatives are threefold:

1. We aim to drive Vafseo to be the standard of care for the treatment of anemia due to CKD in the U.S. in both dialysis and, if approved, non-dialysis patient populations. We are commercializing Vafseo in the U.S. for adult patients on dialysis and began shipping product in January 2025. We have also advanced a plan to explore label expansion to the non-dialysis patient population and submitted a protocol to the FDA for VALOR, a Phase 3 cardiovascular outcome study of approximately 1,500 patients in the U.S. with late-stage CKD anemia not on dialysis. We expect to meet with the FDA to discuss VALOR.
2. Powered by Nobel prize-winning HIF science and in-licensed technology, we plan to work to create a future for Akebia both within and beyond kidney disease. We intend to leverage our cross organizational experience in nephrology gained through the commercialization of Auryxia and our team's robust discovery and research and development capabilities to advance our pipeline.
3. We continue to explore strategic growth, which includes additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics, through external innovation to leverage our fully integrated team.

We plan to make strategic use of capital and will also continue our approach of financial discipline, cross-organizational efficiency and operational effectiveness.

***Drive Vafseo to be Standard of Care in the Treatment of Anemia due to CKD***

Anemia is common in patients with CKD, and its prevalence increases with disease progression. Anemia due to CKD results from inadequate erythropoietin, or EPO, levels, negatively affecting red blood cell production. Left untreated, anemia accelerates the overall deterioration of patient health with increased morbidity and mortality. According to the U.S. Renal Data System 2022 Annual Data Report, there were nearly 558,000 patients in the U.S. on dialysis in 2020, of which 86% were on in-center hemodialysis and the remainder on home dialysis, which includes both peritoneal dialysis and home hemodialysis.

The current standard of care for anemia due to CKD is treatment by injectable recombinant human ESAs such as Epogen® (epoetin alfa), Aranesp® (darbepoetin alfa) or Mircera® (methoxy polyethylene glycol-epoetin beta), or blood transfusion. When administered to a patient, injectable ESAs provide supraphysiological levels of exogenous EPO to stimulate production of red blood cells, or RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects and need to be injected subcutaneously or intravenously.

The current market opportunity for the treatment of anemia due to CKD in adult patients on dialysis is approximately $1 billion in the U.S. based on current ESA pricing. We believe there is a significant opportunity for Vafseo to become the standard of care for the treatment of anemia due to CKD for adult patients on dialysis and, if approved, not on dialysis.

Vafseo is an oral HIF-PH inhibitor that stimulates the body's natural response to hypoxia. Through activation of the HIF pathway, Vafseo stimulates the body's natural production of EPO and improves mobilization of stored iron to help dialysis patients with CKD manage their anemia. Our data from the $INNO_2VATE$ trials show Vafseo corrected and maintained hemoglobin within target range through a gradual increase over time with evidence of fewer hemoglobin overshoots. Further, we saw in our studies fewer dose adjustments in an once daily oral dose for patients. Our clinical data showed that Vafseo has a safety profile similar to the ESA standard of care. These findings contribute to why we believe Vafseo offers a compelling new choice for physicians for anemia management.

***Vafseo – An oral treatment for anemia due to CKD for adult patients on dialysis***

Upon Vafseo approval, we implemented a launch plan to commercialize Vafseo for the treatment of anemia due to CKD in adult patients on dialysis, the critical first step toward Vafseo potentially becoming the standard of care. We have completed certain critical commercialization initiatives, including securing reimbursement for Vafseo under the Transitional Drug Add-on Payment Adjustment, or TDAPA, and securing access to Vafseo for patients through commercial supply agreements with dialysis organizations. In addition, we continue to work to help dialysis organizations establish protocols and to drive prescriber demand.

Medications covered under the ESRD Prospective Payment System, or PPS, in Medicare are known as the ESRD Bundle, a payment structure with a flat base rate per dialysis session adjusted for individual patient and facility characteristics. Dialysis-related drugs are included in the ESRD Bundle if they fall into functional categories such as anemia management. In a final ESRD PPS rule published in November 2018, Centers for Medicare & Medicaid Services, or CMS, confirmed that it will expand the TDAPA to all new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA provides separate payment for new drugs for two years based on the drug's Average Sales Price that is in addition to the base rate in the bundle in order to facilitate the adoption of innovative therapies. Vafseo met the criteria for TDAPA in the anemia management ESRD PPS functional category beginning on January 1, 2025. The TDAPA program provides two years of reimbursement for Vafseo in addition to the ESRD bundled rate to dialysis organizations.

Most dialysis clinics operate within dialysis organization networks, the largest of which are DaVita, Inc., or DaVita, Fresenius KidneyCare Group LLC, or Fresenius, and U.S. Renal Care, or USRC. Following Vafseo's U.S. approval, we engaged with dialysis organizations to secure commercial supply agreements for Vafseo. Prior to first shipping Vafseo in the U.S. in January 2025, we had contracts in place with dialysis organizations caring for nearly 100% of dialysis patients.

Treatment is usually driven by medical protocols that dialysis organizations implement across their entire network of clinics. With commercial supply contracts in place, our medical team is working closely with dialysis organization medical professionals to develop protocols for the use of Vafseo in appropriate patient populations as dictated by the Vafseo label. When implemented, protocols can result in rapid change applicable to large segments of the patient population covered by the protocol.

Today, we have an established and embedded commercial team with approximately 35 key account managers, or KAMs, supported by our commercial operations team. Upon Vafseo's U.S. approval and in parallel with contracting and protocol development, our KAMs began detailing Vafseo to prescribers. Nephrologists have identified particularly underserved patient groups: home dialysis patients, a segment in which injectable ESAs are cumbersome, and patients on a higher ESA dose as higher doses of ESAs may be associated with all-cause mortality and cardiovascular complications independent of hemoglobin level. We anticipate Vafseo near-term adoption in these patient populations.

Effective commercialization provides the foundation for a new treatment to potentially become the standard of care. We believe it is also important to generate new data to educate physicians. We initiated a collaborative clinical trial with USRC. In December 2024 the Vafseo Outcomes In-Center Experience trial began to enroll up to approximately 2,200 patients randomized to oral Vafseo 300 mg tablets administered three times per week or standard-of-care ESAs. The trial will end approximately 18 months after the last patient is randomized. The primary endpoint is all-cause mortality, and the secondary endpoint is all-cause hospitalization. The trial was powered to demonstrate non-inferiority for all-cause mortality and superiority for a 10% reduction in all-cause hospitalization. As of early March, USRC has enrolled more than half of the total target of 2,200 patients in the trial, and we expect the trial to be fully enrolled by the end of 2025.

Separately, additional studies might provide relevant data to support Vafseo label expansion specific to alternative dosing to complement existing alternative dosing data. We previously completed the FO2CUS study and the MO2DIFY study which both evaluated alternative dosing. See Part I, Item 1, Clinical Development Programs, for additional information on the $FO_2CUS$ study and the $MO_2DIFY$ study.

***Vafseo – The potential for label expansion for the treatment of anemia due to CKD for patients not on dialysis.***

There are approximately 550,000 patients with stage 4 or stage 5 CKD who are anemic and not receiving dialysis. Of these patients, only 25 percent are treated for anemia. As CKD is progressive and irreversible, these patients are likely to advance to ESRD and dialysis. Data suggests that if patients start dialysis with a hemoglobin level that is in the range of 9 g/dL to 10 g/dL, they have a significantly higher mortality rate at three months, six months and 12 months, even once their anemia is adequately managed. However, despite an appreciation of the risks of starting dialysis with unmanaged anemia, industry research suggests that the use of ESAs is low and declining in the non-dialysis patient population. Today, ESAs in the non-dialysis CKD patient population are approved but use is limited, typically following label guidance when a patient's hemoglobin is below 10 g/dL and to reduce the likelihood of requiring a red blood cell transfusion. Concerns with the potential risk of hemoglobin instability that is a result of labeling could contribute to non treatment with an ESA. Further, data suggests patients are hesitant to self-administer an injection.

We believe the availability of an oral HIF-PH inhibitor within the non-dialysis patient population could address the issues contributing to the decline in ESA use among that patient population. We believe physicians agree, as third-party data from a 2024 Spherix Global Insights report indicated that 87% of physicians agreed with the statement that their treatment of anemia in CKD non-dialysis dependent patients would increase substantially if HIF-PH inhibitors are FDA approved.

We are committed to pursuing a path for label expansion for Vafseo for CKD non-dialysis dependent patients. We initially submitted a New Drug Application, or NDA, to the FDA for vadadustat in March 2021 and in March 2022, the FDA issued a complete response letter, or CRL, to our NDA. The FDA concluded that the data in the NDA did not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns, noting failure to meet non-inferiority in Major Adverse Cardiovascular Events, or MACE, in the non-dialysis patient population. While we have since secured FDA approval for use in dialysis patients, we believe there are compelling data supporting a positive benefit-risk profile for the use of Vafseo broadly in patients with CKD. In addition, we submitted a protocol to the FDA for VALOR, a Phase 3 cardiovascular outcome study of approximately 1,500 U.S. subjects with late-stage CKD anemia not on dialysis with a comparator to standard of care. We received FDA feedback on the protocol and expect to meet with the FDA to discuss VALOR. We intend to initiate the study by the second half of 2025. The study will be one part of what we believe will be a robust data package that will likely include data from the 1,700 U.S. patients in the Global Phase 3 $PRO_2$TECT Program, as well as safety data from the commercial use of Vafseo in the U.S. in dialysis patients, and data on the use of Vafseo in Japan in dialysis and non-dialysis patients where Vafseo has been in the market since 2020.

***Create a Future for Akebia both within and beyond Kidney Disease***

We believe our leadership in the kidney community and deep understanding of the CKD market creates a competitive advantage and positions us for success particularly through the launch of Vafseo. We seek to explore opportunities where we can leverage our commercial excellence attained over the past decade commercializing Auryxia in the kidney space.

Hyperphosphatemia is a metabolic disorder characterized by elevated serum phosphorus levels. Phosphorus is a vital element required for most cellular processes and, in individuals with normal kidney function, excess dietary phosphorus is removed by the kidneys and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.5 to 4.5 mg/dL. In adults with DD-CKD, elevated phosphorus levels, or hyperphosphatemia, can be associated with adverse effects, including increased risk for cardiovascular disease, bone disease and death.

Phosphate binders and phosphate inhibitors are the only interventions marketed for the treatment of hyperphosphatemia. According to the U.S. Renal Data System 2022 Annual Data Report, there were nearly 558,000 patients in the U.S. on dialysis in 2020, of which approximately 80% were treated with a phosphate binder. Phosphate binders need to be taken with meals and snacks, and it is not uncommon for CKD patients receiving dialysis to be prescribed as many as 12 or more phosphate binder pills per day, among other medications. Patients taking phosphate binders also experience gastrointestinal tolerability issues. As a result of the pill burden and tolerability issues associated phosphate binders, prescribed phosphate binders are often intolerable for many patients, leading to lack of treatment adherence.

In addition, in 2020 approximately 44% of patients treated with a phosphate binder were treated solely with a calcium-based binder, which can lead to side effects such as increased cardiovascular risk, hypercalcemia and gastrointestinal-related adverse events. Due to the risks associated with calcium-based binders, in 2017 Kidney Disease: Improving Global Outcomes, recommended that clinicians limit the use of calcium-based binders.

IDA is a common form of anemia that is caused by patients not having enough iron to manufacture healthy RBCs. Although anyone can develop IDA, it is particularly common in NDD-CKD patients. IDA is associated with fatigue, lethargy, decrease quality of life, cardiovascular complications, hospitalizations and increased mortality.

We estimate that there are more than 500,000 adult patients in the U.S. with NDD-CKD diagnosed with IDA and managed by a nephrologist. Currently, there are two forms of iron therapy used to treat IDA: oral iron supplements and iron delivered via intravenous infusion, or IV. Oral iron is currently the first-line iron replacement therapy for most physicians; however, oral iron supplements are poorly absorbed by many patients, which may adversely impact their effectiveness, and are associated with certain side effects, such as constipation, diarrhea and cramping, that may adversely affect treatment adherence. IV iron is viewed as an effective treatment; however, like other intravenous medicines, it is logistically difficult to administer in an office setting, where NDD-CKD patients are more often treated.

***Auryxia – An oral treatment for hyperphosphatemia and iron deficiency anemia***

We market Auryxia in the U.S. through our well-established, nephrology-focused sales force and commercial organization.

Auryxia, an oral-only phosphate binder, was included in the ESRD PPS bundle payment beginning in January 2025, representing a shift, as Auryxia was previously covered by Medicare under Part D and commercial channels. In addition, dialysis organizations will receive a TDAPA payment for claims that include phosphate binders for the next two years. After two years, CMS will adjust the bundle price based on the amount spent on phosphate binders during that time and no longer include an extra TDAPA payment in claims. The shift in reimbursement initiated a change in the distribution of Auryxia to patients and a change in our contracting strategy. We had previously distributed Auryxia primarily in the retail channel through wholesalers or through large dialysis organization pharmacies, such as Fresenius Rx. Now, patients with hyperphosphatemia have access to Auryxia through dialysis organizations in the U.S. and distribution of Auryxia sits with the dialysis organization through dialysis organizations' pharmacies, or other specialty pharmacies or distributors.

In preparation for this change, throughout 2024 we began contracting directly with dialysis organizations for Auryxia. Some of the dialysis organizations had their own specialty pharmacies and could distribute medication to patients, while others needed to partner with a specialty pharmacy to provide this service. We determined that, in order to ensure patient access, we needed to contract with distribution partners of the dialysis organizations as well. We enabled broad access to Auryxia by executing contracts with dialysis organizations that care for nearly 100% of patients on dialysis in the U.S. Akebia now delivers Auryxia directly to dialysis organizations or to their distribution partners rather than to wholesalers.

We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that protect us from generic drug competition until March 2025. We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B could result in slower revenue decline after the LoE date than in other LoE situations, but the impact of LoE on future Auryxia revenues will depend on many factors including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

Outside the U.S., JT and Torii market Riona in Japan, and we receive tiered double-digit royalties based on their sales in Japan. Averoa applied for marketing authorization for ferric citrate in Europe.

We also leverage our research and development competency and expertise in HIF-based technology to both build on our commitment to kidney disease and also address areas of unmet medical need outside of kidney disease. We have invested resources to build out a preclinical portfolio and have selected two candidates for further preclinical development: AKB-9090 and AKB-10108. We intend to explore AKB-9090 for potential use in CS-AKI and ARDS, and AKB-10108 for potential use in ROP.

*Cardiac Surgery-related Acute Kidney Injury*

AKI is a sudden decline in the ability of the kidneys to work and perform their normal functions. AKI occurs in many settings including in 20-30% of the approximately two million patients who undergo cardiac surgery with use of cardio-pulmonary bypass each year worldwide. There are no current treatments available for CS-AKI. Stabilization of HIF by prolyl hydroxylase inhibition leads to the release of erythropoietin, a shift to anaerobic metabolism (glycolysis) and decreased inflammatory responses that collectively lessen kidney ischemia-reperfusion injury and ameliorate the decline in kidney function seen in many clinical settings including CS-AKI. Data from our preclinical studies showed AKB-9090 to be highly active in lessening the severity of AKI in an animal model of ischemia-reperfusion injury. We expect to initiate a Phase 1 trial of AKB-9090 in 2025.

*Acute Respiratory Distress Syndrome (ARDS)*

ARDS is a life-threatening acute form of lung disease characterized by acute bilateral pulmonary edema and severe hypoxemia (low blood oxygen). Despite improvement in supportive care, a third-party study indicated high hospital mortality rates for patients with ARDS admitted to participating intensive care units. The mortality rate among patients with ARDS in the study was: 34.9% with mild ARDS; 40.3% with moderate ARDS and 46.1% with severe ARDS. There are currently no treatments

available for ARDS except for supportive care. Stabilization of HIF by prolyl hydroxylase inhibition leads to the release of erythropoietin, increased extracellular adenosine signaling, increased glycolytic activity and decreased inflammation in lung epithelial cells that promote resolution of the lung injury. Our plan is to first study HIF activity in vadadustat for the treatment of ARDS due to suspected aspiration, pathogen-associated pneumonia, or sepsis in hospitalized patients, which could provide clinical data from an investigator-initiated trial, and then to use these findings to support clinical development of an alternative HIF-based molecule such as AKB 9090 for ARDS. In earlier studies, vadadustat lessened the severity of COVID-19 pneumonia in a clinical trial (NCT04478071) and improved outcomes in animal models of acute lung injury.

*Retinopathy of Prematurity (ROP)*

ROP is the leading cause of blindness in preterm infants globally and occurs due to incomplete retinal development and abnormal blood vessel growth in the retina. ROP is caused by the high oxygen therapy used to treat preterm babies, which prevents retina growth. Annually, there are approximately 100,000 new cases of infant blindness worldwide due to ROP and currently no preventative therapy. HIF-PH inhibitors can protect the retina by stabilizing HIF, which degrades during hyperoxia, allowing normal retinal development and preventing abnormal blood vessel growth that can lead to scarring, bleeding, retinal detachment and blindness. Data from our preclinical studies of AKB-10108 in mouse and rat models of ROP showed significant improvements in retinal development under hyperoxic conditions, as well as significant reductions in abnormal blood vessel growth after returning to normal oxygen levels.

***Clinical Development Programs***

Below is a summary of the clinical development work completed for vadadustat.

*Vadadustat Global Phase 3 Clinical Program in Anemia Due To CKD*

We conducted a global Phase 3 clinical development program for vadadustat, which included two programs, INNO$_2$VATE and PRO$_2$TECT. INNO$_2$VATE evaluated vadadustat in adult DD-CKD patients with anemia due to CKD in two studies, and PRO$_2$TECT evaluated vadadustat in adult NDD-CKD patients with anemia due to CKD in two studies. Combined, we enrolled approximately 7,500 patients in these studies and evaluated a once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa.

Both the INNO$_2$VATE and PRO$_2$TECT Phase 3 programs were global, multicenter, open-label, sponsor-blind, active-controlled non-inferiority programs. In both programs, patients were randomized 1:1 to receive either oral vadadustat or injectable darbepoetin alfa. The primary efficacy endpoint for each study in the INNO$_2$VATE and PRO$_2$TECT programs was the mean change in hemoglobin between baseline and the primary evaluation period. Non-inferiority, or NI, for the primary efficacy endpoint was achieved if the lower bound of the 95% confidence interval for the between-group difference of the mean hemoglobin change did not fall below the pre-specified NI margin. Both the INNO$_2$VATE and PRO$_2$TECT programs included the primary safety endpoint of the assessment of MACE, with a comparison of vadadustat to darbepoetin alfa. MACE is defined as the composite endpoint of all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke. The primary safety analysis for each program was based on the combined MACE events from the two studies in each of INNO$_2$VATE and PRO$_2$TECT. NI for the primary safety analysis was achieved if the upper bound of the 95% confidence interval for the hazard ratio, or HR, of vadadustat to darbepoetin alfa did not exceed the pre-specified NI margin. We prospectively defined and agreed to non-inferiority margins with the U.S. and European regulatory authorities and agreed with the U.S. regulatory authorities on the key components of our statistical analysis plan.

*Top-line Results from Global Phase 3 INNO$_2$VATE Program within DD-CKD Adult Patients*

The two INNO$_2$VATE studies (Correction/Conversion and Conversion), which collectively enrolled 3,923 patients, evaluated the efficacy and safety of vadadustat versus darbepoetin alfa for the treatment of anemia due to CKD in DD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two INNO$_2$VATE studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in hemoglobin, or Hb, between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat also achieved the primary safety endpoint of the INNO$_2$VATE program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both INNO$_2$VATE studies.

Vadadustat achieved the INNO$_2$VATE program's primary safety endpoint of non-inferiority for MACE. In the primary analysis of time to first MACE event, vadadustat demonstrated non-inferiority to darbepoetin alfa using a non-inferiority margin of 1.25 based on discussion with the FDA and a non-inferiority margin of 1.3 based on discussion with the EMA. INNO$_2$VATE results on key secondary safety endpoints showed that vadadustat also demonstrated non-inferiority to darbepoetin alfa in analyses of expanded MACE, cardiovascular MACE, cardiovascular mortality, and all-cause mortality.

*Top-line Results from Global Phase 3 PRO$_2$TECT Program within NDD-CKD Adult Patients*

The two $PRO_2$TECT studies (Correction and Conversion), which collectively enrolled 3,476 patients, evaluated the efficacy and safety of vadadustat for the treatment of anemia due to CKD in NDD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two $PRO_2$TECT studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in Hb between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat did not meet the primary safety endpoint of the $PRO_2$TECT program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE, across both $PRO_2$TECT studies.

*Primary and Key Secondary Efficacy Endpoint Results*

Vadadustat achieved each of the $PRO_2$TECT studies' primary efficacy endpoints of mean change in Hb between baseline and the primary evaluation period compared to darbepoetin alfa, in adult patients on dialysis, demonstrating non-inferiority to darbepoetin alfa using an NI margin of -0.75 g/dL.

In $PRO_2$TECT's Correction study (n=1,751):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was 0.05 g/dL (95% CI: -0.04, 0.15), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.39 (0.99) g/dL for vadadustat-treated patients compared to 10.35 (1.03) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained the target Hb efficacy response at weeks 40 to 52 achieving non-inferiority compared to darbepoetin alfa. The least square mean difference in Hb was 0.04 g/dL (95% CI: -0.06, 0.14). The mean (SD) Hb level at week 40 to week 52 was 10.48 (1.05) g/dL for vadadustat-treated patients compared to 10.45 (1.01) g/dL for darbepoetin alfa-treated patients.

In $PRO_2$TECT's Conversion study (n=1,725):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was -0.01 g/dL (95% CI: -0.09, 0.07), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.77 (0.98) g/dL for vadadustat-treated patients compared to 10.77 (0.99) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained efficacy in the Conversion study demonstrating non-inferiority to darbepoetin with a least square mean difference in Hb of 0.00 g/dL (95% CI: -0.10, 0.09). The mean (SD) Hb level at week 40 to week 52 was 10.80 (1.04) g/dL in the vadadustat-treated patients compared to 10.79 (1.05) g/dL for darbepoetin alpha-treated patients.

*Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result*

The $PRO_2$TECT program (Correction and Conversion studies) (n=3,471):

- ***Primary Safety MACE Endpoint Result***: Vadadustat did not meet the PRO2TECT program's primary safety endpoint of non-inferiority for MACE. The upper bound of the 95% confidence interval of the HR was above the pre-specified NI margin of 1.25 for primary MACE analysis (HR 1.17, 95% CI: 1.01, 1.36).

Analysis of MACE events conducted by the Company in the $PRO_2$TECT program revealed that the greater number of MACE events observed among vadadustat patients as compared to the active comparator was primarily related to an excess of non-cardiovascular death and death-of-unknown-cause in regions outside of the U.S. where significant differences in treatment patterns for NDD-CKD patients were observed.

The $PRO_2$TECT analysis plan was prospectively designed to analyze the effect of regional differences, most notably, well-known differences in Hb treatment targets. Within $PRO_2$TECT, U.S. patients were treated to a target Hb range of 10 to 11 g/dL and non-U.S. patients were treated to a target Hb range of 10 to 12 g/dL. In October of 2020, we presented a pre-specified regional analysis that showed vadadustat was not associated with a clinically meaningful increase in cardiovascular risk compared to darbepoetin alfa in U.S. patients treated to a target Hb range of 10 to 11 g/dL, in an analysis of MACE (HR 1.06, 95% CI: 0.87, 1.29).

The incidence of treatment emergent adverse events, or TEAEs, during the Correction study in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common TEAEs reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious TEAEs were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of TEAEs during the Conversion study in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common TEAEs reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract

infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious TEAEs were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

*Hepatic Safety Profile of Vadadustat in Clinical Studies*

During the conduct of our Phase 3 program our team and hepatic experts analyzed hepatic cases (unblinded to treatment). Further, following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which included eight completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two then-ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review consisted of a blinded re-assessment of hepatic events conducted by a separate panel of hepatic experts. While hepatocellular injury attributed to vadadustat was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future. In the clinical review of our NDA in March 2024, the FDA concluded that there is a hepatocellular injury risk with the use of vadadustat in patients with CKD, although the risk of serious liver injury appears rare.

*Modified Dosing Studies*

From May 2020 to January 2023, we also conducted additional studies of vadadustat evaluating a modified approach to a once-daily and three-times weekly dosing, including assessment of a vadadustat starting dose based on an individual's pre-conversion ESA dose prior to study entry and higher titration doses of vadadustat (up to 1200 mg).

The $FO_2CUS$ study evaluated the efficacy and safety of vadadustat in hemodialysis patients who were converted from a long-acting ESA to three-times weekly oral vadadustat dosing for the maintenance treatment of anemia. $FO_2CUS$ was an open-label, active-controlled, sponsor-blinded study that evaluated 456 hemodialysis patients who were randomized (1:1:1) into a vadadustat 600mg starting dose, vadadustat 900mg starting dose, or a long-acting ESA (Mircera®) treatment arms.

The $MO_2DIFY$ study evaluated the efficacy and safety of vadadustat in hemodialysis patients using a modified once-daily dosing regimen different from the $INNO_2VATE$ program dosing and a three-times-weekly dosing regimen of oral vadadustat compared to darbepoetin alfa.

*$FO_2CUS$ Study*

*Primary and Secondary Efficacy Endpoint Results*

In the $FO_2CUS$ study, each vadadustat starting dose regimen (600 mg, 900 mg) and the combined vadadustat-treated group achieved the primary efficacy endpoint of the mean change in Hb between baseline and the primary evaluation period (weeks 20-26) compared to Mircera in adult patients on hemodialysis, demonstrating non-inferiority to Mircera based on a non-inferiority margin of -0.75 g/dL. Similarly, each starting dose regimen of vadadustat and the combined vadadustat-treated group achieved the secondary efficacy endpoint of the mean change in Hb between baseline and the secondary evaluation period (weeks 46-52).

In the $FO_2CUS$ study in hemodialysis patients (n=456):

- ***Primary Efficacy Endpoint Results***: Vadadustat demonstrated non-inferiority to Mircera. The least square mean difference in Hb was -0.43 g/dL (-0.67, -0.20) for the vadadustat 600 mg starting dose group, -0.23 g/dL (-0.46, 0.01) for the vadadustat 900 mg starting dose group, and -0.33 g/dL (-0.53, -0.13) for the combined vadadustat-treated group, achieving the pre-specified non-inferiority margin of -0.75 g/dL. The mean Hb level during the primary evaluation period was 10.11 (0.061) g/dL for the combined vadadustat-treated group compared to 10.41 (0.068) g/dL for Mircera-treated group.
- ***Secondary Efficacy Endpoint Results:*** Vadadustat demonstrated non-inferiority to Mircera. The least square mean difference in Hb was -0.27 g/dL (-0.54, -0.00) for the vadadustat 600 mg starting dose group, -0.38 g/dL (-0.67, -0.10) for the vadadustat 900 mg starting dose group, and -0.33 g/dL (-0.56, -0.09) for the combined vadadustat-treated group. The mean Hb level during the secondary evaluation period was 10.03 (0.066) g/dL for the combined vadadustat-treated group compared to 10.28 (0.076) g/dL for the Mircera-treated group.

*Safety Results*

In the $FO_2CUS$ study, a total of 78.7% of patients experienced any TEAEs in the combined vadadustat-treated group, and 75.3% experienced any TEAEs in the Mircera-treated group. The data demonstrated that 44.5% of patients experienced any serious TEAEs in the combined vadadustat-treated group, and 44.7% of patients experienced any serious TEAEs in the Mircera-treated group. During the study, the most common TEAEs reported in vadadustat-/Mircera- treated patients were COVID-19 (14.6%/16.0%), diarrhea (12.3%/8.0%) and hyperkalaemia (9.0%/10.7%).

*$MO_2DIFY$ Study*

*Primary and Secondary Efficacy Endpoint Results*

In the $MO_2$DIFY study, the vadadustat once-daily, or QD, treatment (starting dose: 300 or 450 mg) achieved the primary efficacy endpoint of the mean change in Hb from baseline to the primary evaluation period (weeks 20-26) compared to darbepoetin alfa in adult patients on hemodialysis, demonstrating non-inferiority to darbepoetin alfa based on a non-inferiority margin of -0.75 g/dL. Vadadustat three-times-weekly, or TIW, treatment (starting dose: 600 or 750) did not demonstrate noninferiority to darbepoetin alfa. Based on a sensitivity analysis using the per protocol population, both vadadustat dosing regimens demonstrated noninferiority to darbepoetin alfa of the mean change in Hb between baseline and the primary evaluation period.

Neither dosing regimen of vadadustat achieved the secondary efficacy endpoint of the mean change in Hb between baseline and the secondary evaluation period (weeks 46-52).

In the $MO_2$DIFY study in hemodialysis patients (n=319):

- ***Primary Efficacy Endpoint Results***: Vadadustat QD treatment was non-inferior to darbepoetin alfa. The least square mean difference in Hb was -0.27 g/dL (-0.55, 0.01) for the vadadustat QD-treated group, meeting the pre-specified non-inferiority margin of -0.75 g/dL. The least square mean difference in Hb was -0.53 g/dL (-0.80, -0.25) for the vadadustat TIW-treated group. The mean Hb level during the primary evaluation period was 10.23 (1.07) g/dL and 10.02 (0.87) g/dL for the vadadustat QD and vadadustat TIW groups respectively, compared to 10.45 (0.83) g/dL for the darbepoetin alfa group.
- ***Secondary Efficacy Endpoint Results***: The secondary efficacy endpoint was the change in average Hb between baseline and the secondary evaluation period (Weeks 46 to 52). The least square mean difference in Hb was -0.40 g/dL (-0.79, -0.02) for the vadadustat QD-treated group and -0.42 g/dL (-0.81, -0.02) for the vadadustat TIW-treated group. Since noninferiority for the secondary efficacy endpoint of vadadustat TIW to darbepoetin alfa was not established, no claims of noninferiority were made for the secondary efficacy endpoint.
- ***Other efficacy Endpoint:*** The proportion of subjects with an average Hb value within the target range (US [10.0 to 11.0 g/dL] and Europe [10.0 to 12.0 g/dL]) was similar in the vadadustat QD, vadadustat TIW and darbepoetin alfa treatment groups during the primary evaluation period (weeks 20 to 26) (51.0%, 50.7%, and 54.5%, respectively) and secondary evaluation period (weeks 46 to 52) (50.4%, 48.3%, and 51.3%, respectively).

*Safety Results*

Among all randomized patients who received at least one dose of the study medication (n=317), 84.8% and 84.6% of patients in the vadadustat QD and TIW groups, respectively, experienced any TEAEs, compared to 80.6% in the darbepoetin alfa group. The data showed that 44.8% of patients in the vadadustat QD group and 45.2% in the vadadustat TIW group experienced any treatment-emergent serious adverse events, compared to 43.5% of patients in the darbepoetin alfa group. The most commonly reported TEAEs in patients treated with vadadustat QD, vadadustat TIW, and darbepoetin alfa were COVID-19 (13.3%, 12.5%, and 13.0% respectively), diarrhea (13.3%, 14.4%, and 5.6% respectively), and anemia (7.6%, 10.6%, and 9.3% respectively).

***Manufacturing and Supply***

*Overview*

We neither own nor operate, and currently have no plans to own or operate, any manufacturing or distribution facilities. We rely on third-party contract manufacturing organizations, or CMOs, to produce all of our preclinical, clinical and commercial supply, and third-party distributors to distribute Auryxia and Vafseo. We have established relationships with several CMOs and expect to continue to rely on either existing or alternative CMOs and distributors to manufacture or distribute our products to support ongoing and planned preclinical, clinical and commercial distribution activities. Our CMOs have other clients and may have other priorities that could affect manufacturing line capacity and/or delivery schedules. Both of these occurrences would be beyond our control. All clinical and commercial supplies are manufactured under current Good Manufacturing Practices, or cGMPs, which is a regulatory requirement for the production of pharmaceuticals that will be used in humans.

*Vafseo*

We currently rely on suppliers for the direct manufacture of our drug substance and drug product for clinical and commercial supply of Vafseo. We have entered into supply agreements with STA Pharmaceutical Hong Kong Limited, or STA, for the manufacture of Vafseo drug substance and drug product for commercial use and Patheon Inc. for the manufacture of Vafseo drug product for commercial use. In addition, we and Esteve Química, S.A. have agreed to negotiate the terms of a new supply agreement for the manufacture of Vafseo drug substance for commercial use. We plan to mitigate potential commercial supply risks for Vafseo, if any, through inventory management and we may enter into additional manufacturing arrangements for both drug substance and drug product. For more information about our manufacturing agreements for Vafseo, see Part II,

Item 7. Management's Discussion and Analysis and Note 10, *Commitments and Contingencies*, to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

Vadadustat is a small molecule. The synthesis of vadadustat is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale using no unusual manufacturing equipment. Vadadustat can be formulated into compressed tablets using proprietary processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

*Auryxia*

The active pharmaceutical ingredient of Auryxia, ferric citrate, is a small molecule. The synthesis of ferric citrate is reliable and reproducible from starting materials available from multiple sources at a commercial scale. Ferric citrate can be formulated into compressed tablets using proprietary manufacturing processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

We have established CMO relationships for the supply of Auryxia to help ensure that we will have sufficient material for ongoing commercial sales and clinical trials. We currently rely on single-source suppliers for the manufacture of our drug substance and drug product for clinical and commercial supply of Auryxia. The drug substance for Auryxia is supplied by Siegfried Evionnaz SA, or Siegfried, pursuant to a supply agreement, as amended, with pricing structured on a per-kilogram basis. Auryxia drug product is supplied by Patheon Manufacturing Services LLC (Thermo Fisher) pursuant to a Master Manufacturing Service Agreement with per-bottle pricing structured on a tiered basis, with the price reduced as the product volume increases. The supply agreement with Siegfried requires that we satisfy certain minimum purchase requirements, but we are not obligated to use Siegfried as our exclusive supplier. For more information about our manufacturing agreements for Auryxia, see Part II, Item 7. Management's Discussion and Analysis and Note 10, *Commitments and Contingencies*, to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

We utilize third parties for the commercial distribution of Auryxia, including wholesale distributors and certain specialty pharmacy providers. We have also engaged Cardinal Health, Inc., as the exclusive third-party logistics distribution agent for commercial sales of Auryxia and Vafseo. The third-party logistics provides services to the Company that include storage, distribution, processing product returns, customer service support, logistics support, electronic data interface and system access support.

***License and Collaboration Agreements***

*Vafseo License and Collaboration Agreements*

*Medice License Agreement*

On May 24, 2023, or the Medice Effective Date, we entered into a License Agreement, or the Medice License Agreement, with Medice, under which we granted to Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in adult patients with chronic kidney disease in the EEA, UK, Switzerland and Australia, or the Medice Territory.

Under the Medice License Agreement, we received an up-front payment of $10.0 million and are eligible to receive the following payments:

(i) commercial milestone payments up to an aggregate of $100.0 million, and

(ii) tiered royalties ranging from 10% to 30% of Medice's annual net sales of Vafseo in the Medice Territory, subject to reduction in certain circumstances.

The royalties will expire on a country-by-country basis upon the latest to occur of (i) the date of expiration of the last-to-expire valid claim of ours, Medice or joint patent that covers Vafseo in such country in the Medice Territory, (ii) the date of expiration of data or regulatory exclusivity for Vafseo in such country in the Medice Territory and (iii) the date that is 12 years from first commercial sale of Vafseo in such country in the Medice Territory.

Under the Medice License Agreement, we retain the right to develop Vafseo for non-dialysis patients with anemia due to CKD in the Medice Territory. If we develop Vafseo for non-dialysis patients and Vafseo receives marketing approval for non-dialysis patients in the Medice Territory, Medice will commercialize Vafseo for both indications in the Medice Territory. In this instance, we would receive 70% of the net product margin of any sales of Vafseo in the non-dialysis patient population, unless Medice requests to share the cost of the development necessary to gain approval to market Vafseo for non-dialysis patients in the Medice Territory and the parties agree on alternative financial terms.

We and Medice established a joint steering committee to oversee the development and commercialization of Vafseo in the Medice Territory.

The Medice License Agreement expires on the date of expiration of all payment obligations due thereunder with respect to Vafseo in the last country in the Medice Territory, unless earlier terminated in accordance with the terms of the Medice License Agreement. Either party may, subject to a cure period, terminate the Medice License Agreement in the event of the other party's uncured material breach. Medice has the right to terminate the Medice License Agreement in its entirety for convenience upon twelve months' prior written notice delivered on or after the date that is twelve months after the Medice Effective Date.

The Medice License Agreement includes customary terms relating to, among others, indemnification, confidentiality, remedies, and representations and warranties.

On September 13, 2024, we entered into a supply agreement, or the Medice Supply Agreement, with Medice under which we supply Vafseo drug product to Medice for commercial and developmental use in the Medice Territory.

*MTPC Collaboration Agreement*

In December 2015, we entered into a collaboration agreement with MTPC, as amended, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to Vafseo in Japan and certain other Asian countries, or the MTPC Territory. In addition, we supply Vafseo to MTPC for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory. On July 15, 2020, we entered into a supply agreement with MTPC for the commercial supply of Vafseo for use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement, which was amended effective as of December 5, 2022.

Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: (i) expiration of the last-to-expire patent covering Vafseo in such country in the MTPC Territory; (ii) expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or (iii) ten years after the first commercial sale of Vafseo in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

Under the terms of the MTPC Agreement, we are eligible to receive payments from MTPC of up to approximately $225.0 million in the aggregate based on the achievement of certain development, regulatory and sales milestones, as well as tiered royalty payments ranging from 13% to 20% on annual net sales of Vafseo in the MTPC Territory, subject to reduction upon launch of a generic product on a country-by-country basis.

In February 2021, we entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or HCR, whereby we sold our right to receive royalties and sales milestones for Vafseo in Japan and certain other Asian countries in the MTPC territory under the MTPC Agreement, subject to certain caps and other terms and conditions. For more information on our royalty interest acquisition agreement with HCR, see Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Form 10-K.

*CSL Vifor License Agreement*

On February 18, 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor License Agreement, with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, which amended and restated the License Agreement dated as of May 12, 2017. The Vifor License Agreement granted CSL Vifor an exclusive license to sell Vafseo to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of certain group purchasing organizations and certain non-retail specialty pharmacies, collectively, the Supply Group, in the U.S.

The Vifor License Agreement was structured as a profit share arrangement between us and CSL Vifor in which we would receive approximately 66% of the profits, net of certain pre-specified costs. CSL Vifor made an upfront payment to us of $25.0 million in February 2022 in connection with the amendment and restatement of the Vifor License Agreement. In addition, we entered into certain investment agreements with CSL Vifor, pursuant to which we sold CSL Vifor an aggregate of 7,571,429 shares of our common stock for a total of $70.0 million. The shares have not been registered pursuant to the Securities Act of 1933, as amended, or the Securities Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder as the transaction did not involve any public offering within the meaning of Section 4(a)(2) of the Securities Act.

On July 10, 2024, we and CSL Vifor entered into the Vifor Termination and Settlement Agreement, or the Vifor Termination Agreement, pursuant to which we and CSL Vifor agreed, among other things, to terminate, effective immediately, the Vifor License Agreement.

Pursuant to the terms of the Vifor Termination Agreement, we will pay CSL Vifor decreasing quarterly tiered royalty payments ranging from a high single-digit percentage of our net sales of Vafseo up to $450.0 million to mid-single digit percentage of

our net sales of Vafseo above $450.0 million, in each case, in the U.S. during a calendar year, or the Settlement Royalty Payments. The Settlement Royalty Payments will commence upon the first sale of Vafseo by us, our affiliates or third-party licensees to a third party for use in the U.S., and will continue until the later of the (i) expiration of the last-to-expire valid claim listed in the FDA Orange Book that would be infringed by the making, using, selling or importing of Vafseo in the U.S. or (ii) the expiration of marketing or regulatory exclusivity for Vafseo in the U.S., or the Settlement Royalty Term. Beginning on July 1, 2027 and throughout the Settlement Royalty Term, we have the option to make a one-time payment to CSL Vifor, or the Royalty Buy-Down Option, upon which the Settlement Royalty Payments will be adjusted as of the date of exercise of the Royalty Buy-Down Option such that we will then only pay CSL Vifor quarterly royalty payments based on a mid-single digit percentage of our net sales of Vafseo up to $450.0 million in the U.S. during a calendar year in lieu of the above Settlement Royalty Payments. If we exercise the Royalty Buy-Down Option, the WCF Royalty Payments, as described below, will continue.

The WCF Royalty Payments, as described below, the Settlement Royalty Payments and the Royalty Buy-Down Option are in consideration for the termination of the Vifor License Agreement and all obligations thereunder, and the covenants and agreements set forth in the Vifor Termination Agreement, including the settlement and release of all disputes and claims which could arise from the Vifor License Agreement.

Pursuant to the Vifor License Agreement, CSL Vifor contributed $40.0 million to a working capital facility, or Working Capital Fund, established to partially fund our costs of purchasing Vafseo from our contract manufacturers. On May 3, 2024, we and CSL Vifor entered into Amendment #1 to the Vifor License Agreement, or the Vifor Amendment. Pursuant to the Vifor Amendment, and as modified by the Vifor Termination Agreement, we and CSL Vifor agreed to modify the method of repayment of the Working Capital Fund such that the Working Capital Fund will be repaid through quarterly tiered royalty payments ranging from 8% to 14% of our net sales of Vafseo in the U.S., or the WCF Royalty Payments. The WCF Royalty Payments will commence on July 1, 2025, and will continue until the earlier of (i) the cumulative total of the WCF Royalty Payments equals $40.0 million, or (ii) May 31, 2028, or the WCF Royalty Term. The WCF Royalty Payments are subject to minimum true-up milestones of $10.0 million, $20.0 million and $40.0 million, or the WCF Royalty True-Up Payments, on each of May 31, 2026, May 31, 2027 and May 31, 2028, respectively, or the WCF Royalty True-Up Dates. If the cumulative total of the WCF Royalty Payments paid to CSL Vifor on any given WCF Royalty True-Up Date is less than the respective WCF Royalty True-Up Payment, we will pay CSL Vifor a one-time payment equal to the difference between the WCF Royalty True-Up Payment and the cumulative total of the WCF Royalty Payments paid by us through such WCF Royalty True-Up Date.

*Auryxia License and Collaboration Agreements*

*Averoa License Agreement*

On December 22, 2022, we and Averoa entered into a license agreement, or Averoa License Agreement, pursuant to which we granted to Averoa an exclusive license to develop and commercialize ferric citrate, or Averoa Licensed Product, in the EEA, Turkey, Switzerland and the United Kingdom, and in August 2024, we also granted Averoa an exclusive license to develop and commercialize ferric citrate in the Balkans and certain countries in Eastern Europe and the Middle East, or collectively, the Averoa Territory. We and Averoa have established a joint steering committee to oversee the development, manufacturing and commercialization of the Averoa Licensed Product in the Averoa Territory. In April 2024, Averoa submitted its marketing authorization application for ferric citrate in Europe and the application is still under review.

Under the Averoa License Agreement, we are entitled to receive tiered, escalating royalties ranging from a mid-single digit percentage to a low double-digit percentage of Averoa's annual net sales of the Averoa Licensed Product in the Averoa Territory, including certain minimum royalty amounts in certain years, and subject to reduction in certain circumstances. The royalties will expire on a country-by-country basis upon the last to occur of (a) ten years following the date of first commercial sale of the Licensed Product in such country; (b) expiration of the last valid claim of our patent rights and joint patent rights in such country; and (c) the date of expiration of the data, regulatory, or marketing exclusivity period conferred by the applicable regulatory authority in such country with respect to the Licensed Product. As of December 31, 2024, we have not received any royalties under this agreement.

The Averoa License Agreement expires on the date of expiration of all royalty obligations due thereunder with respect to the Averoa Licensed Product on a country-by-country basis in the Averoa Territory, unless earlier terminated in accordance with the Averoa License Agreement.

The Averoa License Agreement provides that we and Averoa will enter into a supply agreement pursuant to which we will supply the Averoa Licensed Product to Averoa for commercial use in the Averoa Territory. We will have the right to terminate the supply agreement upon twenty-four months' notice. We have not yet entered into a supply agreement with Averoa.

*Sublicense Agreement with Japan Tobacco Inc. and Torii Pharmaceutical Co., Ltd.*

In September 2007, we entered into a Sublicense Agreement with JT and Torii, under which JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate in Japan. Effective June 8, 2009, we entered into

an Amended and Restated Sublicense Agreement, which was amended in June 2013, or the Revised Agreement, with JT and Torii.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate hydrate, which launched in May 2014 and is being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. In July 2019, JT and Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan, which was approved in March 2021. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan. Under the terms of the Revised Agreement with JT and Torii, we are eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that we must pay to Panion & BF Biotech, Inc., or Panion, on JT and Torii's net sales of Riona under the Panion Amended License Agreement, subject to certain reductions upon expiration or termination of the Panion Amended License Agreement, and may also receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones. We recorded $5.4 million in license revenue related to royalties earned on net sales of Riona in Japan during the year ended December 31, 2024.

The sublicense under the Revised Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the Revised Agreement with or without cause upon at least six months prior written notice to us. Additionally, either party may terminate the Revised Agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the Revised Agreement, or after certain insolvency events.

*License Agreement with Panion & BF Biotech, Inc.*

On April 17, 2019, we and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amended and restated in full the license agreement between us and Panion. The Panion Amended License Agreement provides us with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding certain Asian Pacific counties, or the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under our patents covering the rights to sublicense (with our written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Consistent with the Panion License Agreement, under the Panion Amended License Agreement, Panion is eligible to receive from us or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in our licensed territories. We are eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion's licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of our and Panion's obligations to pay royalties thereunder. In addition, we may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in our licensed territory, in either case upon 90 days' notice. We and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, during the term and until the second anniversary of the expiration of our or Panion's obligation, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country. In addition, the Panion Amended License Agreement provides that each of us and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the year ended December 31, 2024, we recorded $9.1 million in royalties due to Panion relating to the sales of Auryxia in the U.S. and JT and Torii net sales of Riona in Japan.

*Cyclerion Therapeutics License Agreement*

In June 2021, we entered into a license agreement, or the Cyclerion Agreement, with Cyclerion under which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral sGC stimulator.

Under the terms of the Cyclerion Agreement, we paid $3.0 million in cash upfront to Cyclerion and expensed the amount to research and development, or R&D, expense in June 2021. In December 2024, we amended the terms of the Cyclerion Agreement, pursuant to which we paid an additional $1.25 million in cash upfront to Cyclerion and we will pay an additional $0.5 million to Cyclerion on or before September 30, 2025. In addition, the parties agreed to the reduction of certain development milestones and the increase of certain royalty rates on net sales and sublicense income. We now control all

clinical and commercial manufacturing of praliciguat, which will be conducted by a third party manufacturer. We will also control patent prosecution and pay intellectual property costs starting April 1, 2025.

In addition, Cyclerion is eligible to receive up to an aggregate of $198.5 million from us in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a mid-single-digit percentage to twenty percent of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product and (iii) 10 years from first commercial sale of such product. We may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. We and Cyclerion also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

***Intellectual Property***

The proprietary nature of, and protection for, our products, product candidates and our discovery programs, processes and know-how are important to our business. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the U.S., Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules.

Our commercial success will depend in part on obtaining and maintaining patent protection of our current products as well as current and future product candidates, methods of their use and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. Even once patents successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held not infringed or unenforceable. For this and more comprehensive risks related to our intellectual property, please see "Risk Factors—Risks Related to our Intellectual Property" in Part I, Item 1A. Risk Factors.

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the U.S. are effective for 20 years from the earliest filing date of a U.S. non-provisional application or an international application filed under the Patent Cooperation Treaty. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, however, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest international filing date. Patent term recapture for loss of term as a result of the regulatory review period is available in some foreign jurisdictions. In the U.S., a patent's term may also be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or USPTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

Changes in either the patent laws or interpretations of patent laws in the U.S. and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or license or may receive or acquire in the future may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical

development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. The patent positions for vadadustat and Auryxia are summarized below.

*Vadadustat Patent Portfolio*

We hold 19 issued patents covering the composition of matter, polymorph, method of treating anemia, pharmaceutical compositions of vadadustat, and processes for manufacturing vadadustat in the U.S. and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration dates for these patents are between 2027 and 2039 plus any extensions or adjustments of term available under national law.

We also hold patents and patent applications directed to starting materials and intermediates in the processes for manufacturing vadadustat, dosing regimens, formulations and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2042 exclusive of possible patent term extensions or adjustments.

We have ongoing opposition proceedings relating to vadadustat. See Part I, Item 3. Legal Proceedings for further information relating to these matters.

*Auryxia Patent Portfolio*

Pursuant to the Panion Amended License Agreement, we have the exclusive rights under a series of patents and patent applications to commercialize Auryxia worldwide, excluding certain Asian-Pacific countries. These patents and patent applications include claims directed to compositions of matter, pharmaceutical compositions, methods of treatment, as well as methods for the manufacture of Auryxia.

Our patent rights currently include 3 issued patents that are listed in the Orange Book covering the composition of matter, method of treating hyperphosphatemia, and pharmaceutical compositions of Auryxia. The expected expiration dates for these patents are between 2026 and 2030 plus any additional patent term extensions that may be available.

Pursuant to the sublicense with our Japanese partner, Japan Tobacco Inc., or JT, and its subsidiary, Torii Pharmaceutical Co. Ltd., or Torii, we have exclusively sublicensed certain Japanese patent rights to JT and Torii. These sublicensed rights include several Japanese patents and pending patent applications with composition of matter claims, methods of synthesizing claims, and methods of use claims covering Riona, the trade name under which JT and Torii market ferric citrate in Japan. The expected expiration dates for these patents and pending patent applications are between 2025 and 2028. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these Japanese patents.

Pursuant to the sublicense with our European partner, Averoa, we have exclusively sublicensed certain European patent rights to Averoa. These sublicensed rights include several European patents and pending patent applications with composition of matter claims and methods of use claims covering ferric citrate. The expected expiration dates for these patents and pending patent applications are between 2024 and 2036. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these European patents.

We received Paragraph IV certification notice letters regarding abbreviated new drug applications, or ANDAs, submitted to the FDA by third parties requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). In response we filed certain complaints for patent infringement against six third parties, and have entered into settlement and license agreements with each of the six ANDA filers. Each settlement agreement granted the defendants a license to market a generic version of Auryxia in the U.S. beginning on March 20, 2025 (subject to FDA approval).

***Other Intellectual Property Rights***

We depend upon trademarks, trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

In addition to patent protection, we may utilize orphan drug regulations, pediatric exclusivity or other provisions of the Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, such as new chemical entity exclusivity or new formulation exclusivity, to provide market exclusivity for a product candidate. In the U.S., the FDA has the authority to grant additional data protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of data protection as well as to the term of a relevant patent, to the extent these protections have not already expired. We may also seek to utilize market

exclusivities in other territories. We cannot assure you that our products or any product candidates we may acquire or in-license, will obtain such orphan drug designation, pediatric exclusivity, new chemical entity exclusivity or any other market exclusivity in the U.S., EU, or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection.

***Know-How***

In addition to patents, we rely upon unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment provisions in the confidentiality agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment provisions, to grant us ownership of technologies that are developed by our employees. These agreements may be breached, and we may not have adequate remedies for any breach.

To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

***The Hatch-Waxman Act***

*Orange Book Listing*

In seeking approval for a drug through an NDA, sponsors are required to list with the FDA each patent whose claims cover the sponsor's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA sponsors are usually not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA sponsor is required to make certain certifications to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the sponsor must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA sponsor may also elect to submit a Section viii statement, certifying that its proposed ANDA label does not contain or carve out any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent.

If the sponsor does not challenge the listed patents, the ANDA will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from receiving the Paragraph IV certification, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA sponsor. Also, the ANDA will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

*Exclusivity*

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the FDA cannot accept any ANDA seeking approval of a generic version of that drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug that includes such changes.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

*Patent Term Extension*

After NDA approval, owners of relevant drug patents or their agents may apply for up to a five-year patent extension for delays caused by FDA regulatory review. The allowable patent term extension is calculated as half of the drug's testing phase which is the time between Investigational New Drug application, or IND submission, and NDA submission, and all of the review phase, which is the time between NDA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the sponsor did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of approval by virtue of the patent term extension.

We have filed applications under the patent term extension provisions of 35 U.S.C. § 156 for U.S. Patent Nos. 8,299,298, 8,093,423, 7,767,851 and 8,338,642 each of which covers Auryxia for delays caused by FDA regulatory review. We have also filed patent term extension applications for U.S. Patent Nos. 7,811,595, 8,343,952, 8,323,671, 8,598,210, and 8,940,773 each of which covers Vafseo for delays caused by FDA regulatory review. If granted, we can utilize the patent term extension on one of the Auryxia patents and one of the Vafseo patents, however, we cannot assure you that we can obtain any extension of the term of these patents. Upon expiration of these patents, competitors who obtain the requisite regulatory approval may potentially offer products with the same composition and/or method of use as our product, so long as the competitors do not infringe any other patents that we may own or license.

For patents that might expire before a determination regarding patent term extension, the patent owner or its agent may request an interim patent term extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely.

In addition, certain jurisdictions outside of the U.S., including Japan, have provisions that provide for patent term extension. In October 2014, following the regulatory approval of Riona in Japan, the Japan Patent office granted the patent term extensions filed by our sublicensee, JT, for Japanese Patents Nos. 4964585 and 4173553. As a result of the extension of patent term, Japanese Patent No. 4173553 expired in November 2022 and Japanese Patent No. 4964585 will expire in November 2025 for hyperphosphatemia and December 2028 for iron deficiency anemia. We also sought and obtained patent term extension for Japanese Patent Nos. 5113838, 6290781, and 6612479 following regulatory approval of Vafseo in Japan. As a result of the extension of patent term, Japanese Patent No. 5113838 will expire in June 2032, Japanese Patent No. 6290781 will expire in October 2034, and Japanese Patent No. 6612479 will expire in January 2035.

In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each product candidate and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

***Competition***

The pharmaceutical and biotechnology industries are highly competitive, with several key players offering innovative solutions. The growing prevalence of CKD and the increasing demand for better anemia management solutions continue to drive competition innovation in this market. Our competitors include public and private pharmaceutical and biotechnology companies, academic institutions, and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in a larger concentration of resources among a smaller number of our competitors. These organizations, as well as others in the broader industries, compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations and license competitive technologies to ours.

While major pharmaceutical companies are continuously investing in R&D and have significantly greater capital resources, larger R&D teams and facilities and more experience in drug development, regulation, manufacturing and marketing than we do; we believe our novel HIF-PH inhibitors have the potential to revolutionize the treatment landscape in multiple areas, including anemia due to CKD. To compete successfully in these industries, we must continue to identify novel and unique drugs or treatment methods and complete the development of those drugs as treatments before our competitors.

*Vadadustat Competitors*

Drugs that may compete with Vafseo include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the U.S. and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by CSL Vifor in the U.S. and Roche Holding Ltd. outside of the U.S. and Evrenzo(R) (roxadustat) in Europe commercialized by Astellas Pharma Inc., or Astellas, Eporatio® (epoetin theta) in Europe commercialized by Teva Pharmaceuticals Ltd., Silapo® (epoetin zeta) in Europe commercialized by Stada Arzneimittel AG, Epoetin Alfa Hexal® (epoetin alfa) in Europe commercialized by Hexal AG, Binocrit® (epoetin alfa-biosimilar) in Europe commercialized by Sandoz, and NeoRecormon® (epoetin beta) in Europe commercialized by Roche.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PH inhibitor product candidates in various stages of development for anemia indications in territories outside of the U.S. that may be in direct competition with Vafseo. These candidates are being developed by companies such as JT and Bayer HealthCare AG, or Bayer. In Europe, roxadustat is approved for the treatment of anemia in patients with CKD.

Furthermore, certain companies are developing new therapies for renal-related diseases that potentially could reduce injectable ESA utilization and thus limit the market potential for Vafseo. Other new therapies are in development for treating conditions, including renal anemia, that may impact the market for anemia-targeted treatment.

In Japan, vadadustat is sold under the name Vafseo, which is approved for patients with CKD, including both DD-CKD and NDD-CKD, and competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of DD-CKD patients and NDD-CKD patients. In addition, daprodustat, GSK's product candidate, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD, and molidustat, Bayer HealthCare AG's product, is approved in Japan for the treatment of renal anemia. In China, roxadustat is commercialized for the treatment of anemia due to CKD in DD-CKD patients and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is licensed based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product (i.e., a reference biologic product). The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without the risk of being sued for patent infringement. In addition, an application for a biosimilar product can only be approved by the FDA 12 years after the existing, branded product was licensed under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the U.S. Because injectable ESAs are biologic products, introducing biosimilars into the injectable ESA market in the U.S. will constitute additional competition for Vafseo. In the U.S., Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Furthermore, Vafseo's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Vafseo.

*Auryxia Competitors*

***Hyperphosphatemia Competition***

Auryxia is competing in the hyperphosphatemia market in the U.S. with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's RENAZORB™ (lanthanum dioxycarbonate) or could otherwise enter the market that may impact the market for Auryxia. In October 2023, the FDA approved XPHOZAH® (tenapanor), a phosphate absorption inhibitor that is marketed by Ardelyx, Inc., or Ardelyx and indicated to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy, which may adversely impact the market for Auryxia.

*Iron Deficiency Anemia Competition*

Auryxia is competing in the IDA market in the U.S. with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutic' plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA, and Accrufer® (ferric maltol), which was launched in the U.S. for the treatment of IDA in July 2021.

In Japan, our Japanese sublicensee, JT and Torii, commercialize Riona (ferric citrate hydrate). In the hyperphosphatemia market, Riona competes with Fosrenol® (lanthanum carbonate hydrate) marketed by Bayer Yakuhin Ltd., generic lanthanum carbonate hydrate products, and Phozevel® (tenapor hydrochloride) marketed by Kyowa Kirin Co., Ltd. In the IDA market in Japan, Riona competes with Ferromia® (sodium ferrous citrate) marketed by Alfresa Pharma Corporation and Fero-Gradumet® (dried ferrous sulfate) marketed by Viatris Inc.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies

have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that protect us from generic drug competition until March 20, 2025. Following LoE, in March 2025, the timing and number of generic versions of Auryxia that enter the market will affect our revenue from Auryxia. We and our licensors, Panion, and, as applicable, Dr. Hsu, entered into settlement agreements with all of the third parties who submitted Paragraph IV certification notice letters regarding ANDAs submitted to the FDA, pursuant to which we granted licenses to market a generic version of Auryxia in the U.S. beginning on March 20, 2025 (subject to FDA approval).

On February 5, 2025, we entered into an Authorized Generic Distribution and Supply Agreement with Mylan Pharmaceuticals, Inc. pursuant to which, on or after March 20, 2025, they will sell an authorized generic version of Auryxia. We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B could result in slower revenue decline after the LoE date than in other LoE situations, but the impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

***Government Regulation and Product Approvals***

Government authorities in the U.S., at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the U.S. and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

*Review and Approval of Drug Products in the U.S.*

In the U.S., the FDA approves and regulates drugs under the FDCA and applicable implementing regulations and guidance.

Our product candidates must be approved by the FDA for therapeutic indications before we or our partners are able to market them in the U.S. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products is referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug product in the U.S. must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations and consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, or ICH, requirements;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must be reviewed and allowed by the FDA before human clinical trials may begin;
- approval by an independent local or central institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed product candidate for each indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product candidate, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites and records to assure compliance with GCPs and good practices, or GxPs, the integrity of the clinical data and that adequate controls and oversight are in place regarding manufacturing, clinical trials, pharmacovigilance, safety, data management, vendor oversight, collection and reporting of serious adverse events and other activities;
- payment of user fees pursuant to the Prescription Drug User Fee Act, or PDUFA;
- approval of an NDA for the new drug product authorizing marketing for particular indications in the U.S.; and

- compliance with any post-approval requirements and/or commitments, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and potentially post-market requirement, or PMR, and post-market commitment, or PMC, studies.

*Preclinical Tests*

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND and are generally referred to as IND-enabling studies. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

*The IND and IRB Processes*

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped through interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be obtained prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In addition to reviewing an IND to assure the safety and rights of patients, the FDA also focuses on the quality of the investigation and whether it will be adequate to permit an evaluation of the drug's safety and efficacy. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research patients will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold or require that the sponsor amend the clinical protocol to include additional safety measurements. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical trial or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a partial clinical hold might state that a specific protocol or part of a protocol may not proceed, while other parts of a protocol or other protocols may do so. No more than 30 days after the imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor with a written explanation of the basis for the hold. Following the issuance of a clinical hold or partial clinical hold, a clinical trial may only resume once the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed or recommence. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical trial subjects.

In addition to the foregoing requirements related to the IND submission and ongoing review, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to study patients. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by a Data Monitoring Committee, which is an independent group of qualified experts organized by the trial sponsor. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed

to an unacceptable health risk. Other reasons for suspension or termination may be made by a sponsor based on evolving business objectives and/or competitive climate.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived by the FDA. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

*Reporting Clinical Trial Results*

Under the Public Health Service Act, or PHSA, sponsors of certain clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both NIH and the FDA have signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

The PHSA grants the Secretary of the U.S. Department of Health and Human Services, or HHS, the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. As of December 19, 2024, the FDA has issued six notices of non-compliance, thereby signaling the government's willingness to begin enforcing these requirements against non-compliant clinical trial sponsors. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinical trials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Violations may also result in injunctions and/or criminal prosecution or disqualification from federal grants.

*Expanded Access to an Investigational Drug for Treatment Use*

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 trial for a covered investigational product; or 15 days after the investigational product receives designation from the FDA as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

*Human Clinical Trials in Support of an NDA*

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research

patients provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- **Phase 1.** The product candidate is initially introduced into a small number of healthy human patients or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- **Phase 2.** The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- **Phase 3.** These clinical trials are commonly referred to as "pivotal" studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product candidate for approval, identify adverse effects, establish the overall risk-benefit profile of the product candidate and to provide adequate information for the labeling of the product candidate.
- **Phase 4.** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA.

In December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. As a result, the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development remain unclear and we will need to carefully navigate such uncertainty.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the ICH's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

*Interactions with the FDA During the Clinical Development Program*

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. Progress reports detailing the results of clinical trials must be submitted annually within 60 days of the anniversary dates that the IND went into effect and more frequently if serious adverse events occur. These reports must include a development safety update report. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the occurrence of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In addition, a sponsor will continue to have interactions with the FDA and the sponsor may meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND, or a pre-IND meeting, at the end of Phase 2 clinical trials and before an NDA is submitted, or a pre-NDA meeting. Meetings at other times may also be requested. These meetings provide an opportunity for the sponsor to share information about the data gathered to date with the FDA and for the FDA to provide advice on the next phase of development.

There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA meetings as well as end of phase meetings such as end-of-phase 2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including for example meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues (typically limited to no more than two focused topics) and should not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

Such meetings may be conducted in person, via teleconference/videoconference, or written response only with minutes reflecting the questions that the sponsor posed to the FDA and the agency's responses. The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure. In September 2023, the FDA issued draft guidance outlining the terms of such meetings in more detail.

*Pediatric Studies*

Under the Pediatric Research Equity Act, or PREA, applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical trials, early phase clinical trials, and/or other clinical development programs.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Pursuant to the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, the FDA must send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. FDASIA further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

*Acceptance and Review of an NDA*

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed

labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the product candidate for one or more indications. The fee required for the submission and review of an application under the PDUFA is substantial (for example, for fiscal year 2025 this application fee is approximately $4.3 million), and the sponsor of an approved application is also subject to an annual program fee, currently approximately $0.4 million per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the sponsor is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. This is known as the filing decision. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File determination to the sponsor. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. A product that has been designated as a breakthrough therapy may also be eligible for review within six months if supported by clinical data at the time of submission of the NDA. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing such as active pharmaceutical ingredients, finished drug product manufacturing, control testing laboratories, as well as packaging and labeling facilities. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the U.S. prior to being imported or offered for import into the U.S.

Moreover, the FDA will review a sponsor's financial relationship with the principal investigators who conducted the clinical trials in support of the NDA. That is because, under certain circumstances, principal investigators at a clinical trial site may also serve as scientific advisors or consultants to a sponsor and receive compensation in connection with such services. Depending on the level of that compensation and any other financial interest a principal investigator may have in a sponsor, the sponsor may be required to report these relationships to the FDA. The FDA will then evaluate that financial relationship and determine whether it creates a conflict of interest or otherwise affects the interpretation of the trial or the integrity of the data generated at the principal investigator's clinical trial site. If so, the FDA may exclude data from the clinical trial site in connection with its determination of safety and efficacy of the investigational product.

Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The sponsor of the NDA may also have their records, processes, procedures, training, and other aspects reviewed during an inspection. The FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks.

Finally, the FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

*Fast Track, Breakthrough Therapy, Priority Review*

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential

to address unmet medical needs for such a disease or condition. The fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's review clock goal for taking action on a marketing application from ten months to six months.

*Accelerated Approval Pathway*

Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

In December 2022, Congress modified certain provisions governing accelerated approval of drug products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded and to submit progress reports on its post-approval studies to the FDA every six months until the study is completed. Moreover, FDORA established expedited procedures authorizing the FDA to withdraw an accelerated approval if certain conditions are met, including where a required confirmatory study fails to verify and describe the predicted clinical benefit or where evidence demonstrates the product is not shown to be safe or effective under the conditions of use. The FDA may also use such procedures to withdraw an accelerated approval if a sponsor fails to conduct any required post-approval trial of the product with due diligence, including with respect to "conditions specified by the Secretary." The new procedures include the provision of due notice and an explanation for a proposed withdrawal, and opportunities for a meeting with the Commissioner or the Commissioner's designee and a written appeal, among other things.

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and generally applies to oncology products and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval. Subsequently, in December 2024, the FDA issued additional draft guidance relating to accelerated approval.

*The FDA's Decision on an NDA*

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with

certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. Although the FDA has not yet finalized that guidance, it did issue additional draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical study.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a CRL or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review. Rather, for those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

*Post-Approval Requirements and Commitments*

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, conditions of NDA approval may include sponsor agreement to PMR or PMC studies, which are designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. These may include additional studies, registries, data collection, analyses, and/or information.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the

approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a product candidate's safety or effectiveness are prohibited before the product candidate is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA or in a manner that is inconsistent with the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. This guidance was finalized by the FDA on January 6, 2025.

In the U.S., healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific conditions, for a manufacturer to engage in non-promotional, truthful and non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In addition, companies may also promote information that it consistent with the prescribing information and have the ability to proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug under some relatively recent guidance from the FDA. Moreover, with the passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

However, if a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act, or DSCSA, which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability. So as not to disrupt supply chains, the FDA has granted certain exemptions from enhanced drug distribution security requirements for eligible trading partners for particular periods of time.

*Section 505(b)(2) NDAs*

NDAs for most new drug products are based on two full clinical trials which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor. Products approved under Section 505(b)(2) are often referred to as follow-on products.

*Abbreviated New Drug Applications for Generic Drugs*

In 1984, with the passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, a sponsor must submit an ANDA to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of regulatory exclusivity for the RLD has expired. The FDCA provides a period of five years of regulatory data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, the FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, a generic or follow-on drug application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of regulatory exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA

from accepting ANDAs or 505(b)(2) applications seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

*Hatch-Waxman Patent Certification and the 30-Month Stay*

As part of the submission of an NDA or certain supplemental applications, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA sponsor files its application with the FDA, the sponsor is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book. Specifically, the ANDA sponsor must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA sponsor is relying on studies conducted for an already approved product, the sponsor also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA sponsor would.

If the generic drug or follow-on drug sponsor does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA application.

*Pediatric Studies and Exclusivity*

Pediatric exclusivity is another type of non-patent marketing exclusivity in the U.S. and, if granted, for drug products, provides for the attachment of an additional six months of marketing protection to the term of any existing patent or regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product is effective in the pediatric population studied, rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) sponsor submitted a Paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

*Patent Term Restoration and Extension*

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

*Federal and State Data Privacy Laws*

There are multiple privacy and data security laws that may impact our business activities, in the U.S. and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, the HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. While we are not a covered entity, as a business associate, we could be subject to penalties, including criminal penalties, and contractual damages if we knowingly obtain or further disclose PHI from a covered entity, such as a health care provider or clinical research site, and therefore we must ensure the proper authorizations are in place before we, or our vendors or business partners, obtain access to any PHI. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In November 2020, California enacted legislation that has been dubbed the first "GDPR-like" law in the U.S. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers rights as it relates to their personal information, and allow for a new cause of action for data breaches. Additionally, starting on January 1, 2023, the California Privacy Rights Act, or CPRA, significantly modified the CCPA, including by expanding consumers' rights, particularly with respect to certain sensitive personal information and creating new principles, such as data minimization, purpose limitation, and storage limitation. The CPRA also created a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities.

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the state of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described

above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

***Review and Approval of Drug Products Outside the U.S.***

In order to market any product outside of the U.S., a sponsor must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

*Non-clinical Studies*

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non-clinical (pharmaco-toxicological) studies must be conducted in compliance with the principles of GLP as set forth in EU Directive 2004/10/EC (unless otherwise justified for certain particular medicinal products such as, for example, radio-pharmaceutical precursors for radio-labeling purposes). In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

*Clinical Trial Approval in the EU*

On January 31, 2022, the Clinical Trials Regulation (EU) No 536/2014 became effective in the EU and replaced the prior Clinical Trials Directive 2001/20/EC. The Clinical Trials Regulation aims to simplify and streamline the authorization, conduct and transparency of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the EU, or an EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the European Medicines Agency, or EMA, and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting EU Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted, or concerned member states. Part II is assessed separately by each concerned member state. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned member state. However, overall related timelines will be defined by the Clinical Trials Regulation.

The Clinical Trials Regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific clinical site after the applicable ethics committee has issued a favorable opinion. The Clinical Trials Regulation will apply to any future clinical trials that we conduct in the EU.

Parties conducting certain clinical trials must, as in the U.S., post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

*PRIME Designation in the European Union*

In March 2016, the EMA launched an initiative, the PRIority MEdicines, or PRIME, scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to

encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application, or MAA, assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies are appointed early in the PRIME scheme, facilitating increased understanding of the product at the EMA's committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

*Pediatric Studies*

Prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for pediatric population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

*Marketing Authorization*

To obtain marketing approval of a product under EU regulatory systems, a sponsor must submit an MAA either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to sponsors who wish to market a product in various EU Member States where such product has not received marketing approval in any EU Member State before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the sponsor, known as the reference member state. Under this procedure, a sponsor submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

A marketing authorization may be granted only to a sponsor established in the EU. Once the marketing authorization is obtained in all member states of the EU and study results are included in the product information, even when negative, the

product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

*Periods of Authorization and Renewals in the EU*

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the EC or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

*Post-Approval Requirements*

As in the U.S., both marketing authorization, or MA, holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC, and the competent authorities of EU Member States. The MA holder must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. In particular, the MA holder must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

The manufacturing process for medicinal products in the EU is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU GMP standards when manufacturing medicinal products and active pharmaceutical ingredient.

In the EU, the advertising and promotion of approved products are subject to laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising, and unfair commercial practices. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the EU. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA.

Failure to comply with EU and EU Member State laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

*Regulatory Data Exclusivity in the EU*

In the EU, innovative medicinal products authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, sponsors for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization

dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to a total of ten years' market exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a NCE so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

In this context, it should be noted that the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products was published in April 2023 and includes, among other things, provisions that would potentially reduce the duration of regulatory data protection. The European Parliament requested several amendments in April 2024. At this time, the proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry in the long term, if and when adopted.

*Pediatric Exclusivity*

If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the EC, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

*Access Consortium*

In October 2020, the Medicines and Healthcare products Regulatory Agency, or MHRA, joined the Access Consortium along with the Australian Therapeutic Goods Administration of Australia, Health Canada, Health Sciences Authority of Singapore and Swissmedic. The consortium is a coalition of these regulatory authorities that work together to promote greater regulatory collaboration and alignment of regulatory requirements. The consortium's goal is to maximize international co-operation between partners in the consortium, reduce duplication, and increase each agency's capacity to ensure patients have timely access to high quality, safe and effective therapeutic products. The MHRA commenced work-sharing applications with Access partners on January 1, 2021. Access Consortium working group members have regular meetings to exchange information on regulatory issues and challenges faced by the participating regulatory agencies, including issues on clinical trials, marketing authorizations, product manufacturing site inspections, post-marketing surveillance, joint development of technical guidelines or regulatory standards, and collaboration on information platforms. The Access consortium has developed three authorization procedures: the New Active Substance and Biosimilar Work Sharing Initiatives and the Generic Medicine Work Sharing Initiative.

*General Data Protection Regulation*

Many countries outside of the U.S. maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the European Union General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the EU, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. This CJEU decision may lead to increased scrutiny on data transfers from the EU to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Additionally, in October 2022, President Biden signed an executive order to implement a new EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt the EU-U.S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

As with other issues related to Brexit, there are open questions about how personal data will be protected in the UK and whether personal information can transfer from the EU to the UK Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. While the Data Protection Act 2018 in the UK that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the UK, it is still unclear whether transfer of data from the EEA to the UK will remain lawful under GDPR. The UK government has already determined that it considers all EU and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the UK to the EU/EEA remain unaffected. In addition, a recent decision from the EC appears to deem the UK as being "essentially adequate" for purposes of data transfer from the EU to the UK, although this decision may be re-evaluated in the future.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products.

*Brexit and the Regulatory Framework in the United Kingdom*

The UK's withdrawal from the EU took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021, and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the UK will form two separate markets governed by two distinct regulatory and legal regimes, except that Northern Ireland will continue to broadly follow EU laws as further described below. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the UK is no longer part of the single market. As of January 1, 2021, the MHRA became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland, and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol.

On February 27, 2023, the UK government and the EC announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide MA will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. As of January 1, 2025, the changes introduced by the Windsor Framework will result in the MHRA being responsible for approving all medicinal products destined for the United Kingdom market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. The Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or HMR, is the primary legal instrument for the regulation of medicines in the UK. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law." However, new legislation such as the (EU) Clinical Trials Regulation will not be applicable in Great Britain. Since a significant proportion of the regulatory framework for pharmaceutical products in the UK covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, MAs, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval, and commercialization of our product candidates in the UK. For example,

the UK is no longer covered by the centralized procedures for obtaining EU-wide MAs from the EMA, and a separate MA will be required to market our product candidates in the UK. A new international recognition framework has been in place since January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs made by the EMA and certain other regulators when determining an application for a new Great Britain MA.

***Pharmaceutical Coverage, Pricing and Reimbursement***

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. In addition, third-party payors may impose prior authorization or step edit requirements requiring patients to have tried other therapies prior to our products for coverage. Payors may also decline to include our products or product candidates on their formulary, which means that unless healthcare providers seek a medical exception for coverage, the payors will not pay for the product.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

Dialysis-related drugs are included in the ESRD PPS bundled payment and are grouped into functional categories such as anemia management and bone and mineral metabolism. In a final ESRD PPS rule published in October 2019, CMS confirmed that TDAPA would be expanded to most new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA provides separate payment for eligible new drugs for two years based on the drug's Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies.

As an oral drug, Auryxia was covered by Medicare under Part D until January 1, 2025, for the treatment of patients with hyperphosphatemia. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home. As of January 2025, oral ESRD-related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, are included in the ESRD bundle and separate Medicare payment for these drugs are no longer available. Vafseo, which we began selling in January 2025, is also included in the ESRD bundle and ESRD facilities will receive TDAPA for Vafseo as a new renal dialysis drug meeting certain criteria for a period of at least two years starting on January 1, 2025. Additionally, in the post-TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that bundled drugs will be reimbursed as part of the single bundled payment for Medicare patients. However, there can be no assurances that any increase in the single bundled payment base rate will be sufficient to adequately reimburse the dialysis facilities for Auryxia or Vafseo at a price that allows us to continue to sell Auryxia at a profit.

In July 2024, Ardelyx filed a complaint in the United States District Court for the District of Columbia against HHS, CMS and other parties, which alleged that CMS's plan to include oral-only phosphate lowering therapies in the ESRD PPS violated its statutory and regulatory authority under the Medicare Improvements for Patients and Providers Act, which established the ESRD PPS bundled payment system for dialysis services. In October 2024, Ardelyx filed a motion for a preliminary injunction to enjoin CMS from including oral-only phosphate lowering therapies in the ESRD PPS. CMS had earlier filed a motion to dismiss the complaint on jurisdictional grounds. On November 8, 2024, the district court denied Ardelyx' motion for a preliminary injunction and it granted the government's motion to dismiss. Thereafter, Ardelyx moved for reconsideration, but the district court also denied that request. On December 26, 2024, Ardelyx filed a notice of appeal with the US Court of Appeals for the DC Circuit.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the U.S., ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its EU Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced EU Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

***Dialysis Organizations Protocols***

Dialysis organizations have their own formularies that list primary or preferred therapeutic options in part based on contracting status with drug manufacturers. While a prescriber may make their own independent decision to prescribe what they determine most appropriate for a given patient, any non-formulary therapeutic options are only available through an exception process based on clinical need. Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. Additionally, dialysis organizations typically assess a product's efficacy before adding it to their formulary. Their process for assessing a product may differ among organizations and the timing of such assessment could delay adding such treatment to formulary, further affecting product sales.

***Healthcare Law and Regulation***

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians, teaching hospitals and other healthcare providers, patient privacy laws and regulations, and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or

recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government
- HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal transparency requirements, known as the federal Physician Payments Sunshine Act (renamed the Open Payments Act), under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the CMS within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- the PDMA and its implementation regulations, as well as the DSCSA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by third-party payors, including private insurers, and state gift ban and disclosure law requirements that differ from the federal Physician Payments Sunshine Act in terms of the nature and type of transfers of value that are reportable and the types of covered recipients.

Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, such as Medicare and Medicaid. Ensuring compliance is time consuming and costly. Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

***Healthcare Reform in the U.S.***

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the U.S.

By way of example, the U.S. and state governments continue to propose and pass legislation designed to reduce the cost of healthcare.

In March 2010, the U.S. Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Other legislative changes have been proposed and adopted

since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act. Under current legislation, the actual reductions in Medicare payments may vary up to 4%.

The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by the prior administration on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. In June 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA after finding that the plaintiffs did not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

*Pharmaceutical Prices in the U.S.*

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U.S. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, the prior administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of products from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) had submitted Section 804 Importation Program proposals to the FDA. On January 5, 2023, the FDA approved Florida's plan for Canadian product importation. That state now has authority to import certain products from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each product selected for importation, which must be approved by the FDA. The state will also need to relabel the products and perform quality testing of the products to meet FDA standards.

Further, the HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would also eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act of 2022, or IRA, has been delayed by Congress to January 1, 2032.

The IRA has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare

Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The law also caps Medicare out-of-pocket drug costs at an estimated $2,000 a year.

On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, chronic kidney disease, and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. On January 17, 2025, HHS announced the selection of 15 additional drugs covered by Part D for the second cycle of negotiations. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027. CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration, and CMS is committed to considering opportunities to bring greater transparency in the negotiation program.

On June 6, 2023, Merck filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the Pharmaceutical Research and Manufacturers of America, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. Litigation involving these and other provisions of the IRA will continue with unpredictable and uncertain results.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

*Healthcare Reform and Pharmaceutical Prices in the EU*

In the EU, similar political, economic, and regulatory developments to those in the U.S. may affect our ability to profitably commercialize our product candidates, if approved. In many countries, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of an MA. To obtain reimbursement or pricing approval in some countries, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or EU Member State level may result in significant additional requirements or obstacles. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU Member States have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could restrict or

regulate post-approval activities and affect the ability of pharmaceutical companies to commercialize their products. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In the EU, potential reductions in prices and changes in reimbursement levels could be the result of different factors, including reference pricing used by various EU Member States, parallel distribution and parallel trade can further reduce prices. It could also result from the application of external reference pricing mechanisms, which consist of arbitrage between low-priced and high-priced EU Member States. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any product candidates, if approved in those countries.

Health technology assessment, or HTA, of medicinal products in the EU is an essential element of the pricing and reimbursement decision-making process in a number of EU Member States. The outcome of HTA has a direct impact on the pricing and reimbursement status granted to the medicinal product. A negative HTA by a leading and recognized HTA body concerning a medicinal product could undermine the prospects to obtain reimbursement for such product not only in the EU Member State in which the negative assessment was issued, but also in other EU Member States.

In 2011, Directive 2011/24/EU was adopted at the EU level. This directive establishes a voluntary network of national authorities or bodies responsible for HTA in the individual EU Member States. The network facilitates and supports the exchange of scientific information concerning HTAs. Further to this, on December 13, 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The regulation intends to boost cooperation among EU Member States in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU Member States to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

***Laws Relating to Foreign Trade***

We are subject to various federal and foreign laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purposes of obtaining or retaining business, or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. Additionally, interactions with or on the part of our partners, collaborators, contract research organizations, vendors or other agents may also implicate the FCPA. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

On February 10, 2025, President Trump issued an Executive Order directing the Attorney General to review the guidelines and policies governing the FCPA investigations and enforcement actions. Per the Executive Order, this review will result in new Department of Justice FCPA guidelines intended to enhance American economic competitiveness and to safeguard national security interests. During the 180-day review period, any new FCPA investigations and enforcement actions are to be suspended absent authorization from the Attorney General, and all existing FCPA investigations and enforcement actions will be reviewed. Additionally, after the Attorney General issues revised guidelines, the Executive Order directs her to assess whether "remedial measures" related to past FCPA actions are warranted.

Our international operations could also be subject to compliance with national laws of other countries, such as the United Kingdom Bribery Act. of 2010, or UK Bribery Act. The UK Bribery Act applies to any company "carrying on business" in the UK, irrespective of where the offending conduct occurs. The UK Bribery Act applies to bribery activities both in the public and private sector and prohibits the provision of an "advantage" intended to induce or reward "improper performance" of the recipient's function. The failure by a company to prevent third parties from providing a bribe on its behalf could also

constitute an offense. Penalties under the UK Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances.

There are local antibribery and anticorruption laws in countries where we are conducting clinical trials, such as Brazil and Russia, and many of these also carry the risk of significant financial or criminal penalties. Our clinical trial operations could also result in enforcement actions by U.S., UK, or other governmental authorities. There are also trade laws within the U.S. and in other regions that regulate the sale, purchase, import, export, reexport, transfer and shipment of goods, currency, products, materials, services and technology. Violations of these laws can lead to serious consequences, including substantial fines.

***Other Regulations***

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

***Buying Patterns***

Fluctuations in wholesaler inventory levels have impacted our product sales. Historically, fourth quarter revenues tended to be stronger than other quarters as our distributors increased their inventory levels, resulting in inventory draw-down by wholesalers in the subsequent first quarter such that first quarter usually had lower revenues than the preceding fourth quarter and the second and third quarters had higher revenues than the first quarter. While buying patterns may affect quarterly comparisons within a fiscal year, it generally is not material to our annual consolidated results.

We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B and Auryxia LoE on March 20, 2025 could result in the buying pattern of certain customers in 2025 and future years being different than historical practices. The impact of LoE on future Auryxia revenues will depend on many factors including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

***Employees and Human Capital Resources***

As of December 31, 2024, we had 181 employees. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

We face competition for our personnel from our competitors and other companies throughout our industry. Over the last several years, the challenges in recruiting and retaining employees across the pharmaceutical and biotechnology industries have increased substantially due to current industry job market dynamics.

Retention, growth, training and development of our employees are integral to our success. We offer competitive compensation, including base salary and incentive bonuses. We conduct bi-annual internal and external pay reviews to ensure fair and equitable pay for our employees, which includes an internal pay equity analysis, as well as a review of our employees' pay against external market data. To foster a stronger sense of ownership and align the interests of employees with shareholders, we grant restricted stock units and common stock options to eligible employees under our broad-based stock incentive program, and employees may purchase stock pursuant to our employee stock purchase plan. In addition, many of our executives participate in our employee stock purchase plan. Further, our benefits packages are designed to attract, motivate and reward talented individuals who possess the skills necessary to support our business objectives, assist in the achievement of our strategic goals and create value for our stockholders. Our compensation program is designed to differentiate us from our competition, incentivize achievement of corporate goals and individual performance and demonstrate our corporate values. In addition, we are committed to developing our team members and provide development and leadership opportunities to our employees to cultivate talent throughout the Company.

We are committed to our employees’ health, safety and well-being. Our work paradigm is flexible and designed to accommodate a range of work profiles. Our workforce is primarily hybrid and fully remote, including field-based, with certain employees being office-based. We offer a wide variety of competitive benefits to support our employees' physical, mental and financial well-being. Our benefits package is comprehensive in coverage and offers options to support all employees in staying healthy, planning for their future and developing their careers. Our management continues to assess and respond to the evolving needs of our workforce.

*Environmental, Social and Governance*

Our commitment is to ensure that every employee is included, supported and treated equitably. In furtherance of this goal, we developed a team to support and guide Akebia as an inclusive and culturally intelligent workplace. Over the past four years this team has worked with executive leadership to identify areas for growth and education and move forward several initiatives that will enable us to continue to build an inclusive workplace and to work toward our aspiration to have a workforce comprised of individuals with different experiences, perspectives and backgrounds. In 2024, this team launched

training focused on promoting equal opportunity and mitigating potential bias for all employees. Other initiatives include learning, coaching, cultural awareness activities and development opportunities for all of our employees.

Our Cambridge office has a Fitwel Certification, a healthy building certification system, and is level two certified. Additionally, we consolidated our office footprint to reduce our use of energy and other resources and have initiated recycling programs, including single stream recycling and recycling cans at every desk. Furthermore, we offer a commuter benefit to all of our hybrid and office-based employees to encourage employees to use public transportation and offer bicycle parking free of charge in the onsite garage.

In addition, we support kidney patient communities where we live and work. In the U.S., we had a patient services program, Akebia Cares, designed to provide one-on-one support to help communicate individual benefits and available resources for patients today facing financial obstacles that keep them from accessing important medications. In 2024, we provided over $7.4 million worth of Auryxia for free to patients needing assistance. Our free drug program ended as of December 31, 2024, however, we continue to offer copay assistance for eligible patients.

We also have a cross-functional Sponsorship Review Committee that reviews and approves sponsorships and donations based on the relevance of each projects to our purpose, business objectives and the communities we serve. We support and work closely with multiple kidney patient advocacy organizations. We believe our involvement with and support of patient advocacy programs demonstrates our commitment to our purpose of bettering the life of each person impacted by kidney disease.

***Available Information***

Our website address is www.akebia.com. The information on our website or that may be accessed by links on our website is not incorporated by reference into this Form 10-K. We make available, free of charge and through our website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they are electronically filed with or furnished to the U.S. Securities and Exchange Commission, or SEC.

***Corporate Information***

Akebia was incorporated in Delaware in 2007 and became a public company in 2014. Our mailing address and principal executive offices and our laboratory are located at 245 First Street, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098.

We are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements, and other information, including amendments and exhibits to such reports, filed or furnished pursuant to the Securities Exchange Act of 1934 are also available free of charge in the "SEC Filings" section of our website located at http://www.akebia.com, as soon as reasonably practicable after the reports are electronically filed with or furnished to the SEC. The information on our website is not part of this Annual Report on Form 10-K.

***Item 1A. Risk Factors.***

*We face a variety of risks and uncertainties in our business. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business, reputation, results of operations, financial condition and stock price which can be materially and adversely affected. If any of the following risks occurs, our business, financial condition, financial statements, results of operations and future growth prospects could be materially and adversely affected.*

**Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy**

***We have incurred significant losses since our inception, and anticipate that we will continue to incur losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.***

Investment in pharmaceutical product development and commercialization is highly speculative because it requires upfront capital expenditures and significant research and development, or R&D, expenses. Despite the investment in assets and R&D, there is significant risk that a product candidate will fail to gain marketing approval or that an approved product will not be commercially viable. Since our inception, we have devoted most of our resources to R&D, including our preclinical and clinical development activities, commercializing Auryxia and Vafseo and providing general and administrative support for these operations. We have funded our operations principally through product sales, payments received from our collaboration and licensing partners, borrowings under term loans, sales of our common stock, including through our employee stock purchase plan, a working capital payment from Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, and a royalty transaction. Prior to our 2018 merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, whereby Keryx became our wholly owned subsidiary, we had no products approved for commercial sale and had not generated any revenue from the sale of products. While we currently have two commercial products, we are not currently profitable and we have incurred net losses each year since our inception, including a net loss of $69.4 million for the year ended December 31, 2024. As of December 31, 2024, we had an accumulated deficit of $1.7 billion. We cannot guarantee when, if ever, we will become profitable.

In March 2022, we received a complete response letter, or CRL, from the United States, or U.S., Food and Drug Administration, or FDA, regarding our new drug application, or NDA, for vadadustat for the treatment of anemia associated with chronic kidney disease, or CKD. Following a Formal Dispute Resolution Request, or FDRR, to the FDA in 2022 for vadadustat, we filed a resubmission to our NDA in 2023. On March 27, 2024, the FDA approved our NDA for vadadustat under the trade name Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. However, we expended significant additional resources to obtain the approval of Vafseo, the commercialization of Vafseo was delayed and Vafseo was approved for a narrower indication than we initially pursued, which had and could continue to have an adverse effect on our business.

Our ability to generate product revenue and achieve profitability depends on our ability to manage expenses and the overall success of Auryxia, Vafseo and any current or future product candidates, including those that may be in-licensed or acquired, which depends on several factors, including:

- obtaining adequate or favorable pricing and reimbursement from private and governmental payors for Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining and maintaining market acceptance of Auryxia, Vafseo and any other product candidate, including those that may be in-licensed or acquired;
- the size of any market in which Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired, receives approval and obtaining adequate market share in those markets;
- maintaining marketing approvals for Auryxia, Vafseo and any other product, including those that may be in-licensed or acquired;
- obtaining regulatory approval for any label expansion for Vafseo, including the timing and scope thereof;
- our ability to maintain contracts with dialysis organizations for the sale of Auryxia and Vafseo in the U.S.;
- actual or perceived advantages or disadvantages of our products or product candidates as compared to alternative treatments, including their respective safety, tolerability and efficacy profiles, the potential convenience and ease of administration and cost;
- maintaining an acceptable safety and tolerability profile of our approved products, including the frequency and severity of any side effects;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, based, in part, on their perception of our clinical trial data and/or the actual or perceived safety, tolerability and efficacy profile;

- the timing and scope of marketing approvals for any product candidate, if approved, including those that may be in-licensed or acquired;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate supplies of products that are compliant with good manufacturing practices, or GMPs, to support the clinical development and the market demand for Auryxia, Vafseo and any other product and product candidate, including those that may be in-licensed or acquired;
- the potential impact of geopolitical pressures or the BIOSECURE Act on our ability to conduct our business as currently conducted;
- current and future restrictions or limitations on our approved or future indications and patient populations or other adverse regulatory actions or in the event that the FDA requires Risk Evaluation and Mitigation Strategies, or REMS, or risk management plans that use restrictive risk minimization strategies;
- the effectiveness of our collaborators' and our sales, marketing, manufacturing and distribution strategies and operations;
- competing effectively with any products for the same or similar indications as our products (including generics);
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and trade secrets; and
- the adverse impact of the COVID-19 pandemic on CKD patients and the phosphate binder market in which we compete.

Our collaboration, license and other revenue also depends on our partners' ability to successfully market and sell Vafseo and Auryxia in the territories in which they have licensed our products. For example, in May 2023, we entered into a license agreement with MEDICE Arzneimittel Pütter GmbH & Co. KG, or Medice, pursuant to which we granted Medice an exclusive license to market and sell Vafseo for the treatment of anemia in patients with CKD in the European Economic Area, or the EEA, the United Kingdom, or UK, Switzerland and Australia, or Medice Territory. Vafseo is currently marketed and sold by Medice in certain countries in the Medice Territory. If Medice's launch of Vafseo in certain countries in the Medice Territory is delayed or their sales are lower than anticipated, we may not receive the revenue that we expect from Medice on the timing anticipated, or at all.

In July 2024, we entered into a Termination and Settlement Agreement with CSL Vifor, or the Vifor Termination Agreement. Pursuant to the Vifor Termination Agreement, we agreed, among other things, to terminate, effective immediately, the Second Amended and Restated License Agreement that we entered into with CSL Vifor in February 2022, as amended in May 2024, or the Vifor License Agreement, pursuant to which we granted CSL Vifor an exclusive license to sell Vafseo to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of certain group purchasing organizations, or GPOs, and to certain non-retail specialty pharmacies in the U.S., which represents a significant portion of the potential market for Vafseo. As a result, we have regained our rights to sell Vafseo to Fresenius Kidney Care North America and its affiliates and certain other third-party dialysis organizations in the U.S.

Pursuant to the Vifor License Agreement, CSL Vifor contributed $40.0 million to a working capital facility, or Working Capital Fund, established to partially fund our costs of purchasing Vafseo from our contract manufacturers. Pursuant to the terms of the Vifor Termination Agreement, we have agreed to repay the Working Capital Fund to CSL Vifor through quarterly tiered royalty payments ranging from 8% to 14% of our net sales of Vafseo in the U.S., or the WCF Royalty Payments. The WCF Royalty Payments will commence on July 1, 2025, and will continue until the earlier of (i) the cumulative total of the WCF Royalty Payments equals $40.0 million, or (ii) May 31, 2028. The WCF Royalty Payments are subject to minimum true-up milestones of $10.0 million, $20.0 million and $40.0 million, or the WCF Royalty True-Up Payments, on each of May 31, 2026, May 31, 2027 and May 31, 2028, respectively, or the WCF Royalty True-Up Dates. If the cumulative total of the WCF Royalty Payments paid to CSL Vifor on any given WCF Royalty True-Up Date is less than the respective WCF Royalty True-Up Payment, we will pay CSL Vifor a one-time payment equal to the difference between the WCF Royalty True-Up Payment and the cumulative total of the WCF Royalty Payments paid by us through such WCF Royalty True-Up Date. If we are not successful in commercializing Vafseo, including maintaining contracts with dialysis organizations on favorable terms, or at all, our expected revenue related to Vafseo would be adversely impacted and we may be unable to repay all or part of the WCF Royalty Payments, which could have a material adverse impact on our consolidated financial statements.

Our ability to achieve profitability also depends on our ability to manage our expenses. We expect to continue to incur substantial additional operating expenses, including additional R&D expenses related to our pipeline, additional R&D and selling, general and administrative expenses for ongoing development and commercialization of Auryxia and Vafseo, which could lead to operating losses for the foreseeable future. We will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia, Vafseo and any other products, including those

that may be in-licensed or acquired, as well as costs relating to the R&D of Vafseo and any other product candidate, including those that may be in-licensed or acquired. Our prior losses have had, and expected future losses will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital.

In addition to any further costs not currently contemplated in our operating plan, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, the timing of our product, collaboration, license and other revenue, the timing and amount of any repayment of the WCF Royalty Payments, our continued compliance with the terms of the Agreement for the Provision of a Loan Facility, as amended, or the BlackRock Credit Agreement, with Kreos Capital VII (UK) Limited, which are funds and accounts managed by BlackRock Inc., collectively, BlackRock, and our ability to obtain additional funding, should it be needed. In addition, we expect to continue to incur significant expenses if and as we:

- continue our commercialization activities for Auryxia, Vafseo and any other product or product candidate for which we obtain approval, including those that may be in-licensed or acquired;
- seek regulatory approval for any label expansion for Vafseo;
- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approval for any product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia, Vafseo and any other product, including those that may be in-licensed or acquired;
- manufacture Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired, for commercial sale and clinical trials;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop and commercialize other product candidates and technologies;
- repay, and pay any associated pre-payment penalties, if applicable, the term loans in an aggregate principal amount of up to $55.0 million, or the Term Loans, that were made available to us pursuant to the BlackRock Credit Agreement;
- make royalty, milestone or other payments under our current and any future in-licensing agreements;
- maintain, protect and expand our intellectual property portfolio;
- make decisions with respect to our personnel, including the retention of key employees;
- make decisions with respect to our infrastructure, including to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any additional delays or encounter issues with any of the above.

We have expended and may in the future expend significant resources on our legal proceedings, as described below under Part I, Item 3. Legal Proceedings, including any legal proceedings that may be brought by or against us in the future.

Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities, or if we otherwise believe it is necessary, to change our manufacturing processes or assays, to amend or replace our study protocols, to perform studies different from or larger than those currently planned, to conduct any additional clinical trials, whether in order to obtain approval or as a post-approval study, including the post-approval studies required for Vafseo and any other additional clinical trial that we decide to conduct for Vafseo, or if there are any delays in completing any of these activities.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses or the associated revenue. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter, our product revenue, the progress of our clinical development and our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

In addition, our ability to generate revenue would be negatively affected if dialysis organizations are unwilling to include Auryxia or Vafseo in their formulary or the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we sought or the patient population for treatment is narrowed by competition, physician choice, coverage or reimbursement, or payor or treatment guidelines. Even though we generate product revenue from Auryxia and royalties from Riona and Vafseo in Japan, generate product revenue from Vafseo in the U.S., generate royalties from Vafseo in Europe and other territories where it is approved, and may generate revenue and

royalties from the sale of any products that may be approved in the future, including those that may be in-licensed or acquired, we may never generate revenue and royalties that are significant enough for us to become and remain profitable, and we may need to obtain additional financing to continue to fund our operating plan.

***We may require substantial additional financing to fund our business. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.***

As of December 31, 2024, our cash and cash equivalents were $51.9 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia; develop and commercialize Vafseo in the U.S.; and develop and commercialize any other product or product candidate, including those that may be in-licensed or acquired. These expenditures will include costs associated with R&D, manufacturing, potentially obtaining marketing approvals and marketing products approved for sale. In addition, other unanticipated costs may arise. Because the outcomes of our current and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete clinical development for any current or future product candidates or to complete post-marketing studies for Auryxia and Vafseo. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical trials or any post-marketing requirements or any other clinical trials for Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired;
- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution costs, for Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects, including on timing of and ability to obtain and maintain marketing approval, label expansion, study design, study size and resulting operating costs;
- any difficulties or delays in conducting our clinical trials, or enrolling patients in our clinical trials, for Auryxia, Vafseo or any other product candidates;
- the outcome of our efforts to obtain marketing approval for any product candidates, including those that may be in-licensed or acquired, including any additional clinical trials or post-approval commitments imposed by regulatory authorities;
- the timing of, and the costs involved in obtaining, label expansion for Vafseo or marketing approvals for any product candidate, including those that may be in-licensed or acquired, including to fund the preparation, filing and prosecution of regulatory submissions;
- the costs of maintaining marketing approvals for Auryxia, Vafseo or any other product, including those that may be in-licensed or acquired;
- the timing and number of generic versions of Auryxia that enter the market following loss of exclusivity, or LoE, for Auryxia on March 20, 2025, the pricing of generic versions of Auryxia and the timing of, and the magnitude of, the impact on the product revenue from Auryxia, including the impact on the price of Auryxia;
- the cost of securing and validating commercial manufacturing for any of our product candidates, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Auryxia and Vafseo or any other product, including those that may be in-licensed or acquired, or securing and validating additional arrangements;
- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs and the outcome of such litigation;
- the costs involved in any legal proceedings to which we are a party;
- our status as a publicly traded company on the Nasdaq Capital Market;
- our decisions with respect to personnel;
- our decisions with respect to infrastructure; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we could develop and market commercial products, or develop other product candidates and technologies.

We may need to obtain substantial additional financing to fund our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our R&D programs or any future commercialization efforts.

We believe our existing cash resources and the cash we expect to generate from product, royalty, supply and license revenues are sufficient to fund our current operating plan for at least twenty-four months. However, if our operating performance deteriorates significantly from the levels expected in our operating plan, it would have an adverse effect on our liquidity and capital resources and could affect our ability to continue as a going concern in the future. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. In addition, if we fail to satisfy any of the covenants under the BlackRock Credit Agreement, and the loan is accelerated, or if certain pre-specified events occur and we are required to make principal payments to BlackRock sooner than we currently anticipate, such event could have a material adverse effect on our business. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources and cash we expect to generate will fund our operating plan for the period anticipated by us, or that additional funding will be available on terms acceptable to us, or at all.

Any additional fundraising efforts may divert our management's attention away from their day-to-day activities, which may adversely affect our ability to develop and commercialize Auryxia, Vafseo and any other products or product candidates, including those that may be in-licensed or acquired. Also, additional funds may not be available to us in sufficient amounts or on acceptable terms or at all. In addition, raising funds in the current economic environment may present additional challenges. For example, any sustained disruption in the capital markets from adverse macroeconomic conditions and an uncertain geopolitical environment, such as rising inflation, increasing interest rates, slower economic growth or recession, global supply chain disruptions, the Russia-Ukraine war, the Israel-Hamas war and the war in the Middle East and tensions between China and Taiwan, could negatively impact our ability to raise capital, and we cannot predict the extent or duration of such macroeconomic disruptions. If we are unable to raise additional capital in sufficient amounts when needed or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development and/or commercialization of Auryxia, Vafseo and any other products or product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

***Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our products and product candidates on unfavorable terms to us.***

We expect to finance future cash needs through product revenue and royalty and license revenue, and we may seek to sell public or private equity, enter into new debt transactions, explore potential strategic transactions or a combination of these approaches or other strategic alternatives. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, our fixed payment obligations may increase, any such securities may have rights senior to those of our common stock, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. For example, since September 12, 2024 (the date our shelf registration statement on Form S-3 went effective) through December 31, 2024, we sold 14,271,631 shares of our common stock in an at-the-market offering with gross proceeds of $24.3 million. Additional debt financing, if available, may involve agreements that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, declare dividends, acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic transactions, we may have to relinquish valuable rights to our portfolio and future revenue streams, and enter into agreements that would restrict our operations and strategic flexibility. If we raise additional funds through strategic transactions with third parties, we may have to do so at an earlier stage than otherwise would be desirable. In connection with any such strategic transactions, we may be required to relinquish valuable rights to our product and product candidates, future revenue streams or research programs or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds when needed, we may not be able to pursue planned development and commercialization activities and we may need to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.***

Although we continue to focus a substantial amount of our efforts to develop and commercialize Auryxia and Vafseo, a key element of our long-term growth strategy is to develop additional product candidates and acquire, in-license, develop and/or market additional products and product candidates.

Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether product candidates are ultimately identified. Our R&D programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;

- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- a product candidate may be shown to have harmful side effects, a lack of efficacy or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance;
- a product candidate we develop and seek regulatory approval for may not be approved by the FDA on a timely basis, or at all;
- product candidates we develop may nevertheless be covered by third party patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer commercially reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third party payors, if applicable.

If any of these events occur, we may be forced to abandon our R&D efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, including those that may be in-licensed or acquired, which may have a material adverse effect on our business.

Because we have limited financial and managerial resources, we have focused on products, research programs and product candidates for specific indications. As a result, we have had to, and in the future may need to, forgo or delay pursuit of opportunities with other product candidates or for other indications, or may out license rights to product candidates, that later prove to have greater commercial potential. For example, as a result of receipt of the CRL and implementation of the reductions in workforce, we delayed certain research activities. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities on a timely basis, or at all. Our spending on current and future R&D programs and product candidates for specific indications may not yield any commercially viable products.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and institutions, and other researchers to sell or license product candidates, products or technology to us. As a result, our rights to these product candidates may be limited or we may be required to make future payments to such third parties if we are successful in developing such product candidates. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of identifying, selecting, negotiating and implementing a license or acquisition of a product candidate or an approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of a product candidate or an approved product. We have limited resources to identify and execute the acquisition or in-licensing of third party products, businesses, and technologies and integrate them into our current infrastructure.

Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA, the EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, or other regulatory authorities, or post-approval testing or other requirements if approved. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any of our products will be manufactured in a cost effective manner, achieve market acceptance or not require substantial post-marketing clinical trials.

Accordingly, there can be no assurance that we will ever be able to identify, acquire, in-license or develop suitable additional products or product candidates, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential products, product candidates or other programs that ultimately prove to be unsuccessful.

***We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.***

As part of our business strategy, we may engage in additional strategic transactions to expand and diversify our portfolio, including through the merger, acquisition or in-license of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing and prior collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on favorable terms, on a cost-effective basis, or at all. Moreover, we may devote resources to potential opportunities that are never completed or we may incorrectly judge the value or worth of such opportunities. Even if we successfully execute a strategic transaction, we may not be able to realize the anticipated benefits of such transaction and may experience

losses related to our investments in such transactions. Integration of an acquired company or assets into our existing business may not be successful and may disrupt ongoing operations, require the hiring of additional personnel and the implementation and integration of additional internal systems and infrastructure, and require management resources that would otherwise focus on developing our existing business. Even if we are able to achieve the long-term benefits of a strategic transaction, our expenses and short-term costs may increase materially and adversely affect our liquidity. Any of the foregoing could have a detrimental effect on our business, results of operations and financial condition. For example, on June 4, 2021, we entered into a license agreement, or the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase stimulator. In December 2024, we entered into an amendment to the Cyclerion Agreement, pursuant to which we amended the terms of the Cyclerion Agreement, and we now control all clinical and commercial manufacturing of praliciguat, which will be conducted by a third party manufacturer. Although we have progressed preclinical studies for praliciguat, we need to do additional work to manufacture product for clinical trials than originally anticipated before we can initiate the trials, and when the clinical trials are started, we may be unsuccessful in developing praliciguat. If any of the assumptions that we made in valuing the transaction, including the costs or timing of development of praliciguat as a result of the additional manufacturing work or otherwise, or the potential benefits of praliciguat, were incorrect, we may not recognize the anticipated benefits of the transaction and our business could be harmed.

In addition, future transactions may entail numerous operational, financial and legal risks, including:

- incurring substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including contingent liabilities, possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations, processes, systems and personnel of any acquired business;
- increased amortization expenses or, in the case of a write-down of the value of acquired assets, impairment losses, and corresponding adjustments to the estimated useful life of the developed product rights for Auryxia;
- impairment of relationships with key suppliers or customers of any acquired business due to changes in management and ownership;
- inability to retain personnel, customers, distributors, vendors and other business partners integral to an in-licensed or acquired product, product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges;
- entry into indications or markets in which we have no or limited development or commercial experience and where competitors in such markets have stronger market positions; and
- other challenges associated with managing an increasingly diversified business.

If we are unable to successfully manage any transaction in which we may engage, our ability to develop new products and continue to expand and diversify our portfolio may be limited.

***Risks Related to our Financial Arrangements***

***Our obligations in connection with the BlackRock Credit Agreement and requirements and restrictions in the BlackRock Credit Agreement could adversely affect our financial condition and restrict our operations.***

We entered into the BlackRock Credit Agreement, which provides for a senior secured term loan facility, in the aggregate principal amount of up to $55.0 million, or the Term Loan Facility. The initial tranche of $37.0 million, or the Tranche A Loan, closed on January 29, 2024, or the Closing Date, an additional amount of $8.0 million, or the Tranche B Loan, was drawn on April 19, 2024, and an additional $10.0 million was drawn on February 3, 2025, or the Tranche C Loan and, together with the Tranche A Loan and the Tranche B Loan, the Term Loans. See Note 7, *Indebtedness*, to our audited consolidated financial statements in Part II, Item 8. Financial Statements of this Form 10-K for additional information regarding our obligations under the BlackRock Credit Agreement. The Term Loan Facility had an initial maturity date of March 31, 2025, which was automatically extended to January 29, 2028, or the Maturity Date, since we received FDA approval for Vafseo prior to June 30, 2024.

The BlackRock Credit Agreement contains certain representations and warranties, affirmative covenants, negative covenants, financial covenants, events of default and other provisions and conditions that are customarily required for similar financings. The financial covenants under the BlackRock Credit Agreement require us to either (i) maintain cash and cash equivalents, measured as of the last day of each fiscal month, greater than or equal to $15.0 million or (ii) earn consolidated revenue, measured as of the last day of each fiscal month for the trailing twelve-month period, of $150.0 million. Failure to maintain compliance with these or other covenants would result in an event of default under the BlackRock Credit Agreement, which

could result in enforcement action, including acceleration of amounts due under the BlackRock Credit Agreement, or limit our ability to make certain payments under the Vifor Termination Agreement.

The Term Loan Facility will accrue interest at a floating annual rate equal to the sum of (x) term Secured Overnight Financing Rate for a tenor of one month (subject to a floor of 4.25% per annum) plus (y) a margin of 6.75% per annum (subject to an overall cap of 15.00% per annum on the all-in interest rate). During the continuance of any payment event of default under the BlackRock Credit Agreement, the interest rate on such overdue sum will automatically increase by an additional 3.0% per annum, and may be subject to an additional late fee of 2.0% of such overdue sum. The Term Loan Facility does not amortize during the period commencing on the Closing Date and ending on December 31, 2025 (which was extended to December 31, 2026 at our option), or the Interest Only Period. We are required to pay interest and, after the Interest Only Period, principal on the first calendar day of each month. In the event of certain prespecified events, the repayment schedule will be accelerated. If any of these events occur, and we are required to repay principal sooner than we anticipate, it would have an adverse effect on our business.

In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the BlackRock Credit Agreement as a result of an event of default or otherwise, we may not have sufficient funds or may be unable to arrange for additional financing to repay the liabilities or to make any accelerated payments, and BlackRock could seek to enforce security interests in the collateral securing the BlackRock Credit Agreement, which would have a material adverse effect on our business, financial condition and results of operations.

In addition, our obligations in connection with the BlackRock Credit Agreement could have additional significant adverse consequences, including, among other things:

- restricting our activities, including limitations on transferring certain of our assets, engaging in certain transactions, terminating certain agreements, incurring certain additional indebtedness, creating certain liens, paying cash dividends or making certain other distributions and investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a possible competitive disadvantage compared to our competitors who have a smaller amount of debt or competitors with comparable debt at more favorable interest rates; and
- limiting our ability to borrow additional amounts for working capital, capital expenditures, R&D efforts, acquisitions, debt service requirements, execution of our business strategy and other purposes.

Any of these factors could materially and adversely affect our business, financial condition and results of operations.

***Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.***

In February 2021, we entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which we sold to HCR our right to receive royalties and sales milestones for Vafseo, collectively the Royalty Interest Payments, in each case, payable to us under our Collaboration Agreement dated December 11, 2015, or the MTPC Agreement, with Mitsubishi Tanabe Pharma Corporation, or MTPC, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. Under the Royalty Agreement, we are required to comply with various covenants, including obligations to take certain actions, such as actions with respect to the Royalty Interest Payments, the MTPC Agreement, our agreement with MTPC for the commercial supply of Vafseo drug product, and our intellectual property. In addition, the Royalty Agreement includes customary events of default upon the occurrence of enumerated events, including failure to perform certain covenants and the occurrence of insolvency events. Upon the occurrence of an event of default, HCR would have the ability to exercise all available remedies in law and equity, which could have a material adverse effect on our financial condition.

***Risks Related to Commercialization***

***Our business is substantially dependent on the commercial success of Auryxia and Vafseo. If we are unable to continue to successfully commercialize Auryxia and Vafseo, our results of operations and financial condition will be materially harmed.***

Our business and our ability to generate product revenue largely depend on our, and our collaborators', ability to successfully commercialize Auryxia and Vafseo. Our ability to generate revenue depends on our ability to execute on our commercialization plans, and the size of the market for, and the level of market acceptance of, Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired. If we are not able to maintain contracts with dialysis organizations and other customers for the sale of Auryxia and Vafseo on favorable terms, or at all, our revenue and results of operations will be adversely affected. If the size of any market for which a product or product candidate is approved decreases or is smaller than we anticipate, our revenue and results of operations could be materially adversely

affected. For example, the approval for Vafseo in the U.S. is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months instead of all such adults. This limitation could affect the level of market acceptance of Vafseo.

We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that protect us from generic drug competition until March 20, 2025. Following LoE, on March 20, 2025, the number of generic versions of Auryxia that enter the market, and the timing thereof, will adversely affect our revenue from Auryxia. The impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia. In addition, we believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B and Auryxia LoE could result in the buying pattern of certain customers in 2025 and future years being different than their historical practices. If Auryxia sales decline faster than we anticipate following LoE, our results of operations and financial condition will be materially harmed.

Given the concentration of dialysis clinics in large networks, with DaVita, Inc., or DaVita, Fresenius Kidney Care Group LLC, or Fresenius, and U.S. Renal Care, or USRC, accounting for a vast majority of the dialysis population in the U.S., treatment is usually driven by medical protocols that are implemented across the entire network of clinics. Dialysis organizations require large data sets to adopt medical protocols. If dialysis organizations do not add Vafseo to their medical protocols in a timely manner, or at all, or if the protocols service smaller populations than the current label, our results of operations could be materially adversely affected.

Oral-only phosphate binders, including Auryxia, are included in the end-stage renal disease, or ESRD, Prospective Payment System, or PPS, bundle payment, as of January 2025, however, it will take time for dialysis organizations to implement internal mechanisms to dispense phosphate binders which could negatively impact the market for phosphate binders, including Auryxia, and divert dialysis organizations' attention from focusing on other therapeutic areas such as anemia management, which in turn could negatively impact the market for Vafseo. In addition, dialysis organizations may choose lower cost binders over Auryxia, or binders that may have features or benefits more aligned with the dialysis organization's operational activities, which could negatively impact Auryxia revenue.

We believe our revenue growth has been negatively impacted by the COVID-19 pandemic since 2021 primarily as the CKD patient populations that we serve experienced both high hospitalization and mortality rates due to COVID-19, and the pandemic had an adverse impact on the phosphate binder market in which Auryxia competes. Labor shortages and costs have also adversely impacted dialysis providers. These impacts have refocused clinical efforts in addressing bone and mineral disorders like hyperphosphatemia to more acute operational issues to ensure patients receive dialysis treatments and still some patients have been rescheduled or missed treatments due to labor shortages. We believe, this and potentially other factors, led to the reduction in the phosphate binder market, which has not experienced growth since early 2020. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, the COVID-19 pandemic and the ongoing impacts from the COVID-19 pandemic continue to adversely and disproportionately impact CKD patients and the phosphate binder market. Therefore, we expect the impacts from the pandemic to continue to have a negative impact on our revenue growth for the foreseeable future.

Market acceptance is also critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If Auryxia, Vafseo or any of our future products is not accepted by the market to the extent that we expect or market acceptance decreases, we may not be able to generate significant product revenue and our business would be materially harmed. Market acceptance of Auryxia, Vafseo or any other approved product depends on a number of factors, including:

- the availability of adequate coverage and reimbursement by, and the availability of discounts, rebates and price concessions to dialysis organizations, third party payors, pharmacy benefit managers, or PBMs, and governmental authorities;
- the availability of discounts and rebates to dialysis organizations to facilitate access for patients;
- use at dialysis organizations and their willingness to include or continue to include Auryxia or Vafseo in their formulary or protocols and the scope of such protocols;
- the safety and efficacy of the product, as demonstrated in clinical trials and in the post-marketing setting;
- the prevalence and complications of the disease treated by the product;
- the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings or limitations that may be required on the label as a consequence of potential safety risks associated with the product;
- the countries in which marketing approvals are obtained;
- the claims we and our partners are able to make regarding the safety and efficacy of the product;

- the success of our physician and patient communications and education programs;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the timing of receipt of marketing approvals and product launch relative to competing products and potential generic entrants;
- the success of, or withdrawal from the market of, competing products;
- relative convenience and ease of administration;
- the frequency and severity of adverse side effects;
- favorable or adverse publicity about our products or favorable or adverse publicity about competing products;
- the effectiveness of our and our partners' sales, marketing, manufacturing and distribution strategies and operations; and
- the restrictions on the use of the product together with other medications, if any.

In addition, our ability to generate net product revenue depends on our ability to control the expenses associated with commercializing a product, including internal expenses, manufacturing costs, rebates, product returns and other adjustments. We do not have control over many of the expenses required to commercialize our products, and if we experience increased costs or expenses, we may not be able to afford the commercial activities required to successfully commercialize our products, which could have an adverse effect on our business. In addition, our net product revenue requires judgement and includes estimates for rebates and product returns, which can fluctuate from quarter-to-quarter and year-over-year. If our net product revenue is lower than anticipated, including as a result of higher expenses or product returns, our business could be harmed.

Several healthcare facilities, including DaVita, have previously restricted access for non-patients as a result of the COVID-19 pandemic, resulting in restricted access for certain members of our sales force. Such precautionary measures have since been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with those customers. Nevertheless, some restrictions remain and restrictions on our customer-facing employees' in-person interactions with healthcare providers have, and could continue to, negatively impact our access to healthcare providers and ultimately our sales, including with respect to Vafseo. In addition, more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19, which may be more contagious and more severe than prior strains of the virus, or due to outbreak of other infectious diseases, such as H1N1 virus (Swine Flu) and H5N1 virus (bird flu). Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand in the U.S. for Auryxia and Vafseo, including the potential for further declines or changes in prescription trends and customer orders, which could have a material adverse effect on our business, results of operations, and financial condition.

***If we are unable to maintain or expand sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, Vafseo or any other product candidates that may be approved.***

In order to market Auryxia, Vafseo and any other approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We have built a commercial infrastructure and sales force in the U.S. for Auryxia and Vafseo. If the sales and marketing team cannot successfully commercialize Auryxia or Vafseo, it could have a material adverse effect on our product revenue and our financial condition. Additionally, training a sales force to successfully sell and market a new commercial product is expensive and time-consuming and could delay any commercial launch or market acceptance of such product. We may underestimate the size of the sales force required for a successful product launch, and we may need to expand our sales and marketing team to a greater extent than we already have, which would increase our costs more than we anticipated.

We devote significant effort to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is significant and retaining qualified personnel with experience in our industry is difficult. If key sales and marketing employees decide to leave, we may not be able to hire and train new employees quickly enough to meet our needs. At the same time, we may face high turnover, requiring us to expend time and resources to source, train and integrate new employees.

There are risks involved with maintaining our own sales and marketing capabilities, including the following:

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

- potential lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales and marketing capabilities, we will not be successful in commercializing Auryxia, Vafseo and any other product candidate that may be approved. Also, if we are unable to maintain our arrangements with third parties with respect to sales and marketing, if we are unsuccessful in entering into additional arrangements with third parties to sell and market our products or we are unable to do so on terms that are favorable to us, or if such third parties are unable to carry out their obligations under such arrangements, it will be difficult to successfully commercialize our product and product candidates, including Vafseo.

***Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, Vafseo or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.***

Market acceptance and sales of any approved products, including Auryxia and Vafseo, depends significantly on the availability of adequate coverage and reimbursement from third party payors and may be affected by existing and future healthcare reform measures. Governmental authorities, dialysis organizations, third party payors, and PBMs decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. We cannot be sure that coverage or adequate reimbursement will be available for Auryxia, Vafseo or any of our potential future products. Even if we obtain coverage for an approved product, third party payors may not establish adequate reimbursement amounts, which may reduce the demand for our product and prompt us to have to reduce pricing for the product. If reimbursement is not available or is limited, we may not be able to successfully commercialize certain of our products. Coverage and reimbursement by a governmental authority, dialysis organization, third-party payor or PBMs may depend upon a number of factors, including the determination that use of a product is:

- a covered benefit under the health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost effective.

Obtaining coverage and reimbursement approval for a product from a governmental authority, dialysis organization, PBM or a third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. In the U.S., there are multiple governmental authorities, PBMs and third-party payors with varying coverage and reimbursement levels for pharmaceutical products, and the timing of commencement of reimbursement by a governmental payor can be dependent on the assignment of codes via the Healthcare Common Procedural Coding System, which codes are assigned on a quarterly basis. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. CMS, local Medicare administrative contractors, Medicare Advantage and/or Part D plans and/or PBMs operating on behalf of such plans, may have some responsibility for determining the medical necessity of such drugs, and therefore coverage, for different patients. Different reimbursement methodologies may apply, and CMS may have some discretion in interpreting their application in certain settings.

As an oral drug, Auryxia was covered by Medicare under Part D until January 1, 2025, for the treatment of patients with hyperphosphatemia. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home. As of January 2025, oral ESRD-related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, are included in the ESRD bundle and separate Medicare payment for these drugs are no longer available. In addition, dialysis organizations will receive a Transitional Drug Add-on Payment Adjustment, or TDAPA, payment for claims that include phosphate binders for the next two years. Vafseo, which we began selling in January 2025, is also included in the ESRD bundle and ESRD facilities will receive a TDAPA for Vafseo as a new renal dialysis drug meeting certain criteria for a period of at least two years starting on January 1, 2025. The TDAPA provides separate payment based on the drug's Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. If the TDAPA reimbursement amount for Auryxia or Vafseo is lower than anticipated, or if the TDAPA is eliminated, it would have an adverse impact on our revenue. Additionally, in the post-TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that bundled drugs will be reimbursed as part of the single bundled payment for Medicare patients. However, there can be no assurances that any increase in the single bundled payment base rate will be sufficient to

adequately reimburse the dialysis facilities for Auryxia or Vafseo at a price that allows us to continue to sell Auryxia or Vafseo at a profit.

In July 2024, Ardelyx, Inc., or Ardelyx, filed a complaint in the United States District Court for the District of Columbia against the U.S. Department of Health and Human Services, or HHS, CMS and other parties, which alleged that CMS's plan to include oral-only phosphate lowering therapies in the ESRD PPS violated its statutory and regulatory authority under the Medicare Improvements for Patients and Providers Act, which established the ESRD PPS bundled payment system for dialysis services. In October 2024, Ardelyx filed a motion for a preliminary injunction to enjoin CMS from including oral-only phosphate lowering therapies in the ESRD PPS. CMS had earlier filed a motion to dismiss the complaint on jurisdictional grounds. On November 8, 2024, the district court denied Ardelyx's motion for a preliminary injunction and it granted the government's motion to dismiss. Thereafter, Ardelyx moved for reconsideration, but the district court also denied that request. On December 26, 2024, Ardelyx filed a notice of appeal with the US Court of Appeals for the DC Circuit. If Ardelyx is successful in its claims, oral-only phosphate lowering therapies, including Auryxia, may be removed from the ESRD bundle, which could reduce anticipated revenue for Auryxia.

In addition, in September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients not on dialysis, or NDD-CKD. While this decision does not impact CMS coverage for the control of serum phosphorus levels in adult patients with anemia due to CKD in patients on dialysis, or DD-CKD, or the Hyperphosphatemia Indication, it requires Part D Plan sponsors to impose prior authorization or other steps to ensure that Auryxia is reimbursed only for the Hyperphosphatemia Indication. We decided beginning in 2022 to terminate certain Part D contracts, as patients no longer had the access benefit given the prior authorization requirement. Now patients must go through a medical exemption process, which is very similar to a prior authorization review. While we believe this had, and may continue to have, a negative impact on our overall sales volume, we believe it had a significant positive impact on our net selling price. However, if we experience additional negative impacts on our sales volume as a result of this change, it could have a negative impact on our product revenue.

Medicaid reimbursement of drugs varies by state. Private third-party payor reimbursement policies also vary and may or may not be consistent with Medicare reimbursement methodologies. Manufacturers of outpatient prescription drugs may be required to provide discounts or rebates under government healthcare programs or to certain third-party payors in order to obtain coverage of such products.

Additionally, we will be required to enter into contracts with dialysis organizations, GPOs, third party payors and/or PBMs offering rebates or discounts on our products in order to obtain favorable formulary status and we may not be able to agree upon commercially reasonable terms with such dialysis organizations, GPOs, third party payors or PBMs, or provide data sufficient to obtain favorable coverage and reimbursement for many reasons, including that we may be at a competitive disadvantage relative to companies with more extensive product lines. In addition, dialysis organizations, GPOs, third party payors, PBMs and/or other entities that purchase our products may impose restrictions on our ability to raise prices for our products over time without incurring additional costs. Three distributors, Fresenius Medical Care Rx, McKesson Corporation and Cencora, Inc., formerly known as AmerisourceBergen Drug Corporation, in the aggregate, accounted for a significant percentage of our gross revenue during the year ended December 31, 2024. However, due to a variety of factors, including coverage of our products in the ESRD bundle and to support commercial availability of Vafseo in 2025, there were changes to the manner in which we distributed our products, which we implemented in January 2025. This included, for example, reducing the number of mainline wholesalers in our distribution network, distribution of products through specialty distributors, and an increased focus on direct sales through contracts with dialysis organizations. If we are not able to enter into and maintain agreements with wholesalers, specialty distributors, the dialysis organizations and other purchasers for the sale of our products on favorable terms, on a timely basis or at all, or if dialysis organizations or other purchasers do not purchase as much product as we anticipate or terminate our arrangements, it would adversely impact the market opportunity for our products, our product revenues and operating results.

Furthermore, the dialysis market is unique and is dominated by three providers: DaVita, Fresenius and USRC, which account for a vast majority of the dialysis population in the U.S. If we are not able to maintain supply agreements with these, and other, dialysis organizations for the sale of Vafseo on favorable terms, in a timely matter or at all, our business may be materially harmed.

Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, or will terminate their contract, resulting in that product not being on that organization's formulary. If any dialysis organization does not add Auryxia or Vafseo to the formulary, or removes Auryxia or Vafseo from the formulary, our business may be materially harmed.

In addition, we may be unable to sell Auryxia or Vafseo to dialysis providers on a profitable basis if CMS significantly reduces the level of reimbursement for dialysis services and providers choose to use alternative therapies or look to re-negotiate their contracts with us. Our profitability may also be affected if our costs of production increase faster than increases in reimbursement levels. Adequate coverage and reimbursement of our products by government and private insurance plans, including Medicare Advantage plans, are central to patient and provider acceptance of any products for which we receive marketing approval. Existing competitive products may enter into sole source agreements with dialysis providers that impact the ability for new product innovations and new competitors may face price pressure based on existing contracts with dialysis providers.

Further, in many countries outside the U.S., a drug must be approved for reimbursement before it can be marketed or sold in that country. In some cases, the prices that we intend to charge for our products are also subject to approval. Approval by the EMA or another regulatory authority does not ensure approval by reimbursement authorities in that jurisdiction, and approval by one reimbursement authority outside the U.S. does not ensure approval by any other reimbursement authorities.

However, the failure to obtain reimbursement in one jurisdiction may negatively impact our ability to obtain reimbursement in another jurisdiction. In addition, we plan to rely on a partner to obtain approval by reimbursement authorities outside the U.S. Our partners may not be able to obtain such reimbursement approvals on a timely basis, if at all, and favorable pricing in certain countries depends on a number of factors, some of which are outside of our partners' control. Vafseo was approved in Japan for the treatment of adult patients with anemia due to CKD and is being marketed by MTPC in Japan under the trade name Vafseo. Pricing and reimbursement strategy is a key component of MTPC's commercialization plans for Vafseo in Japan. If coverage and reimbursement terms change, MTPC may not be able to, or may decide not to, continue commercialization of Vafseo in Japan. Furthermore, Vafseo was approved in Europe and Australia for the treatment of anemia due to CKD in DD-CKD patients. In Europe, reimbursement is obtained on a country-by-country basis and it is a time consuming process. In May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in the Medice Territory. Medice launched and has received pricing and reimbursement for Vafseo in certain countries in Europe and is working on launching and securing pricing and reimbursement for Vafseo in other markets across Europe. There is no guarantee of the timing or extent of reimbursement that they will receive in each country, if at all. If Medice is not able to obtain favorable pricing in the Medice Territory, or if such approvals are delayed, it will affect Medice's sales of Vafseo in the Medice Territory, which could have an adverse effect on our results of operations.

***We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.***

The development and commercialization of new drugs is highly competitive and subject to rapid and significant technological change. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired. Our objective is to successfully commercialize Auryxia and Vafseo and develop and commercialize new products with clinically proven efficacy, convenience, tolerability and/or safety. In many cases, any approved products that we commercialize will compete with existing, market-leading products. If existing or new competitors of Auryxia or Vafseo take market share from us, it could have an adverse impact on our revenue and our business.

We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that protect us from generic drug competition until March 20, 2025. Following LoE, in March 2025, the timing and number of generic versions of Auryxia that enter the market will affect our revenue from Auryxia. We and our licensors, Panion & BF Biotech, Inc., or Panion, and, as applicable, Dr. Hsu, entered into settlement agreements with all of the third parties who submitted Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA, pursuant to which we granted licenses to market a generic version of Auryxia in the U.S. beginning on March 20, 2025 (subject to FDA approval). On February 5, 2025, we entered into an Authorized Generic Distribution and Supply Agreement with Mylan Pharmaceuticals, Inc., or AG Partner, pursuant to which, on or after March 20, 2025, they will sell an authorized generic version of Auryxia. The impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia. In addition, we believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B and Auryxia LoE could result in the buying pattern of certain customers in future years being different than their historical practices. If Auryxia sales decline faster than we anticipate following LoE, our results of operations and financial condition will be materially harmed.

Auryxia is competing in the hyperphosphatemia market in the U.S. with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents

are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's RENAZORB™ (lanthanum dioxycarbonate), or could otherwise enter the market that may impact the market for Auryxia. In October 2023, the FDA approved XPHOZAH® (tenapanor), a phosphate absorption inhibitor that is marketed by Ardelyx and indicated to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy, which may adversely impact the market for Auryxia.

Auryxia is competing in the IDA market in the U.S. with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutics plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which was launched in the U.S. for the treatment of IDA in July 2021.

In Japan, our Japanese sublicensee, Japan Tobacco International, or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona (ferric citrate hydrate). In the hyperphosphatemia market, Riona competes with Fosrenol® (lanthanum carbonate hydrate) marketed by Bayer Yakuhin Ltd., generic lanthanum carbonate hydrate products, and Phozevel® (tenapor hydrochloride) marketed by Kyowa Kirin Co., Ltd. In the IDA market in Japan, Riona competes with Ferromia® (sodium ferrous citrate) marketed by Alfresa Pharma Corporation and Fero-Gradumet® (dried ferrous sulfate) marketed by Viatris Inc.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia.

Drugs that may compete with Vafseo include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the U.S. and Europe, respectively, Mircera® (methoxy PEG-epoetin beta), commercialized by CSL Vifor in the U.S. and Roche Holding Ltd., or Roche, outside of the U.S., Evrenzo® (roxadustat) in Europe commercialized by Astellas Pharma Inc., or Astellas, Eporatio® (epoetin theta) in Europe commercialized by Teva Pharmaceuticals Ltd., Silapo® (epoetin zeta) in Europe commercialized by Stada Arzneimittel AG, Epoetin Alfa Hexal® (epoetin alfa) in Europe commercialized by Hexal AG, Binocrit® (epoetin alfa-biosimilar) in Europe commercialized by Sandoz, and NeoRecormon® (epoetin beta) in Europe commercialized by Roche.

We and our partners may also face competition from potential new anemia therapies. There are several other oral hypoxia-inducible factor prolyl hydroxylase inhibitor product candidates in various stages of development for anemia indications in territories outside the U.S. that may be in direct competition with Vafseo if and when they are approved and launched commercially. These candidates are being developed by companies such as JT and Bayer HealthCare AG, or Bayer. In Europe, roxadustat is approved for the treatment of anemia in patients with CKD.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable erythropoiesis stimulating agent, or ESA, utilization and thus limit the market potential for Vafseo if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

In Japan, vadadustat is sold under the name Vafseo, which is approved for patients with CKD, including both DD-CKD and NDD-CKD, and competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of DD-CKD patients and NDD-CKD patients. In addition, daprodustat, GSK's product candidate, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD, and molidustat, Bayer HealthCare AG's product, is approved in Japan for the treatment of renal anemia. In China, roxadustat is commercialized for the treatment of anemia due to CKD in DD-CKD patients and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is licensed for marketing based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product (i.e., a reference biologic product). The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without the risk of being sued for patent infringement. In addition, an application for a biosimilar product can only be approved by the FDA 12 years after the existing, branded product was licensed under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the U.S. The introduction of biosimilars into the injectable ESA market in the U.S. will constitute additional competition for Vafseo. In the U.S., Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. Large and established companies such as Amgen, Roche and GSK, among others, compete in the market for drug products to treat kidney disease. In particular, these companies have greater experience and expertise in conducting preclinical testing and clinical trials, obtaining marketing approvals, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we are developing obsolete. Smaller and other early-stage companies may also prove to be significant competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval, or discovering, developing and commercializing competitive products, before, or more effectively than, we do. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

***The commercialization of ferric citrate, branded as Riona in Japan, Vafseo in Europe, Japan and other territories where it is approved, and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the U.S. subject us to a variety of risks associated with international operations, which could materially adversely affect our business.***

Our Japanese sublicensee, JT, and its subsidiary, Torii, commercialize Riona, the trade name for ferric citrate hydrate in Japan, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA in Japan. In Japan and certain other countries in Asia, we granted MTPC exclusive rights to commercialize Vafseo, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo. In May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in the Medice Territory. Pursuant to the license agreement, we transferred the marketing authorization issued by the EMA, UK, the Swiss Agency for Therapeutic Products and the Australian Therapeutic Goods Administration to Medice. We also granted Averoa SAS, or Averoa, an exclusive license to develop and commercialize ferric citrate in the EEA, Turkey, Switzerland, UK, Balkans, and certain countries in Eastern Europe and the Middle East, or the Averoa Territory.

In addition, we have conducted and in the future may conduct clinical trials outside of the U.S. for any product or product candidate that may be in-licensed or acquired. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing Auryxia and Vafseo outside the U.S., including, among others:

- political, regulatory, compliance and economic developments, weakness or instability that could restrict our ability to manufacture, market and sell our products;
- changes in international medical reimbursement policies and programs;
- changes in healthcare policies of foreign jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs and our compliance therewith;
- our ability to develop or manage relationships with qualified local distributors and trading companies;
- diminished protection of intellectual property in some countries outside of the U.S.;
- differing labor regulations and business practices;
- compliance with laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation, the EU General Data Protection Regulation, or GDPR, and similar data protection laws, and tax, employment, immigration and labor laws;
- economic weakness, including inflation, increasing interest rates, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, global pandemics, or natural disasters including earthquakes, typhoons, floods and fires.

In addition, we receive revenues from royalty payments converted to U.S. dollars based on net sales of Riona and Vafseo in Japanese yen, the Euro, the Pound Sterling and the Swiss Franc. The exchange rates between these currencies on the one hand, and the U.S. dollar, on the other hand, have changed substantially in recent years and may fluctuate substantially in the future. Our results of operations could be adversely affected over time by certain movements in exchange rates, particularly if these currencies depreciate against the U.S. dollar.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations. As and if we continue to expand our commercialization efforts, we may encounter new risks.

***Risks Related to Product Development***

***Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development of any of our product candidates.***

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Preclinical studies and clinical trials are expensive, difficult to design and implement, can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the process.

We may be unable to successfully complete clinical trials of Auryxia, Vafseo and our product candidates or to successfully obtain approval of label expansion for Vafseo or approval of our product candidates, if the results of those trials and studies are not positive or are only modestly positive, or if there are concerns with the product profile due to efficacy or safety. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, interim results of a clinical trial do not necessarily predict final results, and results of Phase 3 clinical trials for one indication may not be predictive of results of Phase 3 clinical trials for another indication. For example, we announced positive results from the INNO$_2$VATE program; however, while Vafseo achieved the primary and key secondary efficacy endpoints in each of the two PRO$_2$TECT studies, the PRO$_2$TECT program did not meet the primary major adverse cardiovascular event, or MACE, safety endpoint. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. For example, in March 2022, we received the CRL for Vafseo indicating that the FDA had determined that it could not approve the NDA in its present form, thus delaying any potential approval of Vafseo. Following submission of the FDRR to the FDA in 2022, we filed a resubmission to our NDA for vadadustat for the treatment of anemia due to CKD only in adult DD-CKD patients in 2023. On March 27, 2024, the FDA approved our NDA for vadadustat under the trade name of Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. However, we expended significant additional resources to obtain the approval of Vafseo, the approved indication is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months and the commercialization of Vafseo was delayed, which had and could continue to have an adverse effect on our business.

We have several lifecycle management and label expansion opportunities currently under evaluation for Vafseo, one of which is the potential for alternative dosing, and another of which is label expansion for the treatment of adult patients with NDD-CKD. However, we will be required to complete additional clinical trials before seeking approval for label expansion for the treatment of adult patients with NDD-CKD and we may be required to generate additional clinical data before seeking approval for alternative dosing. Clinical trials are time consuming and expensive, and even though Vafseo is approved for adult patients with anemia due to CKD on dialysis for at least three months, we may not be successful in any of our lifecycle management or label expansion opportunities in the timeframe anticipated by us, or at all. For example, we plan to start a Phase 3 trial in the second half of 2025 to potentially expand Vafseo label to include the treatment of late-stage NDD-CKD patients; however, the FDA may not agree with our study design or we may not successfully demonstrate safety and/or efficacy needed to obtain regulatory approval or we may be unable to successfully complete the trial when anticipated, or at all. If the clinical trials for our label expansion opportunities are not successful or take longer than anticipated, or if we do not obtain FDA approval of label expansion for Vafseo for the treatment of adult patients with NDD-CKD or for alternative dosing in a timely manner, or at all, it could impact future revenue and have an adverse effect on our business. In addition, it is impossible to predict when or if any of our other product candidates will prove effective or safe in humans or will receive marketing approval or on what terms.

We may experience numerous unforeseen events during, or as a result of, preclinical development or clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. We may be required to complete additional clinical trials for Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired, in order to obtain or maintain required regulatory approvals.

Our preclinical studies and clinical trials may take longer to complete than currently anticipated, or may be delayed, suspended, required to be repeated, prematurely terminated or may not successfully demonstrate safety and/or efficacy needed to obtain or maintain regulatory approval for a variety of other reasons, such as:

- the costs may be greater than we anticipate;
- the number of patients required for clinical trials may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third party contractors, such as our contract research organizations, or CROs, may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all, or we may fail to communicate effectively or provide the appropriate level of oversight of such third party contractors;
- the supply or quality of our starting materials, drug substance and drug product necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators, independent data monitoring committees, institutional review boards, safety committees, or ethics committees, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using our product candidate, or a finding that the participants are being exposed to unacceptable health risks;
- clinical trials of our product candidates may produce negative or inconclusive results or results that may be interpreted in a manner different than we interpret them, and we may decide, or regulators may require us, to conduct additional clinical trials, repeat a clinical trial or abandon product development programs;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials or repeat a clinical trial and increased expenses associated with the services of our CROs and other third parties;
- we may fail to initiate, delay or fail to complete a clinical trial as a result of an Investigational New Drug application, or IND, being placed on clinical hold by the FDA, the EMA, the PMDA, or other regulatory authorities, or for other reasons, such as failure to recruit or enroll suitable patients or patients' failure to return for post-treatment follow up;
- we may determine to expand or otherwise change a clinical trial, including after it has begun;
- clinical trial sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, or failure by us or our CROs to communicate effectively or provide the appropriate level of oversight of such clinical sites and investigators;
- there may be an inability, delay, or failure in identifying and maintaining a sufficient number of clinical trial sites, many of which may already be engaged in other clinical programs;
- there may be a delay or failure in reaching agreement with the FDA, the EMA, the PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- there may be a delay or failure in obtaining authorization to commence a clinical trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- there may be delays in reaching, or failure to reach, agreement on acceptable terms with prospective clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- the FDA, the EMA, the PMDA or other regulatory authorities may require us to submit additional data or impose further requirements before permitting us to initiate a clinical trial or during an ongoing clinical trial;
- the FDA, the EMA, the PMDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- third parties with which we work may fail to comply with good practice quality guidelines and regulations, or GxP, including good laboratory practice, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- there may be changes in governmental regulations or administrative actions.

If any of the foregoing occurs, the following may result:

- regulators may require that we conduct additional clinical trials, repeat clinical trials or conduct other studies beyond those that we currently contemplate;

- we may be delayed in obtaining marketing approval for our product candidates;
- we may not obtain marketing approval for our product candidates at all;
- we may obtain approval for indications or patient populations that are not as broad as intended or desired;
- we may obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for any approved product or inhibit our ability to successfully commercialize any approved product;
- a REMS or FDA-imposed risk management plan that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, may be required;
- we may be subject to additional post-marketing restrictions and/or requirements; or
- the product may be removed from the market after obtaining marketing approval.

Our product development costs may also increase if we experience development delays or delays in receiving the requisite marketing approvals. Our preclinical studies or clinical trials may need to be restructured or may not be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize Vafseo for potential future indications or any product candidate that is approved, including those that may be in-licensed or acquired, or allow our competitors to bring products to market before we do. This could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

***We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired.***

Identifying and qualifying patients to participate in clinical trials is critical to the success of our clinical trials. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our clinical trials. Patients may be unwilling to participate in our clinical trials because of concerns about investigational research studies, the time and commitment needed to participate in a study, adverse events observed with the product candidate under study, the current standard of care, competitor products and/or other investigational agents, in each case for the same indications and/or similar patient populations. In addition, in the case of clinical trials of any product candidate, patients currently receiving treatment with the current standard of care or a competitor product may be reluctant to participate in a clinical trial with an investigational drug. Additionally, it is often more difficult to enroll special or particular subpopulations of patients, such as pediatric or elderly patients, due to a number of factors including parental or other caregiver considerations, concerns and burdens. For example, we began enrolling sites in a post-approval pediatric study for the Hyperphosphatemia Indication of Auryxia in the second quarter of 2022, which began patient recruitment in the third quarter of 2022, but enrollment of eligible pediatric patients in study sites continues to be very slow despite efforts to do so.

Finally, competition for clinical trial sites may limit our access to patients appropriate for our clinical trials. As a result, the timeline for recruiting patients and conducting studies may be delayed. These delays could result in increased costs, delays in advancing our development of any product or product candidate, or termination of the clinical trial altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment is affected by many factors, including:

- severity of the disease under investigation;
- design of the study protocol;
- size and nature of the patient population;
- eligibility criteria for, and design of, the study in question, including study complexity;
- perceived risks and benefits of the product or product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product or product candidate being studied in relation to available therapies or other product candidates in development;
- efforts to facilitate timely enrollment in clinical trials;
- participation length and demands on patients and caregivers;
- site staffing shortages and turnover;
- clinical trial sites and investigators failing to perform effectively; and
- patient referral practices of physicians.

We may not be able to initiate or complete clinical trials in a timely manner, or at all, if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may delay approval, or result in failure to maintain or obtain approval, of our products or product candidates, which would have a material adverse effect on our business.

Further, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan, or DAP, for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, action plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In June 2024, as mandated by FDORA, the FDA issued draft guidance outlining the general requirements for DAPs. Unlike most guidance documents issued by the FDA, the DAP guidance when finalized will have the force of law because FDORA specifically dictates that the form and manner for submission of DAPs are specified in FDA guidance. On January 27, 2025, in response to an Executive Order issued by President Trump on January 21, 2025, on Diversity, Equity and Inclusion programs, the FDA removed this draft guidance from its website. As a result, the applicability of statutory obligations to submit DAPs and the agency's current thinking on best practices for clinical development remain unclear and we will need to carefully navigate such uncertainty.

In addition, the regulatory landscape related to clinical trials in the European Union recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

***We have conducted and intend to conduct certain of our clinical trials globally. However, there are additional risks unique to conducting trials outside of the U.S., and the FDA and other foreign equivalents may not accept data from such trials, in which case our development plans may be delayed, which could materially harm our business.***

We have conducted and intend to continue conducting certain of our clinical trials globally. The acceptance by the FDA or other regulatory authorities of data from clinical trials conducted outside their jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

In addition, even where foreign clinical trial data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the clinical trial is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the trial through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it could result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;

- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

***Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.***

Undesirable effects caused by, or other undesirable properties of, Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired, or competing commercial products or product candidates in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay, denial or withdrawal of marketing approval by the FDA or other regulatory authorities, and could lead to potential product liability claims. In addition, results of our clinical trials could reveal a high frequency of undesirable effects or unexpected characteristics. For example, in March 2022, we received the CRL from the FDA for our NDA for Vafseo in which the FDA concluded that the data in the NDA did not support a favorable benefit-risk assessment of Vafseo for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. As a result, we filed the FDRR and, following the FDRR, we filed a resubmission to our NDA, and the FDA approved Vafseo on March 27, 2024. However, the approved indication is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months.

If we or others identify undesirable effects caused by, or other undesirable properties of, Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired, or if known undesirable effects are more frequent or severe than in the past, or if any of the foregoing are perceived to have occurred, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our product candidates may not be approved by regulatory authorities;
- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- regulatory authorities may require warnings on the label, such as the warning on Auryxia's label regarding iron overload or the boxed warning on Vafseo's label regarding increased risk of death, myocardial infarction, stroke, venous thromboembolism and thrombosis of vascular access;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies may be required;
- we may decide to, or be required to, send drug warnings or safety alerts to physicians, pharmacists and hospitals (or the FDA or other regulatory authorities may choose to issue such alerts), or we may decide to conduct a product recall or be requested to do so by the FDA or other regulatory authority;
- reformulation of the product, additional non-clinical or clinical trials, restrictive changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of a product within its indicated populations, or studying the product or product candidate in additional indications and populations or in new formulations; and
- we could be investigated by the government or sued and held liable for harm caused to patients, including in class action lawsuits; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining, whether on a restricted basis or at all, marketing approval and, ultimately, market acceptance or penetration of Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired. In addition, any of these events could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, Vafseo or any other product and product candidate, including those that may be in-licensed or acquired, and generate product revenue.

The patient populations treated with Auryxia and the projected patient populations that will be treated with Vafseo have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke and, in its most severe form, results in, kidney failure and the need for dialysis or kidney transplant. Many patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these patients having adverse events, including serious adverse events is high.

With respect to the global $INNO_2VATE$ Phase 3 program, the incidence of treatment emergent adverse events, or TEAEs, during the Correction and Conversion study in Vafseo-treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common TEAEs reported in Vafseo/darbepoetin alfa treated patients were hypertension

(16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious TEAEs were lower in Vafseo-treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of TEAEs during the prevalent dialysis patient study (Conversion) in the Vafseo-treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common TEAEs reported in Vafseo/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious TEAEs were slightly lower for Vafseo-treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 — 1.50) driven by thrombosis of vascular access.

With respect to the global $PRO_2TECT$ Phase 3 program, the incidence of TEAEs during the ESA untreated patients study (Correction) in the Vafseo-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common TEAEs reported in Vafseo/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious TEAEs were 65.3% for Vafseo-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of TEAEs during the ESA-treated patients study (Conversion) in Vafseo-treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common TEAEs reported in Vafseo/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious TEAEs were 58.5% for Vafseo-treated patients and 56.6% for darbepoetin alfa-treated patients.

During the conduct of our Phase 3 program for Vafseo, our team and hepatic experts analyzed hepatic cases (unblinded to treatment) and, following the completion of our global Phase 3 clinical program for Vafseo, there was a review of hepatic safety across the Vafseo clinical program, which included eight completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two then-ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review consisted of a blinded re-assessment of hepatic events conducted by a separate panel of hepatic experts. While hepatocellular injury attributed to Vafseo was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future. Additionally, the FDA expressed safety concerns related to the risk of drug-induced liver injury in the CRL that it issued in March 2022, and these safety concerns were addressed following the FDRR and resubmission to our NDA.

Serious adverse events related to Vafseo, including those noted in the CRL and label, and any other product candidates could have material adverse consequences on the development and potential label expansion of Vafseo or the approval of our other product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of Vafseo or our product candidates may change as we gather more information, the FDA may not agree with our assessment of adverse events and additional unexpected adverse events may be observed in future clinical trials or in the market.

Any of the above safety data or other occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia, Vafseo or any other product or product candidate, including those that may be in-licensed or acquired, increase our expenses and impair or prevent our ability to successfully commercialize Auryxia, Vafseo or any other products or product candidates.

In addition, any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia, Vafseo or any other product we acquire or for which we receive marketing approval, within or outside of their current indications or patient populations, which could result in the identification of previously unknown undesirable effects, increased frequency or severity of known undesirable effects, or result in the identification of unexpected safety signals. In addition, Vafseo and any other products are commercialized, they will be used in significantly larger patient populations, in less rigorously controlled environments and, in some cases, by less experienced and less expert treating practitioners, than in clinical trials, which could result in increased or more serious adverse effects being reported. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia, Vafseo or any other products are associated with serious adverse effects, undermining our commercialization efforts.

***Risks Related to Regulatory Approval***

***We may not be able to obtain marketing approval for any label expansion for Vafseo or any current or future product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.***

Clinical trials, manufacturing and marketing of any product or product candidate are subject to extensive and rigorous review and regulation by numerous governmental authorities in the U.S. and other jurisdictions. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through rigorous and extensive preclinical development and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and marketing approval may never be achieved. Of the large number of drugs in development in the U.S. and in other jurisdictions, only a small percentage successfully complete the FDA's and other regulatory jurisdictions'

marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development efforts, we may be unable to successfully obtain regulatory approval for any label expansion for Vafseo or for any product candidate, including those that may be in-licensed or acquired. Further, any product candidate may not receive marketing approval in the U.S. even if it is approved in other countries. Each regulatory authority makes their own assessment as to the safety and efficacy of a drug, and the FDA's concern about the safety or efficacy of any product candidate could impact the regulatory authority's decision in another country.

In March 2022, we received the CRL from the FDA regarding our NDA for vadadustat for the treatment of anemia due to CKD. Following a FDRR in 2022, we filed a resubmission to our NDA in 2023. On March 27, 2024, the FDA approved our NDA for vadadustat under the trade name Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. However, we expended significant additional resources to obtain the approval of Vafseo, the approved indication is limited to the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months and the commercialization of Vafseo was delayed, which had and could continue to have an adverse effect on our business.

Vafseo is currently approved as a treatment for anemia due to CKD for dialysis dependent patients in the U.S., European Union, United Kingdom, Switzerland and Australia. In Japan, Vafseo is approved as a treatment for anemia due to CKD in both dialysis dependent and non-dialysis dependent patients and is marketed and sold by our collaborator MTPC. In Taiwan and South Korea, Vafseo is approved for the treatment of symptomatic anemia due to CKD in adult patients on chronic maintenance dialysis. We are not permitted to market Vafseo in any additional jurisdictions or other indications until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for Vafseo in additional territories or for other indications, we may be required by regulatory authorities to conduct additional preclinical studies or clinical trials. For example, we have several lifecycle management and label expansion opportunities currently under evaluation for Vafseo, one of which is the potential for alternative dosing, and another of which is label expansion for the treatment of adult patients with NDD-CKD. However, we may be required to complete additional clinical trials before seeking approval for additional indications, which are time consuming and expensive, and even though Vafseo is approved as a treatment for anemia due to CKD for dialysis dependent patients, we may not be successful in any of our lifecycle management or label expansion opportunities in the timeframe anticipated by us, or at all. For example, we plan to start a Phase 3 trial in the second half of 2025 to potentially expand the Vafseo label to include the treatment of late-stage NDD-CKD patients, however, we may not successfully demonstrate safety and/or efficacy needed to obtain regulatory approval or we may be unable to complete the trial when anticipated or at all. If we do not obtain the approval of label expansion for the treatment of adult patients with NDD-CKD or for alternative dosing in a timely manner, or at all, it could impact future revenue and have an adverse effect on our business.

Obtaining marketing approval in the U.S. and other jurisdictions for any product candidate depends upon numerous factors, many of which are subject to the substantial discretion of the regulatory authorities, including that regulatory agencies may not complete their review processes in a timely manner and/or, following completion of the review process, may not grant marketing approval or such marketing approval may be limited. Furthermore, approval of a drug does not ensure successful commercialization. For example, on September 23, 2015, the European Commission, or EC, approved Fexeric (ferric citrate coordination complex) for the control of hyperphosphatemia in adult patients with CKD. Pursuant to the sunset clause under EU law, the EC's approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric within three years; although we successfully negotiated an extension to December 23, 2019, we did not commence marketing Fexeric by such date and therefore the Fexeric approval in the EU has ceased to be valid. In April 2024, our partner Averoa submitted its marketing authorization application for ferric citrate in Europe and the application is still under review.

Safety concerns with a given product may impact marketing approval. For example, safety concerns associated with the current standard of care for the indications for Vafseo may affect the FDA's or other regulatory authorities' review of the safety results of Vafseo. In addition, these regulatory authorities may not agree with our assessment of adverse events. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that our product candidates will never obtain marketing approval in the U.S. or certain other jurisdictions or for some or all of the indications for which we seek approval.

The FDA or other regulatory authorities may delay, limit or deny approval of any product candidate for many reasons including, among others:

- the results of our clinical trials may only be modestly positive, or there may be concerns with the profile due to efficacy or safety;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the relevant regulatory authority for review and/or marketing approval;

- the relevant regulatory authority may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the relevant regulatory authority may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the relevant regulatory authority may not approve the label expansion we request for Vafseo;
- the relevant regulatory authority may approve any product candidate for use only in a small patient population or for fewer or more limited indications than we request;
- the relevant regulatory authority may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA or other relevant regulatory authority may require development of a REMS as a condition of approval or post-approval;
- the relevant regulatory authority may grant approval contingent on the performance of costly post-marketing clinical trials;
- the relevant regulatory authority's onsite inspections may be delayed;
- we, or our CROs or other vendors, may fail to comply with GxP or fail to pass any regulatory inspections or audits;
- we or our third-party manufacturers may fail to perform in accordance with the FDA's or other relevant regulatory authority's cGMP requirements and guidance;
- the relevant regulatory authority could deem that our financial relationships with certain principal investigators constitute a conflict of interest, such that the data from those principal investigators may not be used to support our applications;
- as part of any future regulatory process, the FDA may ask an Advisory Committee to review portions of the NDA, the FDA may have difficulty scheduling an Advisory Committee meeting in a timely manner or, if convened, an FDA Advisory Committee could recommend non-approval, conditions of approval or restrictions on approval, and the FDA may ultimately agree with the recommendations;
- the relevant regulatory authority's review process and decision-making regarding any product candidate may be impacted by the results of our and our competitors' clinical trials and safety concerns of marketed products used to treat the same indications as the indications for which Vafseo and any other product candidate are being developed;
- the relevant regulatory authority may not approve the manufacturing processes or facilities of third-party manufacturers with whom we contract; or
- the policies or regulations of the relevant regulatory authority may significantly change in a manner that renders our clinical data insufficient for approval or requires us to amend or submit new clinical protocols.

Moreover, principal investigators for our future clinical trials may serve as scientific advisors or consultants to us and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or a comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition, we could be adversely affected by several significant administrative law cases decided by the U.S. Supreme Court in 2024. In Loper Bright Enterprises v. Raimondo, for example, the court overruled Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U.S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act, or the APA. Additionally, in Corner Post, Inc. v. Board of Governors of the Federal Reserve System, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, Securities and Exchange Commission v. Jarkesy, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations.

Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U.S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the U.S. District Court for the Northern District of Texas challenging the FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation.

Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA, CMS and other government agencies with jurisdiction over our products and product candidates. Any change in regulations or policies at FDA, CMS or other government agencies could adversely affect our products and product candidates, including the regulatory process or the pricing or reimbursement of our products or product candidates. In addition, the FDA, CMS and other government agencies recently experienced reductions in workforce and could experience additional such actions. Any disruptions at those agencies or uncertainty from any regulatory changes that affect the development or commercialization of our products and product candidates could present new challenges as we navigate the clinical development and approval process for our product candidates and could have an adverse effect on the commercialization of our products.

***If we are unable to obtain or maintain marketing approval in jurisdictions outside the United States, we and our partners will not be able to market any product or product candidates outside of the United States.***

In order to market and sell our product candidates in the European Union, Japan and many other jurisdictions, we or our partners must obtain or maintain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain or maintain approval may differ substantially from that required to obtain or maintain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining or maintaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We and our partners may not obtain or maintain approvals from regulatory authorities outside the United States on a timely basis or at all.

Additionally, we and our partners could face heightened risks with respect to obtaining or maintaining marketing authorizations in the UK as a result of the withdrawal of the UK from the EU, commonly referred to as Brexit. The UK is no longer part of the European Single Market and EU Customs Union. As of January 1, 2025, the Medicines and Healthcare Products Regulatory Agency, or MHRA, is responsible for approving all medicinal products destined for the United Kingdom market (i.e., Great Britain and Northern Ireland). At the same time, a new international recognition procedure, or IRP, will apply, which intends to facilitate approval of pharmaceutical products in the UK. The IRP is open to applicants that have already received an authorization for the same product from one of the MHRA's specified Reference Regulators, or RRs. The RRs notably include EMA and regulators in the EEA member states for approvals in the EU centralized procedure and mutual recognition procedure as well as the FDA (for product approvals granted in the U.S.). However, the concrete functioning of the IRP is currently unclear. Any delay in obtaining, maintaining or an inability to obtain or maintain, any marketing approvals may force us or our partners to restrict or delay efforts to seek regulatory approval in the UK for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

***Products approved for marketing are subject to extensive post-marketing regulatory requirements, including post-approval pediatric studies for Auryxia and Vafseo, and could be subject to post-marketing restrictions or withdrawal from the***

***market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if approved.***

Marketing approvals may be subject to limitations on the approved indicated uses for which the product may be marketed, other conditions of approval, or contain requirements or commitments for potentially costly post-marketing studies and surveillance to monitor the safety and efficacy of the product, including REMS, or registries or observational studies. For example, in connection with the FDA approvals of Auryxia and Vafseo, we committed to the FDA to conduct certain post-approval pediatric studies of Auryxia and Vafseo under the Pediatric Research Equity Act of 2003, or PREA. Under PREA, an NDA or supplement to an NDA for certain drug products must contain data to assess the safety and effectiveness of the drug product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. With regard to the Hyperphosphatemia Indication for Auryxia, we initially committed to completing the original post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. However, we did not complete the study according to the original schedule and therefore did not submit the required final report by December 31, 2019. Consequently, we received a notification of noncompliance with PREA. We have since been released from the original post marketing requirement, or PMR, and a new PMR was issued that provided that the final report was due in April 2024. In June 2023 we requested an extension of time for the submission of the final report and such request was denied by the FDA in August 2023. The PMR trial is ongoing and actively recruiting patients, but the final report for the trial was due in April 2024, so the trial is considered delayed. With regard to Auryxia for the treatment of IDA in adult NDD-CKD patients, or IDA Indication, we initially committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023. We did not meet a required milestone relating to this post-approval pediatric study of Auryxia in a timely manner and received a notification from the FDA. Subsequently, the FDA agreed to extend the pediatric clinical trial timelines for the IDA Indication and required that the final report be submitted in August 2024. We subsequently communicated to the FDA that we would be delaying the start of the clinical trial in the IDA Indication while we work to produce smaller size tablets. In response, the FDA issued a partial clinical hold until we manufacture the smaller tablets and provide the FDA with relevant information regarding the smaller sized tablets for review. The FDA lifted the partial clinical hold in June 2022, and we continued to conduct feasibility, however, we have not commenced start-up of this study. In February 2024, we requested an extension for the submission of the final report and such request was denied by the FDA in April 2024. In October 2024, we received a letter from the FDA regarding our non-compliance with PREA due to our failure to complete the IDA post-approval pediatric study, and we submitted our response, including a proposal to waive the PMR with regard to the IDA Indication, to the FDA on November 1, 2024. If the FDA denies our waiver of the PMR with regard to the IDA Indication, or we are unable to complete these studies successfully or have further delays in completing these studies, we will need to inform the FDA, have further discussions and, if the FDA finds that we failed to comply with pediatric study requirements, in violation of applicable law, it could institute enforcement proceedings to seize or enjoin the sale of Auryxia, seek civil penalties or other adverse consequences, which would have a material adverse impact on our ability to commercialize Auryxia and our ability to generate revenues from Auryxia.

In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for Auryxia, Vafseo and any other product for which we receive regulatory approval will be subject to extensive and ongoing regulatory requirements and guidance. These requirements and guidance include manufacturing processes and procedures (including record keeping), the implementation and operation of quality systems to control and assure the quality of the product, submissions of safety and other post-marketing information and reports, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. If we, our contract manufacturing organizations, or CMOs, or other third parties we engage fail to adhere to such regulatory requirements and guidance, we could suffer significant consequences, including product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, loss of customer confidence, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs, and our development or commercialization efforts may be materially harmed.

Post-approval discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, use or manufacturing of the product;
- withdrawal of the product from the market, or product recalls;
- restrictions on the labeling or marketing of a product;
- fines, restitution or disgorgement of profits or revenues;

- warning or untitled letters or clinical holds;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- REMS; and
- injunctions or the imposition of civil or criminal penalties.

For example, we previously had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future related to Auryxia or Vafseo could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia in the U.S. and Vafseo in the U.S., Japan, Europe or in other countries, for commercial and clinical use.

Non-compliance with the FDA, the EMA, the PMDA and other regulatory authorities' requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

The FDA's policies and those of other regulatory authorities may change, and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulations that may arise from future legislation or administrative action, either in the U.S. or in other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially adversely affect our business.

***Risks Related to Governmental Regulation and Compliance***

***We are subject to complex regulatory schemes that require significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.***

In general, a variety of laws apply to us or may otherwise restrict our activities, including the following:

- laws and regulations governing the conduct of preclinical studies and clinical trials in the U.S. and other countries in which we are conducting such studies;
- anti-corruption and anti-bribery laws, including the FCPA, the UK Bribery Act and various other anti-corruption laws in countries outside of the U.S.;
- data privacy laws existing in the U.S., the EU, the UK and other countries in which we operate, including the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, as amended by the California Privacy Rights Act of 2020, or CPRA, as well as other state consumer protection laws, GDPR, any additional applicable EU member state, or EU Member State, data protection laws in force from time to time, the retained EU law version of the General Data Protection Regulation as saved into United Kingdom law by virtue of section 3 of the United Kingdom's European Union (Withdrawal) Act 2018;
- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws;
- environmental, health and safety laws and regulations; and
- international trade laws, which are laws that regulate the sale, purchase, import, export, re-export, transfer and shipment of goods, products, materials, services and technology.

In addition, our relationships with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse laws that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and Vafseo and any other products for which we may obtain marketing approval. As such, these arrangements are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations at federal, state and international levels. These restrictions include, but are not limited to, the following:

- the Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, which among other things, strictly regulates drug product marketing and promotion and prohibits manufacturers from marketing such products for off-label use;

- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs, and laws requiring notification of price increases;
- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, and violations of the FDCA, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the HITECH, and their respective implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Open Payments Act (the former Physician Payments Sunshine Act) requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous state laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by state Medicaid or other programs, or non-governmental third party payors, including private insurers, and which are not preempted by federal laws and often differ from state to state, thus complicating compliance efforts; and
- U.S. state laws restricting interactions with healthcare providers and other members of the healthcare community or requiring pharmaceutical manufacturers to implement certain compliance standards, which vary from state to state.

Because of the breadth of these U.S. laws, and their non-U.S. equivalents, and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reforms have strengthened these laws. For example, the Health Care Reform Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate the law. The Health Care Reform Act also amended the False Claims Act, such that violations of the Anti-Kickback Statute are now deemed violations of the False Claims Act.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals. Additionally, some state and local laws require the registration and specific training of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Efforts to ensure that our business complies with applicable healthcare laws and regulations involves substantial costs and requires us to expend significant resources. One of the potential areas for governmental scrutiny involves federal and state requirements for pharmaceutical manufacturers to submit accurate price reports to the government. Because our processes for calculating applicable government prices and the judgments involved in making these calculations involve subjective decisions and complex methodologies, these calculations are subject to risk of errors and differing interpretations. In addition, they are subject to review and challenge by the applicable governmental agencies, or potential qui tam complaints, and it is possible that such reviews could result in changes, recalculations, or defense costs that may have adverse legal or financial consequences. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could materially adversely affect our business and would result in increased

costs and diversion of management attention and could negatively impact the development, regulatory approval and commercialization of Auryxia or Vafseo, any of which could have a material adverse effect on our business. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

***We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia, Vafseo or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.***

Physicians are permitted to prescribe drug products for uses that differ from those approved by the FDA or other applicable regulatory agencies. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict manufacturer communications regarding unapproved uses of an approved drug. Companies are not permitted to promote drugs for unapproved uses or in a manner that is inconsistent with the FDA-approved labeling. There are also restrictions about making comparative or superiority claims based on safety or efficacy that are not supported by substantial evidence. Accordingly, we may not promote Auryxia in the U.S. for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia or Vafseo, as applicable.

Promoting a drug off-label is a violation of the FDCA and can give rise to liability under the federal False Claims Act, as well as under additional federal and state laws and insurance statutes. The FDA, the Department of Justice and other regulatory and enforcement authorities enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained, as well as the false advertising or misleading promotion of drugs. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. In addition, laws and regulations govern the distribution and tracing of prescription drugs and prescription drug samples, including the Prescription Drug Marketing Act of 1976 and the Drug Supply Chain Security Act, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. A company that is found to have improperly promoted off-label uses or to have otherwise engaged in false or misleading promotion or improper distribution of drugs will be subject to significant liability, potentially including civil and administrative remedies as well as criminal sanctions. It may also be subject to exclusion and debarment from federal healthcare reimbursement programs.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in January 2025, the FDA published final guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This final guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Securities Exchange Act of 1934, as amended, or the Exchange Act, signed into law as part of the Consolidated Appropriations Act of 2023, or the Consolidated Appropriations Act, companies may also provide information that is consistent with a product's FDA approved-labeling and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We intend to engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program and processes designed to ensure that all such activities are performed in a legal and compliant manner, such program and processes may not be sufficient to deter or detect all violations, and we will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In addition, if a company's activities are determined to have violated the federal Anti-Kickback Statute, this can also give rise to liability under the federal False Claims Act and such violations can result in significant fines, criminal and civil remedies, and exclusion from Medicare and Medicaid. There is increased government focus on relationships between the pharmaceutical industry and physicians, pharmacies (especially specialty pharmacies), and other sources of referrals. Common industry activities, such as speaker programs, insurance assistance and support, relationships with foundations providing copayment assistance, and relationships with patient organizations and patients are receiving increased governmental attention. If any of our relationships or activities is determined to violate applicable federal and state anti-kickback laws, false claims laws, or other laws or regulations, the company and/or company executives, employees, and other representatives could be subject to significant fines and criminal sanctions, imprisonment, and potential exclusion from Medicare and Medicaid, and could harm our reputation or result in significant legal expenses and distraction of management.

***Policy changes or disruptions at the FDA, regulatory authorities outside the U.S., CMS and other government agencies caused by funding shortages, global health concerns or other events could prevent products, product candidates and services from being developed or commercialized in a timely manner, with expected terms or at all, which could negatively impact our business.***

The ability of the FDA and regulatory authorities outside the U.S. to review and approve products and product candidates can be affected by a variety of factors, including government budget and funding levels, staffing shortages, statutory, regulatory, and policy changes, global health concerns and other events that may otherwise affect the FDA's or other regulatory authorities' ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result of certain of these factors. In addition, government funding of other government agencies that fund R&D activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may increase the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our, or our collaboration partners', regulatory submissions, which could have a material adverse effect on our business.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA, CMS and other government agencies with jurisdiction over our products and product candidates. Any change in regulations or policies at FDA, CMS or other government agencies could adversely affect our products and product candidates, including the regulatory process or the pricing or reimbursement of our products or product candidates. In addition, the FDA, CMS and other government agencies recently experienced reductions in workforce and could experience additional such actions. Any disruptions at those agencies or uncertainty from any regulatory changes that affect the development or commercialization of our products and product candidates could present new challenges as we navigate the clinical development and approval process for our product candidates and could have an adverse effect on the commercialization of our products. These and other actions by the new administration could impact our business as a regulated entity and as a biopharmaceutical company, and we cannot anticipate in what ways and the magnitude of the impacts.

***Compliance with privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.***

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which took effect across all member states of the EEA, in May 2018. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data when required, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, when required, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third party processors. The GDPR increases our obligations as a sponsor in clinical trials in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial patients and investigators. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of the total worldwide annual turnover of a group of companies from the preceding financial year or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU Member States may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data and permits EU Member States to adopt further penalties for violations that are not subject to the administrative fines outlined in the GDPR.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S. and, as a result, increases the scrutiny that we should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the U.S. There is ongoing uncertainty about the transfer

mechanisms that companies rely upon to enable the legal transfer of personal data from the EU to other countries. For example, in July 2020, the Court of Justice of the European Union invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. Although a new Data Privacy Framework has been adopted, as court decisions and regulatory guidance evolves, challenges remain with respect to GDPR compliance. Companies must continue to monitor the regulatory landscape and implement necessary changes, all of which may be costly and may put the company out of compliance while any changes are being implemented.

Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. In relation to data transfers, both the UK and the EU have determined, through separate "adequacy" decisions, that data transfers between the two jurisdictions are in compliance with the UK Data Protection Act and the GDPR, respectively. The UK and the U.S. have also agreed to a U.S.-UK "Data Bridge", which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the UK to the U.S. In addition to the UK, Switzerland has approved an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the U.S.). Any changes or updates to these developments have the potential to impact our business.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which serves as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the EC adopted the adequacy decision on July 10, 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the U.S. However, some privacy advocacy groups have challenged or suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business internationally.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the U.S. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns. The Federal Trade Commission, or the FTC, and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC's evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

Laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, and the CPRA, which amends CCPA by expanding the scope and applicability, while also introducing new privacy protections, is creating similar risks and obligations as those created by GDPR. In November 2020, California voters passed a ballot initiative for the CPRA, which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also creates a new agency that is specifically responsible for enforcing the new law and other California privacy laws. Because of this, we may need to engage in additional activities (e.g., data mapping) to identify the personal information we are collecting and the purposes for which such information is collected. In addition, we will need

to ensure that our policies recognize the rights granted to consumers (as that phrase is broadly defined in the CCPA and can include business contact information).

In addition to California, at least eighteen other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Plaintiffs' lawyers are also increasingly using privacy-related statutes at both the state and federal level to bring lawsuits against companies for their data-related practices. In particular, there have been a significant number of cases filed against companies for their use of pixels and other web trackers. These cases often allege violations of the California Invasion of Privacy Act and other state laws regulating wiretapping, as well as the federal Video Privacy Protection Act. The rise in these types of lawsuits creates potential risk for our business.

If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In recent months, the Officer of Civil Rights, or OCR, has been especially active in enforcing the HIPAA rules. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. Additionally, OCR is looking to amend the HIPAA Security Rule, which (if and when finalized) could create additional compliance obligations and risk for our business.

There are also increased restrictions at the federal level relating to transferring sensitive data outside of the U.S. to certain foreign countries. For example, in 2024, Congress passed H.B. 815, which included the Protecting Americans' Data from Foreign Adversaries Act of 2024. This law creates certain restrictions for entities that disclose sensitive data (including potential health data) to countries such as China. Failure to comply with these rules can lead to a potential FTC enforcement action. Additionally, the Department of Justice recently finalized a rule implementing Executive Order 14117, which creates similar restrictions related to the transfer of sensitive US data to countries such as China. These data transfer restrictions (and others that may pass in the future) may create operational challenges and legal risks for our business.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities, and could lead to government enforcement actions, private litigation and significant fines and penalties against us, all of which could increase our cost of doing business and have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Further, we cannot assure you that our third-party service providers with access to our or our customers', suppliers', trial patients' and employees' personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, storage and transmission of such information.

***Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the U.S. or foreign jurisdictions.***

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of any product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and Vafseo. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any FDA approved product, such as Auryxia or Vafseo or any reimbursement that physicians receive for administering any approved product.

In the U.S. the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for Auryxia and any other approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA. In addition, other legislative and regulatory changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031.

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriations Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

The American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, other legislative and regulatory changes have been proposed, but not yet adopted. For example, in July 2019, HHS proposed regulatory changes in kidney health policy and reimbursement. Any new legislative or regulatory changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for Auryxia or Vafseo or the frequency with which Auryxia and Vafseo is prescribed or used.

The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the U.S. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

In addition, in October 2020, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the U.S. That regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Seven states (Colorado, Florida, Maine, New Hampshire, New Mexico, Texas and Vermont) have passed laws allowing for the importation of drugs from Canada. North Dakota and Virginia have passed legislation establishing workgroups to examine the impact of a state importation program. As of May 2024, five states (Colorado, Florida, Maine, New Hampshire and New Mexico) have submitted Section 804 Importation Program proposals to the FDA. Vermont has submitted a concept letter to HHS. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation. Florida now has authority to import certain drugs from Canada for a period of two years once certain conditions are met. Florida will first need to submit a pre-import request for each drug selected for importation, which must be approved by the FDA. The state will also need to relabel the drugs and perform quality testing of the products to meet FDA standards.

As an oral drug, Auryxia was covered by Medicare under Part D until January 1, 2025. In January 2011, CMS implemented the ESRD PPS, a prospective payment system for dialysis treatment. Under the ESRD PPS, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home.

As of January 2025, oral ESRD-related drugs without injectable or intravenous equivalents, including Auryxia and all other phosphate lowering medications, are included in the ESRD bundle and separate Medicare payment for these drugs are no longer available, but ESRD facilities will receive a TDAPA for Auryxia for a period of at least two years starting on January 1, 2025. Vafseo, which we began selling in January 2025, is also included in the ESRD bundle and ESRD facilities will receive a TDAPA for Vafseo as a new renal dialysis drug meeting certain criteria for a period of at least two years starting on January 1, 2025. The TDAPA provides separate payment based on the drug's ASP that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. If the TDAPA reimbursement amount for Auryxia or Vafseo is lower than anticipated, or if TDAPA is eliminated, it would have an adverse impact on our revenue. Additionally, in the post-TDAPA period, CMS currently expects to increase the single bundled payment base rate paid to the dialysis facility for each dialysis treatment to reflect that bundled drugs will be reimbursed as part of the single bundled payment for Medicare patients. However, there can be no assurances that any increase in the single bundled payment base rate will be sufficient to adequately reimburse the dialysis facilities for Auryxia or Vafseo at a price that allows us to continue to sell Auryxia or Vafseo at a profit.

In July 2024, Ardelyx filed a complaint in the United States District Court for the District of Columbia against HHS, CMS and other parties, which alleged that CMS's plan to include oral-only phosphate lowering therapies in the ESRD PPS violated its statutory and regulatory authority under the Medicare Improvements for Patients and Providers Act, which established the ESRD PPS bundled payment system for dialysis services. In October 2024, Ardelyx filed a motion for a preliminary injunction to enjoin CMS from including oral-only phosphate lowering therapies in the ESRD PPS. CMS had earlier filed a motion to dismiss the complaint on jurisdictional grounds. On November 8, 2024, the district court denied Ardelyx's motion for a preliminary injunction and it granted the government's motion to dismiss. Thereafter, Ardelyx moved for reconsideration, but the district court also denied that request. On December 26, 2024, Ardelyx filed a notice of appeal with the US Court of Appeals for the DC Circuit. If Ardelyx is successful in its claims, oral-only phosphate lowering therapies, including Auryxia, may be removed from the ESRD bundle, which could reduce anticipated revenue for Auryxia.

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. We consider many factors when we implement a price increase for a product, including historical and potential future inflation rates. However, there are many variables that are outside of our control and if we increase the price of Auryxia or Vafseo faster than the pace of inflation, we would be subject to additional rebates under Medicare, which could have a material adverse effect on our product revenues.

With respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. On August 15, 2024, HHS published the results of the first Medicare drug price negotiations for ten selected drugs that treat a range of conditions, including diabetes, CKD and rheumatoid arthritis. The prices of these ten drugs will become effective January 1, 2026. Subsequently, on January 17, 2025, HHS announced its selection of 15 additional drugs covered by Part D for the second cycle of negotiations. This second cycle of negotiations with participating drug companies will occur during 2025, and any negotiated prices for this second set of drugs will be effective starting January 1, 2027. CMS issued a public statement on January 29, 2025, declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The law also caps Medicare out-of-pocket drug costs at an estimated $2,000.

On June 6, 2023, Merck & Co. Inc. filed a lawsuit against HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the

Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against HHS and CMS. There have been various decisions by the courts considering these cases since they were filed. The HHS has generally won the substantive disputes in these cases, and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry. Certain of these cases are now on appeal and, on October 30, 2024, the Court of Appeals for the Third Circuit heard oral argument in three of these cases. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products or put pressure on our product pricing.

It is likely that federal and state legislatures within the U.S. and foreign governments will continue to consider changes to existing healthcare legislation. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Auryxia or Vafseo and any product candidates for which we receive marketing approval or additional pricing pressures. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for Auryxia, Vafseo and any product candidates for which we receive marketing approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain and maintain coverage and reimbursement approval for Auryxia, Vafseo or any other approved product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

In addition, in some countries, including EU Member States, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced EU Member States, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product and/or our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product and/or product candidates could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

***Our reporting and payment obligations under the Medicaid Drug Rebate Program, Medicare and other governmental drug pricing programs are complex and may involve subjective decisions. Any failure to properly comply with those obligations could subject us to penalties and sanctions.***

As a condition of reimbursement by various federal and state health insurance programs, we are required to calculate and report certain pricing information to federal and state agencies. The regulations governing the calculations, price reporting and payment obligations are complex and subject to interpretation by various government and regulatory agencies, as well as

the courts. Reasonable assumptions have been made where there is lack of regulations or clear guidance and such assumptions involve subjective decisions and estimates. We are required to report any revisions to our calculation, price reporting and payment obligations previously reported or paid. Such revisions could affect our liability to federal and state payors and also adversely impact our reported financial results of operations in the period of such restatement. Further, a number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers for the untimely, inaccurate, or incomplete reporting of drug pricing information or for otherwise failing to comply with drug price transparency requirements. If we are found to have violated state law requirements, we may become subject to significant penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Uncertainty exists as new laws, regulations, judicial decisions, or new interpretations of existing laws, or regulations related to our calculations, price reporting or payments obligations increases the chances of a legal challenge, restatement or investigation. If we become subject to investigations, restatements, or other inquiries concerning our compliance with price reporting laws and regulations, we could be required to pay or be subject to additional reimbursements, penalties, sanctions or fines, which could have a material adverse effect on our business, financial condition and results of operations. In addition, it is possible that future healthcare reform measures could be adopted, which could result in changes to how we calculate or report certain pricing information to federal and state agencies, or increased pressure on pricing and reimbursement of our products and thus have an adverse impact on our financial position or business operations.

Further, state Medicaid programs may be slow to invoice pharmaceutical companies for calculated rebates resulting in a lag between the time a sale is recorded and the time the rebate is paid. This results in us having to carry a liability on our consolidated balance sheet for the estimate of rebate claims expected for Medicaid patients. If actual claims are higher than current estimates, our financial position and results of operations could be adversely affected.

In addition to retroactive rebates and the potential for 340B Program refunds, if we are found to have knowingly submitted any false price information related to the Medicaid Drug Rebate Program to CMS, we may be liable for civil monetary penalties. Such failure could also be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program. In the event that CMS terminates our rebate agreement, federal payments may not be available under government programs, including Medicaid or Medicare Part B, for our covered outpatient drugs.

Additionally, if we overcharge the government in connection with the Federal Supply Schedule pricing program or Tricare Retail Pharmacy Program, whether due to a misstated Federal Ceiling Price or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the FDCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our collaborators are also subject to similar requirements outside of the U.S. and thus the attendant risks and uncertainties. If our collaborators suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material and adverse impact on our revenues.

***With the passage of the CREATES Act, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs, 505(b)(2) NDAs and biosimilar product applications.***

In December 2019, President Trump signed legislation intended to facilitate the development of generic and biosimilar products. The bill, previously known as the CREATES Act, authorizes sponsors of ANDAs, 505(b)(2) NDAs or biosimilar product applications to file lawsuits against companies holding NDAs or BLAs that decline to provide sufficient quantities of an approved reference drug or biological product on commercially reasonable, market-based terms. Drug or biological products on FDA's drug shortage list are exempt from these new provisions unless the product has been on the list for more than six continuous months or the FDA determines that the supply of the product will help alleviate or prevent a shortage.

To bring an action under the statute, the developer of a product candidate that seeks to develop the product and seek approval under an ANDA, 505(b)(2) NDA, or biosimilar product application must take certain steps to request the reference product from the reference product manufacturer, which, in the case of products covered by a REMS with elements to assure safe use, include obtaining authorization from the FDA for the acquisition of the reference product. If the reference product manufacturer does not provide the reference product and the ANDA, 505(b)(2) NDA, or biosimilar product sponsor does bring an action for failure to provide a reference product, there are certain affirmative defenses available to the reference product manufacturer, which must be shown by a preponderance of evidence, including that the NDA or BLA holder sells the

reference product through agents, distributors, or wholesalers and has placed no restrictions, explicit or implicit, on selling the reference product to ANDA, 505(b)(2) or biosimilar sponsors. If the sponsor prevails in litigation, it is entitled to a court order directing the reference product manufacturer to provide, without delay, sufficient quantities of the applicable product on commercially reasonable, market-based terms, plus reasonable attorney fees and costs.

Additionally, the new statutory provisions authorize a federal court to award the product developer an amount "sufficient to deter" the reference product manufacturer from refusing to provide sufficient product quantities on commercially reasonable, market-based terms, up to a certain maximum amount based on revenue earned while in noncompliance, if the court finds, by a preponderance of the evidence, that the reference product manufacturer did not have a legitimate business justification to delay providing the product or failed to comply with the court's order. For the purposes of the statute, the term "commercially reasonable, market-based terms" is defined as (1) the nondiscriminatory price at or below the most recent wholesale acquisition cost for the product, (2) a delivery schedule that meets the statutorily defined timetable, and (3) no additional conditions on the sale.

Although we intend to comply fully with the terms of these statutory provisions, we are still exposed to potential litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of ANDAs, 505(b)(2) NDA applications or biosimilar product applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. The CREATES Act may facilitate future competition with Auryxia or Vafseo and any of our product candidates, if approved, which could impact our ability to maximize product revenue.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the use and disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by our employees, contractors or consultants, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***Risks Related to our Reliance on Third Parties***

***We depend on collaborations with third parties for the development and commercialization of Auryxia, including an authorized generic version of Auryxia, Riona and Vafseo and, if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona and Vafseo, and our business could be materially harmed.***

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We also entered into a collaboration agreement with MTPC to develop and commercialize Vafseo in Japan and certain other Asian countries. In addition, we granted to Averoa an exclusive license to develop and commercialize ferric citrate in the Averoa Territory. Furthermore, we granted Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in the Medice Territory. We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our and our partners' commercialization efforts with respect to Auryxia, Riona, Vafseo and any other product candidates. We may not be able to maintain our collaborations for development and commercialization. For example, on May 13, 2022, Otsuka Pharmaceutical Co. Ltd., or Otsuka, elected to terminate our collaboration agreements with them, and we subsequently negotiated a Termination and Settlement Agreement with Otsuka. This termination by Otsuka may have delayed the launch of Vafseo in Europe or other territories previously licensed to Otsuka or adversely affected how we are perceived in scientific and financial communities. For example, in August 2023, Medice informed us that their launch of Vafseo in certain countries in the Medice Territory was going to be later than previously anticipated due to the activities required to enable the launch. If we are unable to maintain our

collaborations, we may not be able to capitalize on the market potential of our products or product candidates, and our business could be materially harmed.

In February 2025, in advance of the potential market entry of generic competition to our branded Auryxia on or after March 20, 2025, we entered into an Authorized Generic Distribution and Supply Agreement with our AG Partner, pursuant to which, on or after March 20, 2025, our AG Partner will sell an authorized generic version of Auryxia. We will be relying on our AG Partner for the commercialization of this authorized generic. If competition, including from generics other than our AG Partner, capture sales or if generics are sold at a greater discount to Auryxia's price than anticipated, it could materially and adversely affect our expected revenues. In addition, we are responsible for supplying product to our AG Partner, and if there are problems in the supply chain, we could be subject to certain penalties, which could be substantial.

In addition, our current and any future collaborations may not be successful due to a number of important factors, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborations may be terminated in accordance with the terms of the collaboration agreements and, if terminated, may make it difficult for us to attract new collaborators or adversely affect how we are perceived in scientific and financial communities, and may result in a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates;
- if permitted by the terms of the collaboration agreements, collaborators may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus, availability of funding or other external factors such as a business combination that diverts resources or creates competing priorities;
- if permitted by the terms of the collaboration agreements, collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to our products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration agreements, we and our collaborator may have a difference of opinion regarding the development or commercialization strategy for a particular product or product candidate, and our collaborator may have ultimate decision making authority;
- disputes may arise between a collaborator and us that cause the delay or termination of activities related to research, development, supply or commercialization of Auryxia, Riona or Vafseo and any other product candidate, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may not lead to development or commercialization of products and product candidates, if approved, in the most efficient manner or at all;
- inefficiencies or structural changes in internal operations or processes of our collaborators may lead to increased expenses associated with commercializing a product, including manufacturing costs, rebates, product returns and other adjustments which would negatively impact net product revenue;
- a significant change in the senior management team, a change in the financial condition or a change in the business operations, including a change in control or internal corporate restructuring, of any of our collaborators, could result in delayed timelines, re-prioritization of our programs, decreasing resources or funding allocated to support our programs, or termination of the collaborations; and
- collaborators may not comply with all applicable regulatory and legal requirements.

If any of these events occur, the market potential of Auryxia, including our authorized generic, Riona or Vafseo, where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. Collaborations may also divert resources, including the attention of management and other employees, from other parts of our business, which could have an adverse effect on other parts of our business, and we cannot be certain that the benefits of the collaboration will outweigh the potential risks.

***We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.***

We may decide to enter into additional collaborations for the development and commercialization of Auryxia, Vafseo or our product candidates both within and outside of the U.S. For example, in May 2023, we entered into the license agreement with Medice, pursuant to which we granted Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in the Medice Territory. Any of these relationships may require us to incur non-recurring and

other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, divert management's attention, or disrupt our business.

We may not be successful in entering into additional collaborations as a result of many factors, including the following:

- competition in seeking appropriate collaborators;
- a reduced number of potential collaborators due to recent business combinations in the pharmaceutical industry;
- an inability to negotiate collaborations on acceptable terms, on a timely basis or at all;
- any international rules, regulations, guidance, laws, risks or uncertainties with respect to potential partners outside of the U.S.;
- a potential collaborator's evaluation of Auryxia, Vafseo or any other product or product candidate may differ substantially from ours;
- a potential collaborator's evaluation of our financial stability and resources;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations in a timely manner, or at all, we may have to delay or curtail the commercialization of Auryxia, Vafseo or the development and potential commercialization of any of our product candidates, reduce or delay our development programs, or increase our expenditures and undertake additional development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop or commercialize Auryxia, Vafseo or our other product candidates. For example, following the termination of our collaboration agreements with Otsuka in 2022, we incurred additional expenses in connection with the development of Vafseo in Europe and other countries.

Even if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, we may not be able to maintain them or they may be unsuccessful, which could delay our timelines or otherwise adversely affect our business.

***Royalties from commercial sales of Vafseo under our MTPC Agreement will likely fluctuate and will impact our rights to receive future payments under our Royalty Agreement with HCR.***

Pursuant to the Royalty Agreement with HCR, we sold to HCR our right to receive the Royalty Interest Payments payable to us under the MTPC Agreement, subject to the Annual Cap and the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, we will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or we pay the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to us, and HCR would have no further right to any Royalty Interest Payments. We received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement.

The royalty revenues under the MTPC Agreement may fluctuate considerably because they depend upon, among other things, the rate of growth of sales of Vafseo in the territory covered by the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate our ability to receive 85% of the Royalty Interest Payments after the Annual Cap is achieved in a given calendar year, or our ability to receive 100% of the Royalty Interest Payments after the Aggregate Cap is achieved.

***We rely upon third parties to conduct all aspects of our product manufacturing and commercial distribution, and in many instances only have a single supplier or distributor, and the loss of these manufacturers or distributors, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.***

We do not have any manufacturing facilities and do not expect to independently manufacture any products or product candidates. We currently rely, and expect to continue to rely, on third party manufacturers to produce all of our commercial, clinical and preclinical supply. We also utilize third parties for the commercial distribution of Auryxia and Vafseo, including wholesale distributors and certain specialty pharmacy providers. Our reliance on third party manufacturers, who have control over the manufacturing process, increases the risk that we will not have or be able to maintain or distribute sufficient quantities of Auryxia, Vafseo or any of our product candidates or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our and our partners' development or commercialization efforts.

We currently rely on single source suppliers for each of Auryxia drug substance and drug product, including our authorized generic, and Vafseo drug substance and drug product, and alternate sources of supply may not be readily available. We have

also engaged Cardinal Health, Inc., as the exclusive third-party logistics distribution agent for commercial sales of Auryxia and Vafseo. If any of the following occurs, we may not have sufficient quantities of Auryxia, Vafseo or our product candidates to support our clinical trials, development, commercialization, or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in maintaining our current supply arrangements for commercial quantities of Auryxia and Vafseo;
- we are unsuccessful in validating new sites;
- our commercial supply arrangements for Auryxia or Vafseo are terminated;
- any of our third party manufacturers are unable to fulfill the terms of their agreements with us due to technical issues, natural disasters or other reasons, including with respect to quality and quantity, or are unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings;
- any of our third party manufacturers breach our supply agreements, do not comply with quality or regulatory requirements and guidance, including cGMP or are subject to regulatory review or ceases their operations for any reason; or
- any of our third party distributors fail to perform or encounter any damage or other disruption at their facilities.

If we, or any of our third party manufacturers or distributors cannot or do not perform as agreed or expected, or any of our customers were to experience further shutdowns, delays or other business disruptions, including as a result of catastrophic events, including pandemics, terrorist attacks, wars or other armed conflicts, geopolitical tensions or natural disasters, if they misappropriate our proprietary information, if they terminate their engagements with us, if we terminate our engagements with them, or if there is a significant disagreement, we may be forced to manufacture or distribute the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers or distributors, which we may not be able to do in a timely manner or on favorable or reasonable terms, if at all. If any of these events occur, especially with respect to one of our sole source suppliers, we may not have sufficient quantities of product for the commercialization of Auryxia and/or Vafseo or may experience delays in the development of our products or product candidates, which could materially and adversely impact our business and results of operation. In addition, if we do not have sufficient quantities of Auryxia, including our authorized generic, or Vafseo to satisfy the requirements of our customer and supply contracts, we may be subject to penalties, which could be substantial. In some cases, there may be a limited number of qualified replacement manufacturers, or the technical skills or equipment required to manufacture a product or product candidate may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party, or a feasible alternative may not exist. These factors would increase our reliance on our current manufacturers or require us to obtain necessary regulatory approvals and licenses in order to have another third party manufacture Auryxia or Vafseo. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays and costs associated with the qualification of a new manufacturer and validation of manufacturing processes would negatively affect our ability to supply clinical trials, obtain and maintain marketing approval, or commercialize or satisfy patient demand for Auryxia and Vafseo, where approved, in a timely manner, within budget, or at all.

In addition, the cost of obtaining Auryxia and Vafseo is subject to adjustment based on our third party manufacturers' costs of obtaining raw materials and producing the product. We have limited control over the production costs of Auryxia and Vafseo, including the costs of raw materials, and have seen increases in the production costs of Auryxia and Vafseo, and any significant increase in the cost of obtaining our products could materially adversely affect our revenue for Auryxia and Vafseo.

Moreover, issues that may arise in any scale-up and technology transfer and continued commercial scale manufacture of our products may lead to significant delays in our development, marketing approval and commercial timelines for new products or affect commercial supply of Auryxia or Vafseo and negatively impact our financial performance. For example, a production-related issue resulted in an interruption in the supply of Auryxia in the third and fourth quarters of 2016. This supply interruption negatively impacted our revenues in 2016. This supply interruption was resolved, and we have taken and continue to take actions designed to prevent future interruptions in the supply of Auryxia. However, we had experienced issues in manufacturing Auryxia, and if we experience manufacturing issues going forward, or incur additional costs, or our actions to prevent future interruptions are not successful, we may experience additional supply issues. In addition, before we can manufacture product at a new site, we must validate the process at that site. If the process validation is unsuccessful, or takes longer than we anticipate, we may have to expend additional resources and could experience a supply interruption. Any future supply interruptions, whether quality or quantity based, for Auryxia or Vafseo where approved, would negatively and materially impact our reputation and financial condition.

There are a limited number of manufacturers that are capable of manufacturing Auryxia and Vafseo for us and complying with cGMP regulations and guidance and other stringent regulatory requirements and guidance enforced by the FDA, EMA, PMDA and other regulatory authorities. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our own quality assurance releases. The facilities and

processes used by our third party manufacturers to manufacture Auryxia and Vafseo may be inspected by the FDA and other regulatory authorities at any time, and the facilities and processes used by our third party manufacturers to manufacture Vafseo will be inspected by the FDA, the EMA and other regulatory authorities prior to or after we submit our marketing applications. Although we have general visibility into the manufacturing processes of our third party manufacturers, we do not ultimately control such manufacturing processes of, and have little control over, our third party manufacturers, including, without limitation, their compliance with cGMP requirements and guidance for the manufacture of certain starting materials, drug substance and finished drug product. Similarly, although we review final production, we have little control over the ability of our third party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Our third party manufacturers may experience problems with their manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics. We may also encounter difficulties relating to our own quality processes and procedures, including regulatory compliance, lot release, quality control and quality assurance, as well as shortages of qualified personnel. If our third party manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements and guidance, or if we or our third party manufacturers experience manufacturing, operations and/or quality issues, including an inability or unwillingness to continue manufacturing our products at all, in accordance with agreed-upon processes or on currently validated manufacturing lines, we may not be able to supply patient demand or maintain marketing approval for Auryxia or Vafseo, and we might be required to expend additional resources to obtain material from other manufacturers. If any of these events occur, our reputation and financial condition would be negatively and materially impacted. In addition, if we have high amounts of write-downs to inventory reserves in the future, it could negatively impact our ability to supply Auryxia or Vafseo, and our financial condition could be harmed.

If the FDA, EMA or other regulatory authorities withdraws any approval of the facilities being used to manufacture Auryxia, Vafseo or any of our product candidates, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or Vafseo in Japan, or to commercialize Vafseo in Europe and other countries, or to develop, obtain marketing approval for or market Vafseo our other product candidates, if approved.

Moreover, our failure or the failure of our third party manufacturers or distributors to comply with applicable regulations or guidance, or our failure to oversee or facilitate such compliance, could result in sanctions being imposed on us or our third party manufacturers or distributors, including, where applicable, clinical holds, fines, injunctions, civil penalties, delays in, suspension of or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or Vafseo in the U.S., Japan or Europe, operating restrictions, receipt of a Form 483 or warning letter, or criminal prosecutions, any of which could significantly and adversely affect the supply of Auryxia or Vafseo. For example, we previously conducted three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future and any related write-downs of inventory or other consequences could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia or Vafseo for clinical and commercial use. Also, if our starting materials, drug substance or drug product are damaged or lost while in our or our third party manufacturers’ or distributors' control, it may adversely impact our ability to supply Auryxia or Vafseo, and we may incur significant financial harm.

In addition, Auryxia, Vafseo and our product candidates may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer or distributor may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia, Vafseo or our product candidates due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' or distributors' ability to meet our demand, which could adversely impact our ability to supply Auryxia, Vafseo or our product candidates, and we may incur significant financial harm.

Our current and anticipated future dependence on third parties for the manufacture and distribution of Auryxia, Vafseo and our product candidates may adversely affect our and our partners' ability to commercialize Auryxia, Vafseo and our product candidates, where approved, on a timely and competitive basis and may reduce any future profit margins.

***We rely upon third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, Vafseo or any of our product candidates, and our business could be substantially harmed.***

We do not have the ability to independently conduct certain preclinical studies and clinical trials. We are currently relying, and expect to continue to rely, upon third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and future preclinical studies and clinical trials. The third parties upon whom we rely may fail to perform effectively, or terminate their engagement with us, for a number of reasons, including the following:

- if they experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if they undergo changes in priorities or corporate structure including as a result of a merger or acquisition or other transaction, or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

If the third parties upon whom we rely to conduct our trials fail to adhere to clinical trial protocols or to regulatory requirements, the quantity, quality or accuracy of the data obtained by the third parties may be compromised. We are exposed to risk of fraud or other misconduct by such third parties.

Any of these events could cause our preclinical studies and clinical trials, including post-approval clinical trials, to be extended, delayed, suspended, required to be repeated or terminated, or we may receive untitled warning letters or be the subject of an enforcement action, which could result in our failing to maintain marketing approval of Auryxia or Vafseo, or failing to obtain or maintain marketing approval for any other product candidates on a timely basis or at all, any of which would adversely affect our business operations. In addition, if the third parties upon whom we rely fail to perform effectively or terminate their engagement with us, we may need to enter into alternative arrangements, which could delay, perhaps significantly, the development and commercialization of Auryxia, Vafseo or any other product candidates.

Even though we do not directly control the third parties upon whom we rely to conduct our preclinical studies and clinical trials and therefore cannot guarantee the satisfactory and timely performance of their obligations to us, we are nevertheless responsible for ensuring that each of our clinical trials and preclinical studies is conducted in accordance with the applicable protocol, legal and regulatory requirements, including GxP requirements, and scientific standards, and our reliance on these third parties, including CROs, will not relieve us of our regulatory responsibilities. If we or any of our CROs, their subcontractors, or clinical or preclinical trial sites fail to comply with applicable GxP requirements, the clinical data generated in our trials may be deemed unreliable or insufficient, our clinical trials could be put on hold, and/or the FDA, the EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical and preclinical trials must be conducted with drug product that meets certain specifications and is manufactured under applicable cGMP regulations. These requirements include, among other things, quality control, quality assurance, and the satisfactory maintenance of records and documentation.

We also rely upon third parties to store and distribute drug product for our clinical trials. For example, we use third parties to store product at various sites in the U.S. to distribute to our clinical trial sites. Any performance failure on the part of our storage or distributor partners could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

***If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.***

We do not own all of the rights to our product, Auryxia. We have licensed and sublicensed certain rights, patent and otherwise, to Auryxia from a third party, Panion, who in turn licenses certain rights to Auryxia from one of the inventors of Auryxia. The license agreement with Panion, or the Panion License Agreement, requires us to meet development milestones and imposes development and commercialization due diligence requirements on us. In addition, under the Panion License Agreement, we must pay royalties based on a mid-single digit percentage of net sales of product resulting from the licensed technologies, including Auryxia, and pay the patent filing, prosecution and maintenance costs related to the license. If we do not meet our obligations in a timely manner, or if we otherwise breach the terms of the Panion License Agreement, Panion could terminate the agreement, and we would lose the rights to Auryxia. For example, following announcement of the Merger, Panion notified us in writing that Panion would terminate the Panion License Agreement on November 21, 2018 if we did not cure the breach alleged by Panion, specifically, that we failed to use commercially reasonable best efforts to commercialize Auryxia outside the U.S. We disagreed with Panion's claims, and the parties entered discussions to resolve this dispute. On October 24, 2018, prior to the consummation of the Merger, we and Panion entered into a letter agreement, or the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the Panion License Agreement and waived its rights to terminate the license agreement based on any breach by us of our obligation to use commercially reasonable efforts to commercialize Auryxia outside the U.S. until the parties executed an amendment to the Panion License Agreement in accordance with the terms of the Panion Letter Agreement, following consummation of the Merger. On April 17, 2019, we and Panion entered into an amendment and restatement of the Panion License Agreement, or the Panion Amended License Agreement, which reflects certain revisions consistent with the terms of the Panion Letter Agreement. See Note 10, *Commitments and Contingencies*, to our consolidated financial statements in Part II, Item 8. Financial Statements of this Form 10-K for additional information regarding the Panion Amended License Agreement. Even though we entered into the Panion Amended License Agreement, there are no assurances that Panion will not allege other breaches of the Panion Amended License Agreement or otherwise attempt to terminate the Panion Amended

License Agreement in the future. In addition, if Panion breaches its agreement with the inventor from whom it licenses rights to Auryxia, Panion could lose its license, which could impair or delay our ability to develop and commercialize Auryxia.

From time to time, we may have disagreements with Panion, or Panion may have disagreements with the inventor from whom it licenses rights to Auryxia, regarding the terms of the agreements or ownership of proprietary rights, which could impact the commercialization of Auryxia, could require or result in litigation or arbitration, which would be time-consuming and expensive, could lead to the termination of the Panion Amended License Agreement, or force us to negotiate a revised or new license agreement on terms less favorable than the original. In addition, in the event that the owners and/or licensors of the rights we license were to enter into bankruptcy or similar proceedings, we could potentially lose our rights to Auryxia or our rights could otherwise be adversely affected, which could prevent us from continuing to commercialize Auryxia.

***Changes in U.S. and international trade policies, particularly with respect to China or Canada, may adversely impact our business and operating results.***

The U.S. government has recently made statements and taken certain actions that may lead to potential changes to U.S. and international trade policies, including imposing several rounds of tariffs and export control restrictions affecting certain products manufactured in China, Canada and potentially other countries. In March 2018, the Trump administration announced the imposition of tariffs on steel and aluminum entering the U.S. from China, and in June 2018, the Trump administration announced further tariffs targeting goods imported from China. Recently both China and the U.S. have each imposed tariffs indicating the potential for further trade barriers, including the U.S. Commerce Department adding numerous Chinese entities to its "unverified list," which requires U.S. exporters to go through more procedures before exporting goods to such entities. In March 2025, the U.S. imposed tariffs on certain imports from Canada and Mexico. However, these newly imposed tariffs have resulted in retaliatory tariffs, and threats thereof, against U.S. goods. It is unknown whether and to what extent new tariffs, export controls, or other new laws or regulations will be adopted, or the effect that any such actions would have on us or our industry.

Further, many of our manufacturers and suppliers for Auryxia and Vafseo are located in China and Canada. The manufacturing of our drug product for commercial use of both Auryxia and Vafseo takes place in Canada through a third-party manufacturer, Patheon Inc., or Patheon. Also, the manufacturing of our drug substance and drug product for commercial supply of Vafseo takes place in China through a third-party manufacturer, STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, and we will likely continue to rely on foreign CMOs in the future. We also rely on third parties in China for the supply of raw materials used in the manufacture of Vafseo and for certain early-stage research services. Trade tensions and conflicts between the U.S. and China, Canada or other countries have recently been escalating and, as such, we are exposed to the possibility of product supply disruption and increased costs and expenses in the event of changes to the laws, rules, regulations and policies of the governments of the U.S., China, Canada or other countries, or due to geopolitical unrest and unstable economic conditions. In addition, certain Chinese biotechnology companies may become subject to trade restrictions, sanctions, other regulatory requirements or proposed legislation by the U.S. government, which could restrict or even prohibit our ability to work with such entities, thereby potentially disrupting their supply of material to us. For example, in February 2024, U.S. lawmakers called for investigations into and the imposition of possible economic sanctions against Chinese biotechnology companies WuXi AppTec and WuXi Biologics, or collectively WuXi, over alleged ties to the Chinese military. Further, the recently proposed BIOSECURE Act introduced in the House of Representatives, as well as a substantially similar bill in the Senate, targets certain Chinese biotechnology companies. If these bills become law, or similar laws are passed, they would have the potential to severely restrict the ability of companies to contract with certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the U.S. government. Such disruptions could have adverse effects on our ability to commercialize Vafseo or the development of our product candidates and our business operations.

Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our products and product candidates, affect the demand for our products, the competitive position of our products or product candidates, and import or export of raw materials and finished product candidate used in our preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import from China and Canada, including pursuant to our manufacturing service arrangements with WuXi STA and Patheon. If any new tariffs, export controls, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U.S., Chinese, Canadian or other government takes retaliatory trade actions due to the recent trade tension, such changes could have an adverse effect on our business, financial condition and results of operations.

***Risks Related to our Intellectual Property***

***If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.***

Our commercial success will depend in part on our ability, and the ability of our licensors, to obtain and maintain patent protection on our drug product and technologies, and to successfully defend these patents against third party challenges. We

seek to protect our proprietary products and technology by filing patent applications in the U.S. and certain foreign jurisdictions. The process for obtaining patent protection is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in a cost effective or timely manner. In addition, we may fail to identify patentable subject matter early enough to obtain patent protection. Further, license agreements with third parties may not allow us to control the preparation, filing and prosecution of patent applications, or the maintenance or enforcement of patents. Such third parties may decide not to enforce such patents or enforce such patents without our involvement. Thus, these patent applications and patents may not, under these circumstances, be prosecuted or enforced in a manner consistent with the best interests of the company.

Our pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or potentially sell our products or in countries where others develop, manufacture and potentially sell products using our technologies. Moreover, our pending patent applications, if issued as patents, may not provide additional protection for our products.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical and biotechnology patents has emerged to date. Changes in the patent laws or the interpretation of the patent laws in the U.S. and other jurisdictions may diminish the value of our patents or narrow the scope of our patent protection. Accordingly, the patents we own or license may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative drug products or technologies or design around our patented drug products and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the U.S. that claim technology also claimed by us, we may have to participate in interference or derivation proceedings in front of the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to, or remain in existence for only a short period following, commercialization, which may significantly diminish our ability to exclude others from commercializing products that are similar or identical to ours. The patents we own or license may be challenged or invalidated or may fail to provide us with any competitive advantage. Since we have licensed or sublicensed many patents from third parties, we may not be able to enforce such licensed patents against third party infringers without the cooperation of the patent owner and the licensor, which may not be forthcoming. In addition, we may not be successful or timely in obtaining any patents for which we submit applications.

Generally, the first to file a patent application is entitled to the patent if all other requirements of patentability are met. However, prior to March 16, 2013, in the U.S., the first to invent was entitled to the patent. Since publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, the laws enacted by the Leahy-Smith America Invents Act of 2011, which reformed certain patent laws in the U.S., introduce procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review. Similar laws exist outside of the U.S. The laws of the European Patent Convention, for example, provide for post-grant opposition procedures that permit competitors to challenge, or oppose, our European patents administratively at the European Patent Office, or EPO.

We may become involved in addressing patentability objections based on third party submission of references, or we may become involved in defending our patent rights in oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the U.S. or elsewhere, challenging our patent rights or the patent rights of others. An adverse result in any such proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged on such a basis in the courts or patent offices in the U.S. and abroad. As a result of such challenges, we may lose exclusivity or freedom-to-operate or patent claims may be narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent third parties from using or commercializing similar or identical products, or limit the duration of the patent protection for our products.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and governmental patent agencies in other jurisdictions also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse in many cases can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance

events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market sooner than we expect, which would have a material adverse effect on our business.

In addition, patents protecting our product candidate might expire before or shortly after such candidate is commercialized. Thus, our patent portfolio may not provide sufficient rights to exclude others from commercializing products similar or identical to ours.

We also rely on trade secrets and know-how to protect our intellectual property where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. While we require our employees, licensees, collaborators and consultants to enter into confidentiality agreements, this may not be sufficient to adequately protect our trade secrets or other proprietary information. In addition, in some cases, we share certain ownership and publication rights to data relating to some of our products and product candidates with research collaborators, licensees and other third parties. If we cannot maintain the confidentiality of this information, our ability to receive patent protection or protect our trade secrets or other proprietary information will be at risk.

***We may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting and defending patents on our products and product candidates in all countries throughout the world would be prohibitively expensive. Consequently, the breadth of our intellectual property rights in some countries outside the U.S. may be less extensive than those in the U.S. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the U.S. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories where we have patent protection, but where enforcement is not as strong as in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in countries outside of the U.S. could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage for our products and product candidates from the intellectual property that we develop or license.

***The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia, Vafseo or other future products.***

The patent rights and related non-patent exclusivity that we own or have licensed relating to Auryxia, Vafseo or other future products, are, or may be limited in ways that may affect our ability to exclude third parties from competing against us. For example, a third party may design around our owned or licensed composition of matter patent claims or market a product for the methods of use not covered by our owned or licensed patents.

Obtaining proof of direct infringement by a competitor for a method of use patent requires us to demonstrate that the competitors make and market a product for the patented use(s). Alternatively, we can prove that our competitors induce or contribute to others in engaging in direct infringement. Proving that a competitor contributes to or induces infringement of a patented method by another has additional proof requirements. For example, proving inducement of infringement requires proof of intent by the competitor. If we are required to defend ourselves against claims or to protect our own proprietary rights against others, it could result in substantial costs to us and the distraction of our management. An adverse ruling in any litigation or administrative proceeding could prevent us or our partners from marketing and selling Auryxia, Vafseo or other future products, increase the risk that a generic or other similar version of Auryxia, Vafseo or other future products could enter the market to compete with Auryxia, Vafseo or other future products, limit our or our partners' development and commercialization of Auryxia, Vafseo or other future products, or otherwise harm our competitive position and result in additional significant costs.

Moreover, physicians may prescribe a competitive identical product for indications other than the one for which the product has been approved, or "off-label" indications, that are covered by the applicable patents. Although such off-label prescriptions may directly infringe or contribute to or induce infringement of method of use patents, such infringement is difficult to prevent.

In addition, any limitations of our patent protection described above may adversely affect the value of our drug product and may inhibit our ability to obtain a collaboration partner at terms acceptable to us, if at all.

In addition to patent rights in the U.S., we may seek non-patent exclusivity for any approved or future products under other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, but there is no guarantee that any products will receive such exclusivity. The FDCA provides a five-year period of non-patent exclusivity within the U.S. to the first sponsor to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which consists of the molecule(s) or ion(s) responsible for the action of the drug substance (but not including those portions of the molecule that cause it to be a salt or ester or which are not bound to the molecule by covalent or similar bonds). Vafseo was granted NCE status following its approval in March 2024 and received a five-year NCE exclusivity. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the sponsor does not own or have a legal right of reference to all the data required for approval.

An ANDA that references an NDA product with NCE exclusivity may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of exclusivity for an NDA, particularly a 505(b)(2) NDA or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the sponsor are deemed by the FDA to be essential to the approval of the application (for example, for new indications, dosages, or strengths of an existing drug). This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. The three-year exclusivity period, unlike five-year exclusivity, does not prevent the submission of a competing ANDA or 505(b)(2) NDA. Instead, it only prevents the FDA from granting final approval to such a product until expiration of the exclusivity period. Five-year and three-year exclusivity will not delay the submission (in the case of five-year exclusivity) or the approval (in the case of three-year exclusivity) of a full NDA submitted under section 505(b)(1) of the FDCA; however, a sponsor submitting a full NDA would be required to conduct all of its own studies needed to independently support a finding of safety and effectiveness for the proposed product, or have a full right of reference to all studies not conducted by the sponsor.

In cases where NCE exclusivity has been granted to a new drug product, the 30-month stay triggered by such litigation is extended by the amount of time such that seven years and six months will elapse from the date of approval of the NDA for that product. Without NCE exclusivity, the 30-month stay on FDA final approval of an ANDA runs from the date on which the sponsor of the reference listed drug receives notice of a Paragraph IV certification from the ANDA sponsor.

In addition to NCE, in the U.S., the FDA has the authority to grant additional regulatory exclusivity protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of any non-patent exclusivity that has been awarded as well as to the regulatory protection related to the term of a relevant patent, to the extent these protections have not already expired.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted regarding non-patent exclusivity. For example, EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. The EC's proposal for revision of several legislative instruments related to medicinal products, which may reduce the duration of regulatory data protection and exclusivity periods for orphan drugs, and revise the eligibility for expedited pathways in addition to other changes, was published on April 26, 2023. On April 10, 2024, the European Parliament adopted a position on the proposal requesting several amendments to the package. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may, however, have a significant impact on the pharmaceutical industry and our business in the long term.

We cannot assure you that Auryxia, Vafseo or any of our potential future products will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the U.S., EU or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any non-patent exclusivity protection. We also cannot assure you that Auryxia, Vafseo or any of our potential future products will obtain patent term extension.

***The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia and Vafseo sales and have an adverse impact on our business and results of operation.***

Although the composition and use of Auryxia is currently claimed by 3 issued patents that are listed in the FDA's Orange Book, or OB, and the composition and use of Vafseo is currently claimed by 13 issued patents that are listed in the OB, we cannot assure you that we will be successful in defending against third parties attempting to invalidate or design around our patents or asserting that our patents are invalid or otherwise unenforceable or not infringed, or in competing against third parties introducing generic equivalents of Auryxia, Vafseo or any of our potential future products. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia or Vafseo is approved and launched sooner than we anticipate, revenue from Auryxia or Vafseo, respectively, could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

We previously received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). We filed complaints for patent infringement relating to such ANDAs, and subsequently entered into settlement and license agreements with all such ANDA filers that allow such ANDA filers to market a generic version of Auryxia in the U.S. beginning on March 20, 2025. It is possible that we may receive Paragraph IV certification notice letters from additional ANDA filers and may not ultimately be successful in an ANDA litigation.

While we expect that the availability of generic versions of Auryxia will negatively impact our net product revenue for Auryxia and our results of operations, it is difficult to estimate the impact of generics on Auryxia net product revenue, and if the impact is greater than we currently anticipate, it may materially adversely impact our business and results of operations. Generic competition for Auryxia or any of our potential future products could have a material adverse effect on our sales, results of operations and financial condition.

***Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.***

We may be forced to initiate litigation to enforce our contractual and intellectual property rights, or we may be sued by third parties asserting claims based on contract, tort or intellectual property infringement. Competitors may infringe our patents or misappropriate our trade secrets or confidential information. We may not be able to prevent infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S. In addition, third parties may have or may obtain patents in the future and claim that our products or other technologies infringe their patents. If we are required to defend against suits brought by third parties, or if we sue third parties to protect our rights, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against our licensor, licensees or us that seeks damages or an injunction of commercial activities relating to Auryxia, Vafseo or any product candidates or other technologies, including those that may be in-licensed or acquired, could subject us to monetary liability, a temporary or permanent injunction preventing the development, marketing and sale of such products or such technologies, and/or require our licensor, licensees or us to obtain a license to continue to develop, market or sell such products or other technologies. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. We cannot predict whether our licensor, licensees or we would prevail in any of these types of actions or that any required license would be made available on commercially acceptable terms, if at all.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. However, there may be patents of third parties of which we are currently unaware with claims to compounds, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We have in the past and may in the future become a party to, or be threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our product and product candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the U.S. falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the U.S. or import into the U.S. a patented invention solely for uses reasonably related to the development and submission of information to the FDA. There is an increased possibility of a patent infringement claim against us with respect to commercial products. Our portfolio includes two commercial products: Auryxia and Vafseo. We attempt to ensure that our products and product

candidates and the methods we employ to manufacture them, as well as the methods for their use which we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

FibroGen has filed patent applications in the U.S. and other countries directed to purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. In November 2023, we and our collaboration partner, MTPC, entered into a Settlement and Cross License Agreement, or the Settlement Agreement, with FibroGen and its collaboration partner, Astellas. The Settlement Agreement resolves all patent disputes between us, MTPC, FibroGen and Astellas in the EU, the contracting states to the European Patent Convention, the UK and Japan, or the Settlement Territory. We may in the future initiate invalidity actions or other legal proceedings with respect to FibroGen patents outside of the Settlement Territory. If we are not successful in such proceedings, FibroGen could try to claim that our products infringe their patent rights.

Third parties, including FibroGen, may in the future claim that our products and product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and Vafseo. Parties making claims against us or our licensees may seek and obtain injunctive or other equitable relief, which could effectively block our or their ability to continue to commercialize Auryxia or Vafseo or further develop and commercialize any product candidates, including those that may be in-licensed or acquired. If any third party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our products or product candidates. Should a license to a third party patent become necessary, we cannot predict whether we would be able to obtain a license or, if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our product or product candidate may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

In addition, there may be a challenge or dispute regarding inventorship or ownership of patents or applications currently identified as being owned by or licensed to us. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Competitors may initiate an administrative proceeding challenging our issued patents or pending patent applications, which can be expensive and time-consuming to defend. An adverse result in any current or future defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and held not infringed and could put our patent applications at risk of not issuing. In addition, an unfavorable outcome in any current or future proceeding in which we are challenging third party patents could require us to cease using the patented technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the USPTO or a foreign patent office may result in substantial costs and distract our management and other employees.

We are currently involved in opposition proceedings in the Indian Patent Office and the European Patent Office. The proceedings may be ongoing for a number of years, may be resolved in a manner adverse to the Company and may involve substantial expense and diversion of employee resources from our business, which could have an adverse effect on our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under "Risks Related to our Intellectual Property".

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and some administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure during discovery. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.***

We have received confidential and proprietary information from potential collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

***Risks Related to our Business and Managing Growth***

***If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop and commercialize Auryxia, Vafseo or any of our product candidates.***

Recruiting and retaining qualified personnel is critical to our success. We are also highly dependent on our executives, certain members of our senior management and certain key personnel. The loss of the services of our executives, senior managers or other employees could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Specifically, following receipt of the CRL, we implemented a reduction of our workforce in April and May 2022 by approximately 42% across all areas of our Company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. Losing members of management and other key personnel subjects us to a number of risks, including the failure to coordinate responsibilities and tasks, the necessity to create new management systems and processes, the impact on corporate culture, and the retention of historical knowledge.

Furthermore, replacing executives, senior managers and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop and commercialize Auryxia, Vafseo and any product candidates. Our future financial performance and our ability to develop and commercialize Auryxia and Vafseo and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to hire, train, integrate, and retain additional qualified personnel with sufficient experience. We may be unable to hire, train, retain or motivate these personnel on acceptable terms given the intense competition for our personnel from our competitors and other companies throughout our industry, particularly in our geographic region. Over the last several years, the challenges in recruiting and retaining employees across the pharmaceutical and biotechnology industries have increased substantially due to current industry job market dynamics.

In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our R&D and commercialization strategy. Our contractors, consultants and advisors may become employed by companies other than ours and may have commitments with other entities that may limit their availability to us. If additional members of management or other personnel leave, or we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

***We may encounter difficulties in managing our growth, including with respect to our employee base, and managing our partnerships and operations successfully.***

In our day-to-day operations, we may encounter difficulties in managing the size of our operations as well as challenges associated with managing our business. We have strategic collaborations for the commercialization of Riona in Japan, the development and commercialization of ferric citrate in Europe, and the development and commercialization of vadadustat, which is now being or will be marketed under the trade name Vafseo by our collaboration partner, MTPC, in Japan and potentially other Asian countries and our collaboration partner, Medice, in the Medice Territory. As our operations continue,

we expect that we will need to manage our current relationships and enter into new relationships with various strategic collaborators, consultants, vendors, suppliers and other third parties. These relationships are complex and create numerous risks as we deal with issues that arise.

For example, we supply or have agreed to supply, as applicable, Auryxia in Europe, Vafseo in Japan, Europe and other territories where it is approved for commercial and clinical use to MTPC, Medice and Averoa, which will require us to successfully manage our limited financial and managerial resources. In addition, we may not be able to obtain the raw materials or product that we need, or the cost of the raw materials or product may be higher than expected. If we are unable to successfully manage our supply obligations, our ability to commercialize our products or supply such products to our partners could have a material adverse effect on our relationships with our partners and our results of operations.

Our future financial performance and our ability to commercialize Auryxia and Vafseo, if and where approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. This future growth will impose significant added responsibilities on the business and members of management. To manage any future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes. We may not be able to implement these improvements in an efficient or timely manner and may discover deficiencies in existing systems, procedures and processes. For example, we recently transitioned to a new enterprise resource planning system and if we encounter any difficulties or issues with the new system it could affect our ability to close our books and complete our financial reporting in a timely manner. Moreover, the systems, procedures and processes currently in place or to be implemented may not be adequate for any such growth. Any expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully managing and, as applicable, growing our Company.

In addition, we may need to adjust the size of our workforce as a result of changes to our expectations for our business, which can result in management being required to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth-related activities and related expenses. Further, we rely on independent third parties to provide certain services to us. We structure our relationships with these outside service providers in a manner that we believe results in an independent contractor relationship, not an employee relationship. If any of our service providers are later legally deemed to be employees, we could be subject to employment and tax withholding liabilities and other additional costs as well as other multiple damages and attorneys' fees.

***We have identified a material weakness in our internal control over financial reporting as of December 31, 2024 relating to our accounting for inventory and inventory related transactions. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in our internal control over financial reporting in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately or timely report our financial results or prevent fraud, and we may conclude that our internal control over financial reporting is not effective, which may adversely affect our business.***

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to maintain or implement required new or improved controls, or difficulties encountered in implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act, or Section 404, or any testing by our independent registered public accounting firm may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement.

We identified a material weakness in our internal control over financial reporting as of December 31, 2024. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. Our management concluded that we did not design and maintain effective controls over inventory. Specifically, we did not maintain effective review controls that operated with a sufficient level of precision to evaluate the completeness, accuracy and reasonableness of the product sales forecast, which is used in the evaluation of excess inventory, including the calculation of excess firm purchase commitments and the classification of current and non-current inventory. For further discussion of the material weakness, see Part II, Item 9A, "Controls and Procedures."

We have taken and plan to continue to take actions to remediate this material weakness, including (i) designing and implementing new controls to help ensure the completeness and accuracy of our inventory reconciliations, (ii) engaging accounting personnel with U.S. GAAP experience specific to inventory accounting and (iii) enhancing the monitoring and oversight controls to help to ensure the completeness and accuracy of inventory included in our financial statements and related disclosures. However, we cannot provide assurance that we will be able to correct this material weakness in a timely manner or that our remediation efforts will be adequate to allow us to conclude that our internal control over financial reporting will be effective in the future. Even if this material weakness is remediated in the future, we could identify additional material weaknesses or deficiencies in our internal control over financial reporting that could require correction or

remediation. For example, we previously identified a material weakness in our internal control over financial reporting as of December 31, 2022 relating to our product return reserves that resulted in a revision of our financial statements for the years ended December 31, 2022, 2021 and 2020.

In addition, our conclusion that we have a material weakness could give rise to increased scrutiny, review, audit and investigation over our accounting controls and procedures, which could then lead to additional areas of deficiency or errors in our financial statements.

We will need to continue to dedicate internal resources, engage outside consultants and maintain a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to remediate the material weakness relating to our accounting for inventory and inventory related transactions described above and any future control deficiencies or material weaknesses, and improve control processes as appropriate, validate through testing that controls are functioning as documented and maintain a continuous reporting and improvement process for internal control over financial reporting. If we are not able to correct material weaknesses or deficiencies in internal controls in a timely manner or otherwise comply with the requirements of Section 404 in a timely manner, our ability to record, process, summarize and report financial information accurately and within applicable time periods may be adversely affected, and we could be subject to sanctions or investigations by the Securities Exchange Commission, or the SEC, the Nasdaq Stock Market or other regulatory authorities as well as stockholder litigation which, even if resolved in our favor, would require additional financial and management resources and could adversely affect the market price of our common stock. Any failure to maintain or implement required effective internal control over financial reporting, or any difficulties we encounter in their implementation, could result in additional material weaknesses, cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock and could also affect our ability to raise capital to fund future business initiatives.

***Security breaches and unauthorized use of our information technology systems and information, or the information technology systems or information in the possession of our collaborators and other third parties, could damage the integrity of our clinical trials, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties.***

We, our collaborators, contractors and other third parties rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively. In addition, we and our collaborators, contractors and other third parties rely on information technology networks and systems, including the Internet and artificial intelligence based software, to process, transmit and store clinical trial data, patient information, and other electronic information, and manage or support a variety of business processes, including operational and financial transactions and records, personal identifying information, payroll data and workforce scheduling information. We purchase most of our information technology from vendors, on whom our systems depend. We rely on commercially available systems, software, tools and monitoring to provide security for the processing, transmission and storage of company and customer information.

In the ordinary course of our business, we and our third party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial patients and business partners. In particular, we rely on CROs and other third parties to store and manage information from our clinical trials. We also rely on third parties to manage patient information for Auryxia and Vafseo. Additionally, the use of artificial intelligence based software is increasingly being used in the biopharmaceutical industry. Use of artificial intelligence based software may lead to the release of confidential proprietary information, which may impact our ability to realize the benefit of our intellectual property. The secure maintenance of this sensitive information is critical to our business and reputation.

Companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Attackers have used artificial intelligence and machine learning to launch more automated, targeted and coordinated attacks against targets. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our vendors or third party service providers. A security breach, cyberattack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trials, impact our regulatory filings, cause significant risk to our business, compromise our ability to protect our intellectual property, and subject us to regulatory actions, including under the GDPR and CCPA discussed elsewhere in these risk factors and the privacy or security rules under federal, state, or other local laws outside of the U.S. protecting confidential or personal information, that could be expensive to defend and could result in significant fines or other penalties. Cyberattacks can include malware, computer viruses, hacking, social engineering, zero day vulnerabilities or other unauthorized access or other significant compromise of our computer, communications and related systems. Although

we take steps to manage and avoid these risks and to be prepared to respond to attacks, our preventive and any remedial actions may not be successful and no such measures can eliminate the possibility of the systems' improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyberattacks. Security breaches, whether through physical or electronic break-ins, computer viruses, ransomware, impersonation of authorized users, attacks by hackers or other means, can create system disruptions or shutdowns or the unauthorized disclosure of confidential information.

Although we believe our collaborators, vendors and service providers, such as our CROs, take steps to manage and avoid information security risks and respond to attacks, we may be adversely affected by attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers to remedy any harm to our business caused by such event. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other contractors to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using "spoofing" and "phishing" emails or other types of attacks. Our employees may be targeted by such fraudulent activities. Outside parties may also subject us to distributed denial of services attacks or introduce viruses or other malware through "trojan horse" programs to our users' computers in order to gain access to our systems and the data stored therein. Cyber-attacks have become more prevalent and much harder to detect and defend against. Because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, including the use of artificial intelligence to generate sophisticated spoofed emails and deep fake voice and video, often are not recognized until launched against a target and may be difficult to detect for a long time, we may be unable to anticipate these techniques or to implement adequate preventive or detective measures, and we might not immediately detect such incidents and the damage caused by such incidents.

Such attacks, whether successful or unsuccessful, or other compromises with respect to our information security and the measures we implement to prevent, detect and respond to them, could:

- result in our incurring significant costs related to, for example, rebuilding internal systems, defending against litigation, responding to regulatory inquiries or actions, paying damages or fines, or taking other remedial steps with respect to third parties;
- lead to public exposure of personal information of participants in our clinical trials, Auryxia patients and others;
- damage the integrity of our studies or delay their completion, disrupt our development programs, our business operations and commercialization efforts;
- compromise our ability to protect our trade secrets and proprietary information;
- damage our reputation and deter business partners from working with us; or
- divert the attention of our management and key information technology resources.

Any failure to maintain proper functionality and security of our internal computer and information systems could result in a loss of, or damage to, our data or marketing applications or inappropriate disclosure of confidential or proprietary information, interrupt our operations, damage our reputation, subject us to liability claims or regulatory penalties, under a variety of federal, state or other applicable privacy laws, such as HIPAA, the GDPR, or state data protection laws including the CCPA, harm our competitive position and delay the further development and commercialization of our products and product candidates, or impact our relationships with customers and patients.

***Our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading. In addition, laws and regulations governing any international operations we have or may have in the future may require us to develop and implement costly compliance programs.***

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate applicable laws, including the following:

- FDA and other healthcare authorities' regulations, including those laws that require the reporting of true, complete and accurate information to regulatory authorities, and those prohibiting the promotion of unapproved drugs or approved drugs for an unapproved use;
- quality standards, including GxP;
- federal and state healthcare fraud and abuse laws and regulations and their non-U.S. equivalents;
- anti-bribery and anti-corruption laws, such as the FCPA and the UK Bribery Act or country-specific anti-bribery or anti-corruption laws, as well as various import and export laws and regulations;
- laws that require the reporting of true and accurate financial information and data; and

- U.S. state and federal securities laws and regulations and their non-U.S. equivalents, including those related to insider trading.

We conducted our global clinical trials for Vafseo, and may in the future conduct additional trials, in countries where corruption is prevalent, and violations of any of these laws by our personnel or by any of our vendors or agents, such as our CROs or CMOs, could have a material adverse impact on our clinical trials and our business and could result in criminal or civil fines and sanctions. We are subject to complex laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their intermediaries, such as CROs or CMOs, from making improper payments to foreign government officials for the purpose of obtaining or keeping business or obtaining any kind of advantage for the company. The FCPA also requires companies to keep accurate books and records and maintain adequate accounting controls. A number of past and recent FCPA investigations by the Department of Justice and the SEC have focused on the life sciences sector.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. Some of the countries in which we have conducted clinical trials and in which we have CMOs have a history of corruption, which increases our risks of FCPA violations. In addition, the FCPA presents unique challenges in the pharmaceutical industry because in many countries' hospitals are operated by the government, and doctors and other hospital employees are considered foreign government officials. Certain payments made by pharmaceutical companies, or on their behalf by CROs, to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Additionally, the UK Bribery Act applies to our global activities and prohibits bribery of private individuals as well as public officials. The UK Bribery Act prohibits both the offering and accepting of a bribe and imposes strict liability on companies for failing to prevent bribery, unless the company can show that it had "adequate procedures" in place to prevent bribery. There are also local anti-bribery and anti-corruption laws in countries where we have conducted clinical trials, and many of these also carry the risk of significant financial or criminal penalties.

We are also subject to trade control regulations and trade sanction laws that restrict the movement of certain goods, currency, products, materials, services and technology to, and certain operations in, various countries or with certain persons. Our ability to transfer commercial and clinical product and other clinical trial supplies, and for our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors ability to travel, between certain countries is subject to maintaining required licenses and complying with these laws and regulations.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of non-U.S. jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us.

The internal controls, policies and procedures, and training and compliance programs we have implemented to deter prohibited practices may not be effective in preventing our employees, contractors, consultants, agents or other representatives from violating or circumventing such internal policies or violating applicable laws and regulations. The failure to comply with laws governing international business practices may impact any future clinical trials, result in substantial civil or criminal penalties for us and any such individuals, including imprisonment, suspension or debarment from government contracting, withdrawal of our products, if approved, from the market, or being delisted from The Nasdaq Capital Market. In addition, we may incur significant costs in implementing sufficient systems, controls and processes to ensure compliance with the aforementioned laws. The laws and regulations referenced above may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements that could adversely affect our business.

Additionally, it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling known or unknown risks or preventing losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, or if any such action is instituted against our employees, consultants, independent contractors, CROs, CMOs, vendors or principal investigators, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, curtailment of our operations, disclosure of our confidential information and imprisonment, any of which could adversely affect our ability to operate our business and our results of operations.

***Our financial statements include long-lived assets, including goodwill as a result of the Merger. Other long-lived assets, including property and equipment, right-of-use assets or goodwill, could become impaired in the future under certain***

***conditions. Any potential future impairment of property and equipment, our right-of-use assets or goodwill may significantly impact our results of operations and financial condition.***

As of December 31, 2024, we had approximately $59.0 million in the aggregate of goodwill from the Merger, $2.2 million of property and equipment and $8.2 million right-of-use assets. In accordance with ASC 350, *Goodwill and Other*, we are required annually for goodwill, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill. In addition, under ASC 360, *Property, Plant and Equipment*, we are required to review our property and equipment and right-of-use assets whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. Events giving rise to impairment of long-lived assets are an inherent risk in the pharmaceutical industry and often cannot be predicted.

Conditions that could indicate impairment and necessitate such a review include, but are not limited to, Auryxia's and Vafseo's commercial performance, our inability to execute on our strategic initiatives, the deterioration of our market capitalization such that it is significantly below our net book value, a significant adverse change in legal factors, unexpected adverse business conditions, and an adverse action or assessment by a regulator. To the extent we conclude our long-lived assets have become impaired, we may be required to incur material write-offs relating to such impairment and any such write-offs could have a material impact on our future operating results and financial position. The estimates, judgments and assumptions used in our impairment analyses, and the results of our analyses, are discussed in Note 2, *Summary of Significant Accounting Policies*, to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Form 10-K. If these estimates, judgments and assumptions change in the future, additional impairment charges related to plant and equipment, right-of-use assets or goodwill could be recorded in the future and additional corresponding adjustments may need to be made to the estimated useful life of the developed product rights for Auryxia, which could materially impact our financial position, certain of our material agreements, and our future operating results.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia or Vafseo.***

We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and Vafseo and our product candidates. For example, we may be sued if Auryxia, Vafseo or our product candidates allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product or product candidate, negligence, strict liability and breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Auryxia or Vafseo or affect the development of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for Auryxia or Vafseo;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- our inability to continue to develop Auryxia, Vafseo or our product candidates;
- significant costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for Auryxia or Vafseo;
- loss of revenue;
- the inability to commercialize Auryxia or Vafseo; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance that we believe is appropriate for our Company. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have insufficient or no coverage. If we have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, we may not have, or be able to obtain, sufficient capital to pay such amounts. In addition, insurance

coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost. We also may not be able to obtain additional insurance coverage that will be adequate to cover additional product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

***We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.***

As a public company, we operate in a demanding regulatory environment, and we have and will continue to incur significant legal, accounting, auditing, directors and officers insurance and other expenses. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and certain corporate governance practices. In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Capital Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees, our business and results of operations would likely be materially and adversely affected.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

***Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.***

Our Ninth Amended and Restated Certificate of Incorporation, as amended, or Charter, and our Second Amended and Restated Bylaws, or Bylaws, as amended to date, contain provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, or DGCL, the personal liability of our directors and executive officers for monetary damages for breach of their fiduciary duties as a director or officer. Our Charter and our Bylaws also provide that we will indemnify our directors and executive officers and may indemnify our employees and other agents to the fullest extent permitted by the DGCL.

In addition, as permitted by Section 145 of the DGCL our Bylaws and our indemnification agreements that we have entered into with our directors and executive officers provide that:

- We will indemnify our directors and officers, as defined in our Bylaws, for serving us in those capacities or for serving other related business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of Akebia and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- The rights conferred in our Bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

Any claims for indemnification made by our directors or officers could impact our cash resources and our ability to fund the business.

***Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.***

Under Section 382 of the Internal Revenue Code, or Section 382, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. On December 12, 2018, we completed the Merger, which we believe has resulted in an ownership change under Section 382. In addition, the Tax Cuts and Jobs Act, including amendments made by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating

losses to fully offset taxable income in the future. Future changes in our stock ownership, many of which are outside of our control, could result in an additional ownership change under Section 382. As a result, if we generate taxable income, our ability to use our pre-change NOL carryforwards to offset federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. At the state level, state net operating losses generated in one state cannot be used to offset income generated in another state and there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. taxable income. As described above under "—Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy," we have incurred significant net losses since our inception and anticipate that we will continue to incur losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. taxable income necessary to utilize our NOLs.

***Our Charter designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.***

Our Charter provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the DGCL our Charter or our Bylaws, or (iv) any other action asserting a claim against us, our directors, officers or other employees that is governed by the internal affairs doctrine. Under our Charter, this exclusive forum provision will not apply to claims that are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act, or the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Charter described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our Charter inapplicable to, or unenforceable with respect to, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

***Risks Related to our Common Stock***

***Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors and could result in substantial costs and divert management's attention.***

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for similarly situated biopharmaceutical companies specifically have experienced extreme volatility that has often been unrelated to the operating performance of particular companies, such as rising inflation and increasing interest rates. Since our initial public offering in March 2014, the price of our common stock as reported on The Nasdaq Stock Market has ranged from a low of $0.24 on October 24, 2022 to a high of $31.00 on June 20, 2014. The daily closing market price for our common stock varied between a high price of $2.24 on March 27, 2024 and a low price of $0.86 on June 25, 2024 in the twelve-month period ending on December 31, 2024. During that time, the price of our common stock ranged from an intra-day low of $0.80 per share to an intra-day high of $2.48 per share. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, including, among others, developments related to and results of our research or clinical trials, developments related to our regulatory submissions and meetings with regulatory authorities, commercialization of Auryxia, Vafseo, and any other product candidates, announcements by us or our competitors of significant transactions or strategic collaborations, negative publicity around Auryxia or Vafseo, regulatory or legal developments in the U.S. and other countries, developments or disputes concerning our intellectual property, the recruitment or departure of key personnel, actual or anticipated changes in estimates as to financial results, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector, potential delisting from The Nasdaq Stock Market and other factors beyond our control. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it.

In addition, securities class actions, shareholder derivative lawsuits and other legal proceedings are often brought against companies for any of the risks described in this Form 10-K following a decline or volatility in the market price of their securities. We could be the target of such litigation or other legal proceedings in the future. Class actions, shareholder derivative lawsuits and other legal proceedings, whether successful or not, could result in substantial costs, damage or settlement awards and such costs and any related settlements or judgments may not be covered by insurance. Monetary

damages or any other adverse judgment would have a material adverse effect on our business and financial position. In addition, if other resolution or actions taken as a result of legal proceedings were to restrain our ability to operate or market our products and services, our consolidated financial position, results of operations or cash flows could be materially adversely affected. We could also suffer an adverse impact on our reputation, negative publicity and a diversion of management's attention and resources, which could have a material adverse effect on our business.

***If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.***

We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share and timely filing of all periodic financial reports, or risk delisting, which would have a material adverse effect on our business. If we fail to maintain compliance with Nasdaq's continued listing requirements, it could affect our ability to raise capital on acceptable terms, or at all. In the event we are delisted from Nasdaq, the only established trading market for our common stock would be eliminated, and we would be forced to list our shares on the OTC Markets or another quotation medium, depending on our ability to meet the specific listing requirements of those quotation systems. As a result, an investor would likely find it more difficult to trade or obtain accurate price quotations for our shares. Delisting would likely also reduce the visibility, liquidity, and value of our common stock, reduce institutional investor interest in our Company, and may increase the volatility of our common stock. Delisting could also cause a loss of confidence of potential industry partners, lenders, and employees, which could further harm our business and our future prospects.

***The issuance of additional shares of our common stock or the sale of shares of our common stock by any of our directors, officers or significant stockholders will dilute our stockholders' ownership interest in Akebia and may cause the market price of our common stock to decline.***

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock.

As of December 31, 2024 and based on the amounts reported in the most recent filing made by BlackRock under Section 13(g) of the Exchange Act, BlackRock beneficially owned approximately 6.2% of our outstanding shares of common stock. By selling a large number of shares of common stock, BlackRock could cause the price of our common stock to decline. In addition, as of December 31, 2024, CSL Vifor beneficially owned 7,571,429 shares of common stock, which have not been registered pursuant to the Securities Act and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder, but if they are registered in the future, those shares would become freely tradable and, if a large portion of such shares are sold, could cause the price of our common stock to decline.

Further, we entered into a warrant agreement with Kreos Capital VII Aggregator SCSp, an affiliate of Kreos, or the Warrant Holder, pursuant to which (i) we issued a warrant to the Warrant Holder to purchase 3,076,923 shares of our common stock, at an exercise price per share of $1.30 (subject to standard adjustments for stock splits, stock dividends, rights offerings and pro rata distributions), or the Exercise Price, and (ii) we issued a warrant to the Warrant Holder to purchase 1,153,846 shares of our common stock, at an exercise price per share equal to the Exercise Price. Each warrant is exercisable for eight years from the date of issuance. If any or all of the warrants are exercised, our stockholders could realize dilution, and the value of their shares could decrease.

We have a significant number of shares that are subject to outstanding options, restricted stock units and other securities convertible into our common stock, and in the future we may issue additional options, restricted stock units, or other securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, or other securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline.

In addition, we currently have on file with the SEC a shelf registration statement on Form S-3, which allows us to offer and sell up to $250.0 million in registered securities, such as common stock, preferred stock, debt securities, warrants and units, from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale, including a sales agreement prospectus that covers the offering, issuance and sale by us of up to a maximum aggregate offering price of up to $75.0 million of our common stock that may be issued and sold from time to time under a sales agreement with Jefferies LLC.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other stockholders or by us under our shelf registration statement, pursuant to at-the-market offerings or otherwise, could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

***Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.***

As of December 31, 2024, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our Company on terms that other stockholders may desire.

***Provisions in our organizational documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our Charter and our Bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing certain members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified Board of Directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our Board of Directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of 75% of the holders of our capital stock entitled to vote or the majority vote of our Board of Directors to amend our Bylaws; and
- require a supermajority vote of 85% of the holders of our capital stock entitled to vote to amend the classification of our Board of Directors and to amend certain other provisions of our Charter.

These provisions, alone or together, could delay or prevent hostile takeovers, changes in control or changes in our management.

In addition, Section 203 of the DGCL prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

***Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.***

We have never declared or paid cash dividends on our capital stock and we currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. Any payment of cash dividends in the future would be at the discretion of our Board of Directors and would depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations that the Board of Directors deems relevant. In addition, the terms of the BlackRock Credit Agreement preclude us from paying cash dividends without prior written consent of the lender and future debt agreements may preclude us from paying cash dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

**Item 1B. Unresolved Staff Comments**

None.

**Item 1C. Cybersecurity.**

**Cybersecurity Risk Management and Strategy**

We have certain processes for assessing, identifying, and managing material risks from cybersecurity threats, which are integrated into our enterprise risk management processes. Specifically, we have processes for:

- **Identifying and Managing Cybersecurity Risks** — We have implemented a cross-functional approach to assessing, identifying and managing material cybersecurity threats and incidents. We periodically review, assess, update and test our policies, standards, processes and practices in a manner intended to address cybersecurity threats and events. The results of such reviews, assessments and tests are evaluated by management and reported to our Audit Committee of the Board of Directors, or the Audit Committee, and our Board of Directors.
- **Technical Safeguards** — We have integrated cybersecurity into our overall information technology operations and designed our processes and systems to help protect our information assets and operations from internal and external cyber threats, protect employee and patient information from unauthorized access or attack as well as secure our networks and systems.
- **Incident Response and Recovery Planning —** To better facilitate our cybersecurity program, our cybersecurity team works collaboratively across our Company to implement programs designed to protect our information systems from cybersecurity threats and to promptly respond to any material cybersecurity incidents. We conduct periodic tabletop exercises, including incident simulations to test these plans and ensure personnel are familiar with their roles and responsibilities in a response scenario.
- **Third-Party Risk Management** — We maintain a risk-based approach to identifying and overseeing material cybersecurity threats presented by third parties and the systems of third parties that could adversely impact our business in the event of a material cybersecurity incident affecting those third-party systems. Also, we engage certain external cybersecurity firms to enhance our cybersecurity oversight and cybersecurity breach detection over third party service providers.
- **Education and Awareness** — We provide training regarding cybersecurity threats as a means to equip our employees and consultants with tools to make employees and consultants aware of and to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices. We also use technology-based tools to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

We adjust our cybersecurity policies, standards, processes, and practices as necessary based on the information provided by our assessments, audits and reviews. Such processes include (i) procedural and technical safeguards, (ii) response plans, (iii) periodic tests on our systems, (iv) incident simulations and (v) routine review of our cybersecurity policies and procedures to identify risks and improve our practices. We engage certain external cybersecurity firms to enhance our cybersecurity oversight. We include confidentiality provisions in all contracts with third-party service providers, and data protection provisions in certain contracts with third-party service providers where applicable, to help protect us and our employees and patients from any related vulnerabilities.

**Governance**

Our Board of Directors is responsible for exercising oversight of management's identification and management of, and planning for, risks from cybersecurity threats. While the full Board of Directors has overall responsibility for risk oversight, the Board of Directors has delegated oversight responsibility related to risks from cybersecurity threats to the Audit Committee of our Board of Directors. The Audit Committee reports to the Board of Directors at least annually, and notifies the Board of Directors as necessary regarding significant new cybersecurity threats or incidents. The Audit Committee meets annually to discuss our approach to overseeing cybersecurity threats with management, including with members of our internal cybersecurity team.

We use an internal management team to run our information technology and cybersecurity functions, which includes our information and cybersecurity team leads who have collectively served in various roles in information technology and information security for over 25 years, including at other public companies. Through ongoing communications with this management committee, senior management is informed about and monitors the prevention, detection, mitigation and remediation of cybersecurity threats and incidents in real-time and reports such threats and incidents to the Audit Committee, when appropriate. Management updates the Audit Committee quarterly regarding our cybersecurity threat risk management and strategy programs. Members of the Audit Committee are also encouraged to regularly engage in ad hoc

conversations with management on cybersecurity-related topics and discuss any updates to our cybersecurity risk management and strategy programs. The Audit Committee is notified between such updates regarding significant new cybersecurity threats or incidents that meet pre-established reporting thresholds and any ongoing updates regarding any risk, as needed.

We have not identified any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected or are reasonably likely to materially affect our company, including our business strategy, results of operations or financial condition. However, as discussed under "Risk Factor — Risks Related to our Business and Managing Growth" in Part I, Item 1A of this Form 10-K, cybersecurity threats could pose multiple risks to us. As cybersecurity threats become more frequent, sophisticated, and coordinated, it is reasonably likely that we will be required to expend greater resources to continue to modify and enhance our protective measures.

**Item 2. Properties**

We currently lease approximately 65,167 square feet of office, storage and laboratory space in Cambridge, Massachusetts, which is our corporate headquarters. Excluding renewal options, the lease for our Cambridge, Massachusetts office, storage and lab space expires on September 11, 2026. Due to our primarily hybrid workforce, we are marketing up to 59,216 square feet of furnished office space for sublease. We believe our existing facilities are adequate to meet our operational needs.

**Item 3. Legal Proceedings**

From time to time, we may be involved in legal proceedings arising from the normal course of business activities.

*Opposition Proceedings Against Akebia*

In September 2018, Dr. Reddy's Laboratories Limited filed an opposition to our issued Indian Patent No. 287720 covering the composition of matter of vadadustat in the Indian Patent Office.

On November 6, 2024, Sandoz AG filed an opposition against our issued European Patent No. 3007695 covering vadadustat once daily dosing regimen in the European Patent Office.

**Item 4. Mine Safety Disclosures**

Not applicable.

**PART II**

**Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**

***Market Information***

Our common stock is traded on The Nasdaq Capital Market under the symbol "AKBA".

***Holders***

At March 10, 2025, there were approximately 26 holders of record of our common stock. The number of record holders is based upon the actual number of holders registered on our books at such date and does not include shares held in street name by brokers or other nominees, and shares held by persons, partnerships, associations, corporations or other entities whose shares are held by depository trust companies.

***Dividends***

We have never declared or paid any cash dividends on our common stock and we do not anticipate paying cash dividends in the foreseeable future. In addition, the terms of our BlackRock Credit Agreement preclude us from paying cash dividends without prior written consent and future debt agreements may preclude us from paying cash dividends.

***Issuer Purchases of Equity Securities***

None.

***Recent Sales of Unregistered Securities***

We did not sell any securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act, during the year ended, other than pursuant to transactions previously disclosed in our Current Reports on Form 8-K.

***Purchases of Equity Securities by the Issuer and Affiliated Purchasers***

None.

***Comparative Stock Performance Graph***

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act, and are not required to provide a stock performance graph.

***Securities Authorized for Issuance under Equity Compensation Plans***

Information about our equity compensation plans is incorporated herein by reference to Item 12, *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*, of this Form 10-K.

**Item 6. [Reserved]**

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

*This Annual Report on Form 10-K, or* Form 10-K*, including this management's discussion and analysis of financial condition and results of operations, contains forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results may differ materially from those described in or implied in these forward-looking statements as a result of various factors, including those factors set forth in the "Risk Factors" section included in Part I, Item 1A of this Form 10-K. All references to years, unless otherwise noted, refer to our fiscal years, which end on December 31. For purposes of this section, all references to "we," "us," "our," "Akebia," or the "Company" refer to Akebia Therapeutics, Inc. and its consolidated subsidiaries.*

The following discussion and analysis should also be read in conjunction with the accompanying audited consolidated financial statements and related notes included in Part II, Item 8 of this Form 10-K. This section discusses 2024 and 2023 financial condition, and results of operations and year-to-year comparisons between 2024 and 2023. For discussion of 2023 items and year-over-year comparisons between 2023 and 2022 that are not included in this 2024 Form 10-K, refer to "Item 7. – Management's Discussion and Analysis of Financial Condition and Results of Operations" found in our Form 10-K for the year ended December 31, 2023, that was filed with the Securities and Exchange Commission on March 14, 2024.

**Business Overview**

We are a fully integrated, biopharmaceutical company with two commercial products for patients impacted by kidney disease. We have built a business focused on developing and commercializing innovative therapeutics that we believe serve as a foundation for future growth. Our team has significant expertise in hypoxia-inducible factor, or HIF, science having developed

and commercialized Vafseo® (vadadustat), an oral HIF factor prolyl hydroxylase, or HIF-PH, inhibitor and have selected two additional HIF-based molecules for preclinical development.

We have established the company as a leader in the kidney community, and we believe our cross-organizational expertise in renal disease positions the company for success. Chronic kidney disease, or CKD, is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient's blood, leading to other health problems, including anemia, cardiovascular disease and bone disease. CKD significantly impacts the U.S. healthcare system, potentially affecting approximately 37 million patients and costing Medicare nearly $125 billion annually for treating Medicare beneficiaries with CKD or end-stage renal disease, or ESRD, according to the Centers for Disease Control and Prevention. Our two commercial products address certain complications of kidney disease.

Our current portfolio includes:

**Vafseo** was approved by the U.S. Food and Drug Administration, or the FDA, in March 2024 for the treatment of anemia due to CKD in adult patients on dialysis for at least three months. Shipment of Vafseo commenced in January 2025. We have commercial supply agreements for the purchase of Vafseo in place with dialysis organizations caring for nearly 100% of dialysis patients in the U.S. The current U.S. market opportunity for the treatment of anemia due to CKD in patients with dialysis is approximately $1 billion based on current ESA pricing and Vafseo is the only oral HIF-based treatment available in the U.S.

In the European Union, or EU, the United Kingdom, or UK, Switzerland and Australia, Vafseo is approved for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. Our partner MEDICE Arzneimittel Pütter GmbH & Co. KG, or Medice, has an exclusive license to develop and commercialize Vafseo for the treatment of anemia in patients with CKD in defined territories and launched Vafseo in Germany, Austria, Switzerland, the Netherlands and certain other countries in Europe in 2024.

In Japan, Vafseo is approved as a treatment for anemia due to CKD in both dialysis dependent and non-dialysis dependent patients and is marketed and sold by our collaborator Mitsubishi Tanabe Pharma Corporation, or MTPC. In Taiwan, Vafseo is approved for the treatment of symptomatic anemia due to CKD in adult patients on chronic maintenance dialysis and launched in October 2024 by Tai Tien Pharmaceutical Company, an affiliate of MTPC. In Korea, Vafseo is approved as an anemia treatment for patients with CKD on hemodialysis.

**Auryxia® (ferric citrate)** is an orally administered medicine approved and marketed in the U.S. for two indications: (1) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis-dependent chronic kidney disease, or NDD-CKD.

Today, we market Auryxia in the U.S. Auryxia became part of our portfolio in 2018 and has historically contributed meaningful revenue to the business. In March 2025, Auryxia will lose exclusivity, or LoE. We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B could result in slower revenue decline after the LoE date than in other LoE situations, but the impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

Ferric citrate hydrate has also been approved in Japan, and is marketed and sold by our Japanese sublicensee, Japan Tobacco, Inc., and its subsidiary, Torii Pharmaceutical Co., Ltd., collectively, JT and Torii, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA under the trade name as Riona in Japan. Averoa SAS, or Averoa, has an exclusive license to develop and commercialize ferric citrate in the European Economic Area, or EEA, Turkey, Switzerland, the UK, the Balkans and certain countries in Eastern Europe and the Middle East. Averoa applied for marketing authorization for ferric citrate in Europe in April 2024.

**Our HIF-based product candidates and other pipeline assets** are being evaluated to target areas of unmet needs. The discovery of HIF laid the foundation to explore the central role of oxygen sensing in many diseases. As we have seen through the development of Vafseo as a treatment for anemia due to CKD, when stabilized, HIF triggers wide-ranging adaptive, protective responses during hypoxic or ischemic conditions. We have selected two additional HIF molecules for preclinical development: AKB-9090, potentially for cardiac surgery-related acute kidney injury, or CS-AKI, or acute respiratory distress syndrome, or ARDS, and AKB-10108 for retinopathy of prematurity, or ROP, in neonates.

In June 2021, we acquired from Cyclerion Therapeutics, Inc., or Cyclerion, an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator. We believe there is potential to explore the use of praliciguat for indications within kidney disease.

We continue to explore additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation to leverage our fully integrated team.

***Factors Affecting Our Performance and Results of Operations***

**Financial Highlights**

Net product revenue was $152.2 million and $170.3 million for the years ended December 31, 2024 and 2023, respectively.

We have incurred net losses in each year since inception. Our net losses were $69.4 million and $51.9 million for the years ended December 31, 2024 and 2023, respectively. Substantially all of our net losses resulted from costs incurred in connection with the continued commercialization of Auryxia and development and commercialization efforts relating to Vafseo, including conducting clinical trials of, and seeking regulatory approval for, Vafseo, providing general and administrative support for these operations and protecting our intellectual property.

**Financial Components**

***Product Revenue***

We generate product revenue from commercial sales of Auryxia in the U.S. to a limited number of customers, including dialysis organizations, wholesale distributors and certain specialty pharmacy providers. Our net product revenue includes many variables, including judgments and estimates of discounts, rebates and product returns, which can fluctuate from quarter-to-quarter and year-over-year. We evaluate, at least annually and more frequently, if needed, the price of Auryxia, which will lose exclusivity in March 2025. We expect our product revenue to continue to be generated from our commercial sales of Auryxia as well as to be generated from our commercial sales of Vafseo following its U.S. market entry in January 2025.

We believe the dynamics of Auryxia reimbursement being included in the end-stage renal disease, or ESRD, bundle under Medicare Part B and Auryxia LoE on March 20, 2025, could result in the buying pattern of certain customers in future years being different than their historical practices. In addition, we believe the dynamics of Auryxia reimbursement moving to Medicare Part B could result in slower revenue decline after the LoE date than in other LoE scenarios, but the impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

***License, Collaboration and Other Revenue***

License, collaboration and other revenue includes revenue earned under our agreements with our partners, including license fees, royalty payments and revenue from product we supply.

We expect to continue to generate revenue from our collaboration, license, and supply agreements with Medice, MTPC, JT and Torii and any other collaborations into which we have entered or may enter.

***Cost of Goods Sold***

Cost of goods sold, or COGS, - Cost of product and other revenue includes costs closely correlated or directly related to the costs to manufacture commercial drug substance and drug product, including at our contract manufacturing organizations, or CMOs, as well as indirect costs. Direct and indirect costs include fees for packaging, shipping, insurance and quality assurance, idle capacity charges, changes in reserves for excess inventory, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, including scrap, changes in our firm purchase commitment liability and royalties due to the licensor of Auryxia related to U.S. and Japan product sales recognized during the period.

COGS also includes costs to manufacture drug product provided to MTPC and Medice for commercial sale of Vafseo in Japan and the European Economic Area, or EEA, the United Kingdom, or UK, Switzerland and Australia, or the Medice Territory, respectively, as well as personnel-related costs, including salaries and bonuses, employee benefits and stock-based compensation attributable to employees in particular functions and associated directly with the manufacturing of our commercial products.

Cost of product and other revenue for a newly launched product does not include the full cost of manufacturing until the initial pre-launch inventory is depleted and additional inventory is manufactured and sold. Until we received regulatory approval for Vafseo in the U.S. we recorded costs incurred to manufacture the U.S. pre-launch inventory, such as raw materials, drug substance and drug product conversion costs as research and development, or R&D, expense.

Cost of goods sold - Amortization of intangible asset - In addition, COGS included the amortization of development product rights for Auryxia through the end of 2024.

***Research and Development Expenses***

R&D expenses consist primarily of costs incurred for the development of Vafseo prior to regulatory approval and costs associated with our pipeline which includes:

- personnel-related expenses, including salaries, bonuses, employee benefits, stock-based compensation and travel expenses for employees engaged in R&D functions;
- costs associated with feasibility and potential new manufacturing processes and methods for our commercial products;
- regulatory registration and related fees for non-commercial products;
- expenses incurred under agreements with contract research organizations, or CROs, and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical trial materials through CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies associated with our laboratory space as well as our R&D team;
- costs associated with discovery and development for preclinical, clinical and regulatory activities; and
- costs associated with the pre-launch inventory build for Vafseo in the U.S. prior to FDA approval in March 2024 and in Europe prior to the European Commission, or EC, approval in April 2023.

R&D costs are expensed as incurred. Advance payments made for goods or services to be received in the future for use in R&D activities are recorded as prepaid expenses and other current assets. The prepaid amounts are expensed as the benefits are consumed. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of our R&D projects, the costs of related clinical development, or if, when, or to what extent we will generate revenue from the commercialization or sale of any of our product candidates.

From inception through December 31, 2024, we have incurred $1.7 billion in R&D expenses. We expect to incur significant R&D expenditures for the foreseeable future as we continue the development of Auryxia, Vafseo and any other product or product candidate, including those that may be in-licensed or acquired.

A significant portion of our R&D costs have been external costs, which we track on a program-by-program basis as well as costs related to possible new manufacturing processes and methods associated with our commercial products. These external costs include fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials and costs related to acquiring and manufacturing clinical trial materials, including costs paid to CMOs to manufacture clinical trial materials.

We do not track our internal personnel and facilities costs on a program-by-program basis as our personnel are deployed across multiple R&D projects.

Each of our products and product candidates has technical, clinical, regulatory, and commercial risk, including those discussed more fully under the heading “Risk Factors” in Part I, Item 1A of this Form 10-K. A change in the outcome of any of the variables with respect to the development of Auryxia, Vafseo or any other product or product candidate could result in a significant change in the costs and timing associated with that development.

***Selling, General and Administrative Expenses***

Selling, general and administrative, or SG&A, expenses consist primarily of compensation for personnel, including stock-based compensation related to commercial, marketing, executive, finance and accounting, information technology, corporate and business development and human resource functions. Other SG&A expenses include costs for marketing initiatives for our commercial products, market research and analysis on our commercial products and potential product candidates, conferences and trade shows, travel expenses, professional services fees (including legal, patent, accounting, audit, tax, and consulting fees), insurance costs, general corporate expenses and allocated facilities-related expenses, including rent and maintenance of facilities.

***License Expense***

License expense relates to royalties due to Panion & BF Biotech, Inc., or Panion, for sales of Auryxia in the U.S. and Riona in Japan.

***Other Income (Expense), Net***

Other income (expense), net consists primarily of interest income on our interest-bearing accounts, interest expense related to our term loans, accretion of the debt discount on our term loans as well as changes in the fair value of our derivative liability and amortization of the discount on the liability related to the termination fees associated with the termination agreement with BioVectra Inc., or BioVectra, entered into in December 2022, or the BioVectra Termination Agreement. See Note 10, *Commitments and Contingencies,* in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information on the BioVectra Termination Agreement. Other income (expense), net also includes non-cash interest on our liability related to settlement royalties and the amortization of the discount and deferred gain related to our Working Capital Fund (as defined below) liability to Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information on our arrangements with CSL Vifor.

***Change in Fair Value of Warrant Liability***

Change in fair value of warrant liability relates to the change in fair value of our warrant liability related to a warrant agreement with Kreos Capital VII Aggregator SCSp, an affiliate of Kreos Capital VII (UK) Limited, or Kreos. See Note 3, *Fair Value of Financial Instruments*, and Note 7, *Indebtedness*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information on the warrant liability.

**Recent Events**

***Borrowing Under BlackRock Term Loans***

On February 3, 2025, we and Kreos, which are funds and accounts managed by BlackRock Inc., collectively, BlackRock, entered into the Second Amendment to the Agreement for the Provision of a Loan Facility, or the Second Amendment, which amended certain provisions of the Agreement for the Provision of a Loan Facility, dated January 29, 2024, or the BlackRock Credit Agreement. The BlackRock Credit Agreement provides for a senior secured term loan facility in the aggregate principal amount of up to $55.0 million, subject to certain customary conditions, or the Term Loan Facility.

The Term Loan Facility provided us access to three tranches: (i) an initial tranche of $37.0 million, which was funded on January 29, 2024, (ii) an additional tranche of $8.0 million, which was funded on April 19, 2024, and (iii) a final tranche of $10.0 million, which was available in a single draw through an expiry date of December 31, 2024, or the Prior Tranche C Loan. As a result of the Second Amendment, the Prior Tranche C Loan expiry date was extended until February 3, 2025, or the Extended Tranche C Loan. The terms of the Extended Tranche C Loan are substantially similar to the terms of the Prior Tranche C Loan, however, interest will accrue on the Extended Tranche C Loan as if it was advanced on December 31, 2024.

On February 3, 2025, we received $9.3 million on the Extended Tranche C Loan, after deducting debt issuance costs, interest, fees and expenses.

On February 3, 2025, in connection with the drawdown of the Extended Tranche C Loan, in accordance with the warrant agreement, dated as of January 29, 2024, between the Company and Kreos Capital VII Aggregator SCSp, or the Warrant Holder, we issued a warrant to the Warrant Holder to purchase 1,153,846 shares of our common stock, at an exercise price per share of $1.30. The warrant shall be exercisable for eight years from the date of issuance.

See Note 7, *Indebtedness*, and Note 18, *Subsequent Events*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

***Cyclerion Amendment***

In June 2021, we entered into a license agreement, or the Cyclerion Agreement, with Cyclerion under which we obtained an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase stimulator.

In December 2024, we amended the terms of the Cyclerion Agreement, pursuant to which we made an upfront payment of $1.25 million, and we will also pay Cyclerion $0.5 million on or before September 30, 2025. In addition, we and Cyclerion agreed to the reduction of certain development milestones and the increase of certain royalty rates on net sales and sublicense income. We now control all clinical and commercial manufacturing of praliciguat, which will be conducted by a third party manufacturer. We will also control patent prosecution and pay intellectual property costs starting April 1, 2025.

See Note 10, *Commitments and Contingencies*, for further details on the Cyclerion Agreement.

***U.S. Approval and Commercialization of Vafseo (vadadustat)***

In March 2024, we received approval from the FDA for Vafseo (vadadustat) Tablets for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months. Upon Vafseo approval, we implemented a launch plan to commercialize Vafseo for the treatment of anemia due to CKD in adult patients on dialysis, the critical first step toward Vafseo potentially becoming standard of care. We have completed certain critical commercialization initiatives, including securing

reimbursement for Vafseo under the Transitional Drug Add-on Payment Adjustment, or TDAPA, and securing access to Vafseo for patients through commercial supply agreements with dialysis organizations. The TDAPA program provides at least two years of reimbursement for Vafseo in addition to the end-stage renal disease, or ESRD, bundled rate to dialysis organizations. Additionally, we received a Level II Healthcare Common Procedure Coding System code for Vafseo which is used by dialysis organizations for billing the product for Medicare enrollees. Shipment of Vafseo commenced in January 2025.

***At-the-Market (ATM) Offering***

On September 3, 2024, in connection with the filing of a new shelf registration statement on Form S-3, we filed a prospectus related to our amended and restated sales agreement with Jefferies LLC (which amended and restated the prior sales agreement), pursuant to which we are able to offer and sell up to $75.0 million of our common stock at current market prices from time to time. Since September 12, 2024 (the date our shelf registration statement on Form S-3 went effective) through December 31, 2024, we sold 14,271,631 shares of our common stock under this program with gross proceeds of $24.3 million ($23.8 million, net of offering expenses). Including the amount sold during the year ended December 31, 2024 through the date of the filing of this Form 10-K, we sold 23,708,995 shares of our common stock under the sales agreement with gross proceeds of $43.0 million ($42.2 million, net of offering expenses).

***CSL Vifor Termination and Settlement Agreement***

On July 10, 2024, we and CSL Vifor entered into a Termination and Settlement Agreement, or the Vifor Termination Agreement. Pursuant to the Vifor Termination Agreement, we and CSL Vifor agreed, among other things, to terminate, effective immediately, the Second Amended and Restated License Agreement, dated February 18, 2022 and as amended May 3, 2024, or the Vifor License Agreement, pursuant to which we granted to CSL Vifor an exclusive license to sell Vafseo to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of certain group purchasing organizations, and to certain non-retail specialty pharmacies in the U.S. We and CSL Vifor agreed to terminate the Vifor License Agreement for business reasons.

See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the audited consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information on the Vifor Termination Agreement.

**Results of Operations**

***Comparison of the years ended December 31, 2024 and 2023***

| | Years ended December 31, | | Change | |
|---|---|---|---|---|
| *(dollars in thousands)* | **2024** | **2023** | **$** | **%** |
| Revenues | | | | |
| Product revenue, net | $ 152,180 | $ 170,301 | $ (18,121) | (11)% |
| License, collaboration and other revenue | 8,000 | 24,322 | (16,322) | (67)% |
| Total revenues | 160,180 | 194,623 | (34,443) | (18)% |
| Cost of goods sold | | | | |
| Cost of product and other revenue | 27,135 | 38,107 | (10,972) | (29)% |
| Amortization of intangible asset | 36,042 | 36,042 | — | — % |
| Total cost of goods sold | 63,177 | 74,149 | (10,972) | (15)% |
| Operating expenses | | | | |
| Research and development | 37,652 | 63,079 | (25,427) | (40)% |
| Selling, general and administrative | 106,545 | 100,233 | 6,312 | 6 % |
| License | 3,220 | 3,237 | (17) | * |
| Restructuring | 58 | 181 | (123) | (68)% |
| Total operating expenses | 147,475 | 166,730 | (19,255) | (12)% |
| Operating loss | (50,472) | (46,256) | (4,216) | 9 % |
| Other expense, net | (18,091) | (5,145) | (12,946) | 252 % |
| Change in fair value or warrant liability | (330) | — | (330) | * |
| Loss on extinguishment of debt | (517) | — | (517) | * |
| Loss on termination of lease | — | (524) | 524 | * |
| Net loss | $ (69,410) | $ (51,925) | $ (17,485) | 34 % |

*Percentage change not meaningful.

*Product Revenue, Net*—Net product revenue was derived solely from sales of Auryxia in the U.S. until Vafseo's U.S. market entry in January 2025. We distribute Auryxia principally through a limited number of dialysis organizations, wholesale distributors and certain specialty pharmacy providers.

Net product revenue was $152.2 million for the year ended December 31, 2024, compared to net product revenue of $170.3 million for the year ended December 31, 2023. The decrease was primarily due to a reduction in volume, partially offset by price increases and execution of our contracting strategy with third party payors.

Auryxia will lose exclusivity in the U.S. in March 2025, which may have a negative impact on revenue. We believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medicare Part B could result in slower revenue decline after the LoE date than in other LoE scenarios. However, our ability to continue to generate revenue from sales of Auryxia following LoE will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics that enter the market and the pricing of generics and other products on the market that compete with Auryxia.

*License, Collaboration and Other Revenue*—License, collaboration and other revenue was $8.0 million for the year ended December 31, 2024, compared to $24.3 million for the year ended December 31, 2023. The decrease was due primarily to a one-time $10.0 million upfront payment recognized in connection with the Medice License Agreement during the year ended December 31, 2023 as well as a reduction in revenue under our supply agreement with MTPC as a result of the assignment of our supply agreement with Esteve Química, S.A. to MTPC in December 2022. We also recognized $2.2 million in revenue in connection with the Packaging Validation Transfer Agreement we entered into with Otsuka during the year ended December 31, 2023.

See Note 12, *License, Collaboration and Other Revenue*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

A further breakdown of the license, collaboration and other revenue is as follows:

| | Years Ended December 31, | |
|---|---|---|
| **License, Collaboration and Other Revenue (dollars in thousands)** | **2024** | **2023** |
| ***License Fees:*** | | |
| Medice upfront license payment | $ — | $ 10,000 |
| ***Drug Product Supply:*** | | |
| MTPC Vafseo drug product supply | 717 | 3,738 |
| Medice Vafseo drug product supply | — | 968 |
| ***Drug Product Supply Subtotal*** | 717 | 4,706 |
| ***Royalties:*** | | |
| JT and Torii royalties | 5,366 | 5,394 |
| MTPC royalties | 1,895 | 1,997 |
| Medice royalties | 22 | — |
| ***Royalties Subtotal*** | 7,283 | 7,391 |
| Otsuka U.S. and International Agreements (Terminated) | — | 2,225 |
| Total License, Collaboration and Other Revenue | $ 8,000 | $ 24,322 |

*Cost of Goods Sold: Cost of Product and Other Revenue—Cost of product and other revenue* was $27.1 million for the year ended December 31, 2024, compared to $38.1 million for the year ended December 31, 2023. The decrease was primarily due to a $12.3 million benefit that we recorded during the year ended December 31, 2024 due to our ability to commercially sell inventory previously written down as excess inventory and lower year-over-year sales volume, which was partially offset by a $2.1 million charge related to our firm purchase commitment liability.

During the year ended December 31, 2023, we recorded a $4.3 million benefit due to our ability to commercially sell inventory previously written down as excess inventory, offset by a $1.5 million charge related to our firm purchase commitment liability.

*Cost of Goods Sold: Amortization of Intangible Asset*—Amortization of intangible asset relates to the acquired developed product rights for Auryxia, which was amortized using a straight-line method over its estimated useful life of approximately six years. Amortization of the intangible asset during each of the years ended December 31, 2024 and 2023 was $36.0 million. The intangible asset was fully amortized as of December 31, 2024.

R&D Expenses— R&D expenses were $37.7 million for the year ended December 31, 2024, compared to $63.1 million for the year ended December 31, 2023. The decrease was largely due to the completion of activities related to certain clinical trials, a reduction in consulting expenses associated with pursuing Vafseo regulatory approval in the Medice Territory in 2023, lower headcount related costs, including stock-based compensation and decreased professional service expenses. Additionally, during the year ended December 31, 2023, prior to receiving regulatory approval in the U.S., we recorded costs incurred to manufacture the U.S. pre-launch inventory as R&D expenses.

The following table summarizes our R&D expenses for the years ended December 31, 2024 and 2023 (in thousands):

| | Years ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Vafseo clinical trial and other external costs | $ 11,837 | $ 14,792 |
| Vafseo pre-launch inventory | — | 6,434 |
| External costs for other programs, including feasibility and new processes and methods associated with commercial products | 6,311 | 7,902 |
| Total external R&D expenses | 18,148 | 29,128 |
| Internal personnel, consulting, facilities and other | 19,504 | 33,951 |
| Total R&D expenses | $ 37,652 | $ 63,079 |

We expect to incur significant R&D expenses in future periods in support of ongoing or planned studies with respect to the development of our product candidates as well as Vafseo.

*Selling, General and Administrative Expenses*—SG&A expenses were $106.5 million for the year ended December 31, 2024, compared to $100.2 million for the year ended December 31, 2023. The increase was primarily due to higher headcount related costs and marketing costs in connection with the Vafseo U.S. launch in January 2025, as well as increased promotional expenses and registration and filing fees.

*License Expenses*—License expenses related to royalties due to Panion for sales of Riona in Japan were $3.2 million for each of the years ended December 31, 2024 and 2023.

*Restructuring Expenses*—Restructuring expenses were $0.1 million and $0.2 million for the years ended December 31, 2024 and 2023, respectively.

*Other Expense, Net*—Other expense, net, was $18.1 million for the year ended December 31, 2024, compared to $5.1 million for the year ended December 31, 2023. The increase was primarily due to $9.3 million of non-cash interest expense in 2024 related to the settlement royalty liability in connection with the Vifor Termination Agreement. In addition, during the year ended December 31, 2023, we recorded the change in the fair value of the embedded debt derivative related to the Pharmakon Term Loans (as defined below) as other income. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the audited consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Change in Fair Value of Warrant Liability*—Change in fair value of warrant liability was $0.3 million for the year ended December 31, 2024. There was no change in fair value of warrant liability for the year ended December 31, 2023 since the warrant agreement was entered into in January 2024.

*Loss on Extinguishment of Debt*—During the year ended December 31, 2024, we recorded a $0.5 million loss on the extinguishment of debt in connection with the repayment of the Pharmakon Term Loans.

*Loss on Lease Termination*—On May 26, 2023 we incurred a loss on lease termination of $0.5 million in connection with the assignment of our Boston Lease. In accordance with ASC 842, *Leases*, we wrote off the right-of-use asset and lease liability associated with the Boston Lease, and recognized the difference between the right-of-use asset and the lease liability offset by the $1.3 million payment we made to LG Chem Life Sciences Innovation Center, Inc. in connection with the assignment.

**Liquidity and Capital Resources**

As of December 31, 2024, we had cash and cash equivalents of approximately $51.9 million and restricted cash of $1.7 million.

To date, we have funded our operations principally through sales of our common stock, including through our employee stock purchase plan, product sales, payments received from our collaboration and licensing partners, borrowings under term loans, a working capital payment from CSL Vifor also referred to as a Working Capital Fund liability and a royalty transaction. From

inception through December 31, 2024, we raised approximately $862.8 million of net proceeds from the sale of equity, including $519.8 million from various underwritten public offerings, $273.0 million from at-the-market offerings pursuant to our sales agreement with Jefferies LLC and prior sales agreements with Cantor Fitzgerald & Co., and $70.0 million from the sale of 7,571,429 shares of common stock to CSL Vifor. From January 1, 2025 through the date of the filing of this Form 10-K, we sold 9,437,364 shares of our common stock under our current sales agreement with Jefferies LLC, resulting in proceeds to us of $18.4 million, net of offering expenses, which are not included in the above amounts reported under the ATM sales agreement.

We have incurred recurring losses and negative cash flow from operations in each year since inception and anticipate net losses for the near future. For the years ended December 31, 2024 and 2023, we incurred net operating losses of $69.4 million and $51.9 million, respectively. As of December 31, 2024 and 2023, we had an accumulated deficit of $1.7 billion.

We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that protect us from generic drug competition until March 2025. Following LoE in the U.S., we may not be able to realize enough product revenue from sales of Auryxia to realize net profits from product sales. While we believe the dynamics of Auryxia reimbursement being included in the ESRD bundle under Medical Part B could result in slower revenue decline after the LoE date than in other LoE scenarios, the impact of LoE on future Auryxia revenues will depend on many factors, including our ability to maintain contracts with dialysis organizations, the timing and number of generics and the pricing of generics and other products on the market that compete with Auryxia.

We believe our existing cash resources and the cash we expect to generate from product, royalty, supply and license revenues are sufficient to fund our current operating plan for at least twenty-four months. However, if our operating performance deteriorates significantly from the levels expected in our operating plan, it would have an adverse effect on our liquidity and capital resources and could affect our ability to continue as a going concern in the future. In addition, we may also seek to sell additional private or public equity, enter into new debt transactions, explore potential strategic transactions or a combination of these approaches or other strategic alternatives. If we raise additional funds by issuing equity securities, our shareholders would experience dilution. Debt financing, if available, may involve covenants restricting our operations or our ability to incur additional debt. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. Additional financing may not be available to us in amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital in sufficient amounts when needed or on attractive terms, we may not be able to pursue development and commercial activities related to Auryxia and Vafseo, or any additional products and product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period of time anticipated by us, or that additional funding will be available on terms acceptable to us, or at all. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both near- and long-term, will depend on many factors including, but not limited to, those described under Part I, Item 1A. Risk Factors under the heading "Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy."

***Contractual Obligations and Commitments***

*Debt Agreements and Other Funding Arrangements*

*BlackRock Term Loans*

On January 29, 2024, or the Closing Date, we entered into the BlackRock Credit Agreement, which provides for a senior secured term loan facility, in the aggregate principal amount of up to $55.0 million, or the Term Loan Facility. The Term Loan Facility was available in three tranches: (i) Tranche A — $37.0 million was funded on the Closing Date and used to repay the Pharmakon Term Loans; (i) Tranche B — $8.0 million was funded on April 19, 2024, and (ii) Tranche C — $10.0 million was funded on February 3, 2025, collectively, the Term Loans. The Term Loan Facility matures on January 29, 2028, or the BlackRock Maturity Date.

We are required to make interest-only payments until December 31, 2026 after which, we will begin making equal monthly principal payments. In the event of certain prespecified events, the repayment schedule will be accelerated.

The Term Loan Facility will accrue interest at a floating annual rate equal to the sum of (i) term Secured Overnight Financing Rate, or SOFR, for a tenor of one month (subject to a floor of 4.25% per annum) plus (ii) a margin of 6.75% per annum (subject to an overall cap of 15.00% per annum on the all-in interest rate). During the continuance of any payment event of default the

interest rate on such overdue sum will automatically increase by an additional 3.0% per annum, and may be subject to an additional late fee of 2.0% of such overdue sum.

All obligations under the Term Loan Facility are secured by substantially all of our existing and after-acquired assets. The BlackRock Credit Agreement requires us to either (i) maintain cash and cash equivalents, measured as of the last day of each fiscal month, greater than or equal to $15.0 million or (ii) earn consolidated revenue, measured as of the last day of each fiscal month for the trailing twelve-month period, of $150.0 million. The BlackRock Credit Agreement contains certain representations and warranties, affirmative and negative covenants that limit our ability to engage in specified types of transactions and other provisions typical within a credit agreement. If an event of default occurs and is continuing under the BlackRock Credit Agreement, BlackRock is entitled to take enforcement action, including acceleration of amounts due which could limit our ability to make certain payments under the Vifor Termination Agreement. If we prepay the Term Loans prior to the BlackRock Maturity Date, we will be required to pay a prepayment fee ranging from 1.0% to 4.0% of the amount prepaid.

On the Closing Date, Kreos Capital VII Aggregator SCSp, an affiliate of Kreos, or the Warrant Holder, received a warrant to purchase 3,076,923 shares of our common stock, at an exercise price per share of $1.30, and upon the borrowing of Tranche C in February 2025, we issued additional warrants to purchase 1,153,846 shares of our common stock at an exercise price per share of $1.30. Each warrant is exercisable for eight years from the date of issuance.

See Note 7, *Indebtedness,* in the accompanying notes to the audited consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Liability Related to Settlement Royalties*

Pursuant to the terms of the Vifor Termination Agreement, we will pay CSL Vifor decreasing quarterly tiered royalty payments ranging from a high single-digit percentage of our net sales of Vafseo up to $450.0 million to mid-single digit percentage of our net sales of Vafseo above $450.0 million, in each case, in the U.S. during a calendar year, or the Settlement Royalty Payments. The Settlement Royalty Payments will commence upon the first sale of Vafseo by us, our affiliates or third-party licensees to a third party for use in the U.S., and will continue until the later of the (i) expiration of the last-to-expire valid claim listed in the FDA Orange Book that would be infringed by the making, using, selling or importing of Vafseo in the U.S. or (ii) the expiration of marketing or regulatory exclusivity for Vafseo in the U.S., or the Settlement Royalty Term. Beginning on July 1, 2027 and throughout the Settlement Royalty Term, we have the option to make a one-time payment to CSL Vifor, or the Royalty Buy-Down Option, upon which the Settlement Royalty Payments will be adjusted as of the date of exercise of the Royalty Buy-Down Option such that we will then only pay CSL Vifor quarterly royalty payments based on a mid-single digit percentage of our net sales of Vafseo up to $450.0 million in the U.S. during a calendar year in lieu of the above Settlement Royalty Payments. If we exercise the Royalty Buy-Down Option, the WCF Royalty Payments will continue as described below.

The WCF Royalty Payments, as described below, the Settlement Royalty Payments and the Royalty Buy-Down Option are in consideration for the termination of the Vifor License Agreement and all obligations thereunder, and the covenants and agreements set forth in the Vifor Termination Agreement, including the settlement and release of all disputes and claims arising from the Vifor License Agreement.

As a result of the Vifor Termination Agreement, we concluded that CSL Vifor no longer met the definition of a customer and, therefore, the arrangement should not be considered a revenue contract with a customer under ASC 606, *Revenue from Contracts with Customers.* We therefore determined that the $43.3 million received from Vifor in connection with the Vifor License Agreement and related investment agreements should be classified as debt and we are amortizing such amount using the effective interest method over the Settlement Royalty Term. The liability related to settlement royalties and the amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. The annual effective interest rate as of December 31, 2024 was 41% which is reflected as interest expense in the consolidated statements of operations and comprehensive loss. We recognized interest expense of $9.3 million for the year ended December 31, 2024. As of December 31, 2024, $5.9 million and $46.7 million of the settlement royalties liability is classified as a current and non-current liability, respectively.

See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the audited consolidated financial statements in Part II, Item 8 of this Form 10-K for further information.

*Working Capital Fund Liability (Previously Referred to as Refund Liability to Customer)*

In February 2022, we amended our agreement with CSL Vifor and they contributed $40.0 million to a working capital fund, or the Working Capital Fund, established to partially fund our costs of purchasing Vafseo from our contract manufacturers.

Pursuant to the terms of the Vifor Termination Agreement, and generally consistent with the terms of the Vifor License Agreement, we agreed to repay the Working Capital Fund to CSL Vifor through quarterly tiered royalty payments ranging from 8% to 14% of our net sales of Vafseo in the U.S., or the WCF Royalty Payments. The WCF Royalty Payments will commence on

July 1, 2025, and will continue until the earlier of (i) the cumulative total of the WCF Royalty Payments equals $40.0 million, or (ii) May 31, 2028, or the WCF Royalty Term. The WCF Royalty Payments are subject to certain minimum true-up milestones.

The Working Capital Fund is considered a debt arrangement with zero coupon interest, and we impute interest on the Working Capital Fund liability at a rate of 15.0% per annum. As of December 31, 2024, $2.3 million and $38.0 million of the Working Capital Fund liability is classified as a current and non-current liability, respectively, based on management's estimated timing of the repayment of the Working Capital Fund liability to CSL Vifor.

See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the consolidated financial statements in Part II, Item 8 of this Form 10-K for further information.

*Liability Related to Sale of Future Royalties*

In February 2021, we sold to HealthCare Royalty Partners IV L.P., or HCR, our right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries, such countries collectively, the MTPC Territory, such payments collectively the Royalty Interest Payments, in each case, payable to us under the MTPC Agreement. The Royalty Interest Payments are subject to an annual maximum "cap" of $13.0 million, after which we will receive 85% of the Royalty Interest Payments for the remainder of that year. The Royalty Interest Payments are also subject to an aggregate maximum "cap" of $150.0 million, after which the Royalty Interest Payments will revert back to us.

We received $44.8 million from HCR, net of certain transaction expenses, which we recorded as a liability at the transaction date. We amortize the liability related to the sale of future royalties using the effective interest method over the life of the arrangement. The annual effective interest rate as of December 31, 2024 was 0%. We retain the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. During the year ended December 31, 2024 and 2023, we recorded $1.9 million and $2.0 million of non-cash royalty revenue, respectively. As of December 31, 2024, $2.0 million and $52.1 million of the liability related to the sale of future royalties is classified as a current and non-current liability, respectively.

See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, in the accompanying notes to the consolidated financial statements in Part II, Item 8 of this Form 10-K for further information.

***Off-Balance Sheet Arrangements***

*Letter of Credit*

As of December 31, 2024, in connection with the Cambridge Lease (as defined below), we had $1.7 million in a letter of credit outstanding.

*Director and Officer Indemnification*

We have entered into indemnification agreements with our directors and certain officers that will require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. No demands have been made upon us to provide indemnification under such agreements and there are no claims that we are aware of that could have a material effect on our consolidated financial statements.

***Contractual Obligations and Commitments Other Than Debt Agreements***

We are party to contractual obligations involving commitments to make payments to third parties in the future. Certain contractual obligations are reflected on our consolidated balance sheet as of December 31, 2024, while others are considered future obligations. Our material cash requirements as of December 31, 2024, include contractual obligations and commitments arising in the normal course of business, including leases, license agreements, manufacturing agreements and unconditional purchase commitments which are described in more detail below.

*Cambridge Lease*

We lease approximately 65,167 square feet of office, storage and laboratory space in Cambridge, Massachusetts under non-cancelable operating leases, collectively the Cambridge Lease. The office, storage and lab lease expires on September 11, 2026, and we are currently marketing the furnished office space for sublease.

See Note 9, *Leases*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*License Agreements*

*Panion License Agreement*

We have a license agreement with Panion, under which we are required to pay royalties related to the sale of Auryxia. The royalty payment obligations are contingent upon generating product revenue, and the amount and timing of such payments are not known. See Note 10, *Commitments and Contingencies*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Cyclerion Agreement*

In June 2021, we entered into the Cyclerion Agreement with Cyclerion, as amended in December 2024, under which we obtained an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase stimulator.

Under the Cyclerion Agreement, as amended, Cyclerion is eligible to receive up to an aggregate of $198.5 million from us in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from mid-single-digit percentage to twenty percent of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

See Note 10, *Commitments and Contingencies*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Manufacturing Agreements*

We have various supply arrangements to which we are a party, and we are obligated to pay for drug substance and drug product for commercial use. Under one of our agreements, we are required to purchase a minimum quantity of Auryxia drug substance at a predetermined price. We are also obligated to purchase a certain percentage of the global demand for Vafseo drug substance and drug product based on certain quarterly and annual forecasts we provide to certain suppliers. Our supply agreements for Vafseo drug substance and drug product provide for a volume-based pricing structure. We may also be required to reimburse certain suppliers for reasonable expenses.

See Note 10, *Commitments and Contingencies*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Amounts Due Under Former Manufacturing and Unconditional Purchase Commitments*

On December 22, 2022, we terminated any and all existing agreements with BioVectra for the supply of Auryxia drug substance. Under the BioVectra Termination Agreement, we agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million that was paid in December 2022 and (ii) six quarterly payments of $2.5 million which commenced in April 2024. In addition, we and BioVectra have released one another from all existing and future claims and liabilities and agreed to return certain materials and documents.

See Note 10, *Commitments and Contingencies*, in the accompanying notes to the consolidated financial statements included in Part II, Item 8 of this Form 10-K for further information.

*Other Third Party Contracts*

We enter into agreements in the normal course of business with various vendors, which are generally cancellable upon notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancellable obligations of service providers, up to the date of cancellation. In addition, we contract with various organizations to conduct R&D activities with remaining contract costs to us of approximately $48.0 million as of December 31, 2024. The scope of the services under these R&D contracts can be modified and the contracts cancelled by us upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

***Cash Flows***

The following table provides a summary of cash flow data for each applicable period:

| | Years ended December 31, | |
|---|---|---|
| **NET CASH PROVIDED BY/(USED IN)** *(in thousands)*: | **2024** | **2023** |
| Operating activities | $ (40,659) | $ (23,384) |
| Investing activities | (33) | — |
| Financing activities | 49,663 | (25,206) |
| Net increase (decrease) in cash, cash equivalents and restricted cash | **$ 8,971** | **$ (48,590)** |
| Cash, cash equivalents and restricted cash — beginning of period | 44,579 | 93,169 |
| **Cash, cash equivalents and restricted cash — end of period** | **$ 53,550** | **$ 44,579** |

***Operating Activities***

Net cash used in operating activities during the year ended December 31, 2024 was $40.7 million. Net cash used in operating activities during the year ended December 31, 2024 consisted of a net loss of $69.4 million and net non-cash adjustments of $68.4 million, including amortization of our intangible asset of $36.0 million, and a reduction of $39.7 million in working capital.

Net cash used in operating activities during the year ended December 31, 2023 was $23.4 million. Net cash used in operating activities during the year ended December 31, 2023 consisted of a net loss of $51.9 million and non-cash adjustments of $49.3 million, including amortization of our intangible asset of $36.0 million, and a reduction of $20.7 million in working capital.

***Investing Activities***

Net cash used in investing activities was immaterial during the year ended December 31, 2024.

No net cash was used in investing activities during the year ended December 31, 2023.

***Financing Activities***

Net cash provided by financing activities for the year ended December 31, 2024 was $49.7 million, which primarily consisted of proceeds of $45.0 million from the issuance of debt under the BlackRock Credit Agreement and net proceeds of $42.5 million from the sale of common stock under our ATM facility partially offset by principal payments of debt of $37.1 million primarily related to the Pharmakon Term Loans which were repaid in January 2024.

Net cash used in financing activities for the year ended December 31, 2023 was $25.2 million, which primarily consisted of principal payments of $32.0 million, partially offset by $6.7 million of net proceeds from the sale of common stock under our ATM facility and from the sale of stock under our employee stock purchase plan.

***Recent Accounting Pronouncements***

For a discussion of recent accounting pronouncements not yet adopted, see Note 2, *Summary of Significant Accounting Policies,* to our consolidated financial statements included in Part II, Item 8 of this Form 10-K.

**Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements included elsewhere in this Form 10-K, which consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, including the current or long-term classification of such assets, liabilities and expenses, classification of the expenses and the related disclosure of contingent assets and liabilities. We monitor our estimates on an ongoing basis for changes in facts and circumstances, and material changes in these estimates could occur in the future. Changes in estimates are recorded in the period in which they become known. We base our estimates on historical experience and other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate.

While our significant accounting policies are described in more detail in Note 2, *Summary of Significant Accounting Policies*, to our consolidated financial statements in Part II, Item 8 of this Form 10-K, we believe the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements and to understanding of our results of operations.

***Excess Firm Purchase Commitment Liability***

At each reporting period, we assess whether there are excess firm non-cancelable purchase commitment liabilities, resulting from supply agreements with third-party CMOs. The determination of excess firm purchase commitment liabilities requires judgment, including consideration of many factors, such as estimates of future product demand, current and future market conditions, impact of our loss of exclusivity, expiration and utilization of drug substance under firm purchase commitments, and contractual minimums. Any changes in the firm purchase commitment liability are recorded in cost of product and other revenue in the consolidated statements of operations and comprehensive loss.

***Product Revenue, Net***

We recognize revenue on product sales when the customer obtains control of our product, which occurs at a point in time, typically upon delivery to the customer. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

The most significant estimate we are required to make is related to government and private payor rebates, chargebacks, discounts and fees, collectively rebates (collectively considered variable consideration). The values of the rebates provided to third-party payors vary significantly and are based on government-mandated discounts and our arrangements with other third-party payors. To estimate our total rebates, we estimate the percentage of prescriptions that will be covered by each third-party payor, which is referred to as the payor mix. Thus, revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration, which are described below. We track available information regarding changes, if any, to the payor mix for our products, to our contractual terms with third-party payors and to applicable governmental programs and regulations and levels of our products in the distribution channel. We adjust our estimated rebates based upon new information as it becomes available, including information regarding actual rebates for our products and forecasted customer buying and payment demands. Claims by third-party payors for rebates are submitted to us significantly after the related sales, potentially resulting in adjustments in the period in which the new information becomes known. Our adjustments to revenue related to prior period sales have not been significant.

Further details on the variable consideration components or reserves include:

- *Trade Discounts and Allowances*—Discounts that include incentive fees that are explicitly stated in our contracts. In addition, we compensate (through trade discounts and allowances) our customers for sales order management, data and distribution services.
- *Product Returns*—Consistent with industry practice, subject to certain caps for certain customers, we generally offer customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer, or is subject to a recall. This right of return generally lapses once the product is provided to a patient. We estimate the amount of our product sales that may be returned for credit by our customers. Product return reserves are estimated primarily based on our gross sales multiplied by an estimated return rate calculated using our historical actual rate of return for product sales as well as recent trends on lots still subject to the return window. In addition, certain customers are subject to an annual cap on returns of 2% of gross sales in any given year.
- *Provider Chargebacks and Discounts*—Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period end that we expect will be sold to qualified healthcare providers and chargebacks that customers have claimed but for which we have not yet issued a credit.
- *Commercial and Medicare Part D Rebates*—We contract with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate the rebates for commercial and Medicare Part D payors based upon (i) our contracts with the payors and (ii) information obtained from our customers and other third parties regarding the payor mix for Auryxia.
- *Other Government Rebates*—We are subject to discount obligations under state Medicaid programs and other government programs. We estimate Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

- *Other Incentives*—Other incentives that we offer include voluntary patient assistance programs such as our co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount we expect to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts. Our calculation of the reserves, include estimates and judgments that materially affect our recognition of net product revenues. Changes in our estimates of net product revenues could have a material effect on net product revenues recorded in the period in which we determine that change occurs.

**Item 7A. Quantitative and Qualitative Disclosures about Market Risk**

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act, and are not required to provide information under this item.

**Item 8. Financial Statements and Supplementary Data**



All financial statement schedules have been omitted, since the required information is not applicable or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements and accompanying notes.

**Report of Independent Registered Public Accounting Firm**

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' (deficit) equity and cash flows for each of the two years in the period ended December 31, 2024, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 13, 2025 expressed a qualified opinion thereon.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

**Critical Audit Matter**

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

***Valuation of Excess Firm Purchase Commitment Liability***

*Description of the Matter*

As of December 31, 2024, the Company's liability for excess firm purchase commitments related to its commercial supply agreement with a third-party contract manufacturing organizations was $3.6 million. As described in Note 2 and Note 10, the Company records a liability for its firm purchase commitment that exceeded the Company's estimates of future demand and expiry of inventory. The Company re-evaluates its liability for excess firm purchase commitments each reporting period to assess whether any adjustments are necessary. The Company's evaluations of purchase commitments for Auryxia resulted in the Company recording charges to cost of product and other revenue sold of $2.1 million during the year ended December 31, 2024.

Auditing management's estimate for its excess firm purchase commitment liability is especially challenging because the estimate relies on subjective management assumptions about the estimates of future product demand, which is affected by current and future market conditions and the impact of the Company's loss of exclusivity that can have a material effect on the liability.

*How We Addressed the Matter in Our Audit*

To test the Company's determination of its excess firm purchase commitment liability, our audit procedures included, among other procedures, testing the completeness and accuracy of the underlying data used in the evaluation of the Company's excess firm purchase commitment liability, including evaluating the reasonableness of the Company's estimates of future product demand. We compared the expectations of demand to contractual arrangements with customers, industry trends, historical financial results, and evaluated the consistency of the forecast with those used by management for other purposes. We also performed sensitivity analyses over the significant assumptions used to measure the excess firm purchase commitment liability and evaluated any contrary evidence identified when considering the reasonableness of the significant assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 13, 2025

**AKEBIA THERAPEUTICS, INC.**
**CONSOLIDATED BALANCE SHEETS**

| *(dollars in thousands, except per share amounts)* | December 31, 2024 | December 31, 2023 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 51,870 | $ 42,925 |
| Inventories | 16,243 | 15,691 |
| Accounts receivable, net | 34,368 | 39,290 |
| Prepaid expenses and other current assets | 11,350 | 20,243 |
| **Total current assets** | 113,831 | 118,149 |
| Property and equipment, net | 2,200 | 3,629 |
| Operating right-of-use assets | 8,218 | 12,416 |
| Intangible asset, net | — | 36,042 |
| Goodwill | 59,044 | 59,044 |
| Other long-term assets | 37,377 | 12,423 |
| **Total assets** | $ 220,670 | $ 241,703 |
| **Liabilities and stockholders' deficit** | | |
| Current liabilities: | | |
| Accounts payable | $ 15,180 | $ 14,635 |
| Accrued expenses and other current liabilities | 63,460 | 67,735 |
| Current portion of long-term debt | — | 17,500 |
| Working Capital Fund liability, current portion | 2,274 | — |
| **Total current liabilities** | 80,914 | 99,870 |
| Long-term deferred revenue | — | 43,296 |
| Long-term operating lease liabilities | 3,547 | 8,947 |
| Long-term debt, net | 38,693 | 17,183 |
| Liability related to settlement royalties, net of current portion | 46,697 | — |
| Liability related to sale of future royalties, net of current portion | 52,066 | 54,013 |
| Working Capital Fund liability, net of current portion | 38,013 | 40,093 |
| Warrant liability | 5,176 | — |
| Other long-term liabilities | 4,749 | 8,885 |
| **Total liabilities** | 269,855 | 272,287 |
| **Commitments and contingencies (Note 10)** | | |
| **Stockholders' deficit:** | | |
| Preferred stock $0.00001 par value, 25,000,000 shares authorized; no shares issued and outstanding at December 31, 2024 and 2023 | — | — |
| Common stock: $0.00001 par value; 350,000,000 shares authorized at December 31, 2024 and 2023; 224,848,992 and 194,582,539 shares issued and outstanding at December 31, 2024 and 2023, respectively | 2 | 2 |
| Additional paid-in capital | 1,629,167 | 1,578,358 |
| Accumulated other comprehensive income | 6 | 6 |
| Accumulated deficit | (1,678,360) | (1,608,950) |
| **Total stockholders' deficit** | (49,185) | (30,584) |
| **Total liabilities and stockholders' deficit** | $ 220,670 | $ 241,703 |

The accompanying notes are an integral part of these consolidated financial statements.

**AKEBIA THERAPEUTICS, INC.**
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**

| *(dollars in thousands, except per share amounts)* | Years Ended December 31, 2024 | 2023 |
|---|---|---|
| **Revenues:** | | |
| Product revenue, net | $ 152,180 | $ 170,301 |
| License, collaboration and other revenue | 8,000 | 24,322 |
| Total revenues | 160,180 | 194,623 |
| **Cost of goods sold:** | | |
| Cost of product and other revenue | 27,135 | 38,107 |
| Amortization of intangible asset | 36,042 | 36,042 |
| Total cost of goods sold | 63,177 | 74,149 |
| **Operating expenses:** | | |
| Research and development | 37,652 | 63,079 |
| Selling, general and administrative | 106,545 | 100,233 |
| License | 3,220 | 3,237 |
| Restructuring | 58 | 181 |
| Total operating expenses | 147,475 | 166,730 |
| **Loss from operations** | (50,472) | (46,256) |
| **Other income (expense):** | | |
| Interest expense | (18,185) | (6,032) |
| Other income | 94 | 887 |
| Change in fair value of warrant liability | (330) | — |
| Loss on extinguishment of debt | (517) | — |
| Loss on termination of lease | — | (524) |
| **Net loss before income taxes** | (69,410) | (51,925) |
| **Net loss** | $ (69,410) | $ (51,925) |
| **Comprehensive loss** | $ (69,410) | $ (51,925) |
| | | |
| Net loss per share: | | |
| Basic and diluted | $(0.33) | $(0.28) |
| | | |
| Weighted average number of common shares outstanding: | | |
| Basic and diluted | 210,946,658 | 187,465,448 |

The accompanying notes are an integral part of these consolidated financial statements.

**Akebia Therapeutics, Inc.**
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY**

| *(dollars in thousands)* | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Accumulated Deficit | Total Stockholders' (Deficit) Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| **Balance at December 31, 2022** | **184,135,714** | **$ 2** | **$ 1,562,247** | **$ 6** | **$ (1,557,025)** | **$ 5,230** |
| Issuance of common stock, net of issuance costs | 6,189,974 | — | 6,708 | — | — | 6,708 |
| Proceeds from sale of stock under employee stock purchase plan | 200,194 | — | 85 | — | — | 85 |
| Stock-based compensation expense | — | — | 9,317 | — | — | 9,317 |
| Restricted stock unit vesting | 4,054,407 | — | — | — | — | — |
| Exercise of options | 2,250 | — | 1 | — | — | 1 |
| Net loss | — | — | — | — | (51,925) | (51,925) |
| **Balance at December 31, 2023** | **194,582,539** | **$ 2** | **$ 1,578,358** | **$ 6** | **$ (1,608,950)** | **$ (30,584)** |
| Issuance of common stock, net of issuance costs | 27,532,942 | — | 42,495 | — | — | 42,495 |
| Proceeds from sale of stock under employee stock purchase plan | 189,732 | — | 153 | — | — | 153 |
| Stock-based compensation expense | — | — | 7,775 | — | — | 7,775 |
| Restricted stock unit vesting | 2,099,540 | — | — | — | — | — |
| Exercise of options | 444,239 | — | 386 | — | — | 386 |
| Net loss | — | — | — | — | (69,410) | (69,410) |
| **Balance at December 31, 2024** | **224,848,992** | **$ 2** | **$ 1,629,167** | **$ 6** | **$ (1,678,360)** | **$ (49,185)** |

The accompanying notes are an integral part of these consolidated financial statements.

**Akebia Therapeutics, Inc.**
**CONSOLIDATED STATEMENT OF CASH FLOWS**

| *(dollars in thousands)* | Years Ended December 31, 2024 | 2023 |
|---|---|---|
| **Operating Activities:** | | |
| Net loss | $ (69,410) | $ (51,925) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation | 1,462 | 1,585 |
| Amortization of intangible asset | 36,042 | 36,042 |
| Bad debt expense | 876 | — |
| Change in fair value of warrant liability | 330 | — |
| Non-cash interest expense | 13,069 | (2,228) |
| Non-cash royalty revenue related to sale of future royalties | (1,895) | (1,977) |
| Non-cash research and development expense | — | 782 |
| Amortization of right-of-use assets | 4,198 | 4,219 |
| Non-cash write-off on termination of lease | — | (825) |
| Loss on extinguishment of debt | 294 | — |
| Write-down of inventory | 4,208 | 1,580 |
| Change in firm purchase commitments | 2,068 | 1,533 |
| Stock-based compensation expense | 7,775 | 9,317 |
| Change in fair value of embedded debt derivative | — | (760) |
| Changes in operating assets and liabilities: | | |
| Accounts receivable | 4,046 | 994 |
| Inventories | (28,401) | (2,542) |
| Prepaid expenses and other current assets | 8,893 | 11,839 |
| Other long-term assets | 622 | (1,361) |
| Accounts payable | (1,364) | (5,244) |
| Accrued expense and other current liabilities | (12,777) | (10,021) |
| Lease liabilities | (4,491) | (4,963) |
| Deferred revenue | — | (3,738) |
| Other long-term liabilities | (6,204) | (5,691) |
| **Net cash used in operating activities** | (40,659) | (23,384) |
| **Investing Activities:** | | |
| Purchase of property and equipment | (33) | — |
| **Net cash provided by (used in) investing activities** | (33) | — |
| **Financing Activities:** | | |
| Proceeds from the issuance of debt | 45,000 | — |
| Payments of issuance costs related to BlackRock Credit Agreement | (1,272) | — |
| Proceeds from the issuance of common stock, net of issuance costs | 42,495 | 6,708 |
| Proceeds from the sale of stock under employee stock purchase plan | 154 | 85 |
| Proceeds from the exercise of common stock options | 385 | 1 |
| Repayment of term debt | (37,099) | (32,000) |
| **Net cash (used in) provided by financing activities** | 49,663 | (25,206) |
| Increase (decrease) in cash, cash equivalents and restricted cash | 8,971 | (48,590) |
| Cash, cash equivalents and restricted cash at beginning of the period | 44,579 | 93,169 |
| **Cash, cash equivalents and restricted cash at end of the period** | $ 53,550 | $ 44,579 |
| | | |
| **Non-cash financing activities** | | |
| Issuance of warrants in connection with BlackRock Credit Agreement | $ 4,846 | $ — |
| **Supplemental disclosure of cash flow information:** | | |
| Cash paid for interest | $ 5,035 | $ 6,059 |

The accompanying notes are an integral part of these consolidated financial statements.

**Akebia Therapeutics, Inc.**
**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS**

## 1. NATURE OF BUSINESS

***Organization***

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007 and became a public company in 2014. Akebia is a fully integrated commercial-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics.

The Company has two products approved by the Food and Drug Administration, or FDA, in the United States, or U.S. Vafseo® (vadadustat) is an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor. Vafseo (vadadustat) Tablets were approved in the U.S. in March 2024 for the treatment of anemia due to chronic kidney disease, or CKD, in adults who have been receiving dialysis for at least three months. Vafseo entered the U.S. market in January 2025. Auryxia® (ferric citrate) is marketed for two indications: (i) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, and (ii) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis dependent chronic kidney disease, or NDD-CKD. Auryxia will lose exclusivity in the U.S. in March 2025.

Vafseo is also approved for the treatment of symptomatic anemia associated with CKD in the European Economic Area, or EEA, the United Kingdom, or the UK, Switzerland, Australia, South Korea and Taiwan in adult patients on chronic maintenance dialysis and in Japan for adult dialysis-dependent and non-dialysis patients. Vafseo is marketed and sold by the Company's collaboration partners in certain countries.

Ferric citrate is also approved in Japan, and is marketed and sold by the Company's collaboration partner, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA under the trade name Riona (ferric citrate hydrate).

Since its inception, the Company has devoted most of its resources to research and development, or R&D, including its preclinical and clinical development activities, commercializing Auryxia and Vafseo and providing general and administrative support for these operations. The Company began recording revenue from the U.S. sales of Auryxia and revenue from sublicensing rights to Auryxia in Japan from the Company's Japanese partners, Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively, JT and Torii, in 2018. In addition, the Company continues to explore additional development opportunities to expand its pipeline and portfolio of novel therapeutics.

As of December 31, 2024, the Company had cash and cash equivalents of approximately $51.9 million. Based on its current operating plan, the Company believes that its cash resources and the cash the Company expects to generate from product, royalty, supply and license revenues will be sufficient to fund its current operating plan through at least twelve months from the filing of this Annual Report on Form 10-K, or Form 10-K. However, if the Company's operating performance deteriorates significantly from the levels expected in the Company's operating plan, it would affect the Company's liquidity and its ability to continue as a going concern in the future. The Company expects to finance future cash needs through product and collaboration, license and other revenue, including royalties and revenue from supply agreements. In addition, the Company may seek to sell public or private equity, enter into new debt transactions, explore potential strategic transactions, consider other cash-generating or saving measures or a combination of these approaches or other strategic alternatives. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by the Company or that its cash resources will fund its operating plan for the period of time anticipated by the Company, or that additional funding will be available on terms acceptable to the Company, or at all.

## 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

***Basis of Presentation and Principles of Consolidation***

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S., or GAAP. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in the consolidated financial statements herein.

Certain monetary amounts, percentages and other figures included elsewhere in these consolidated financial statements have been subject to rounding adjustments. Accordingly, figures shown as totals in certain tables may not be the arithmetic aggregation of the figures that precede them, and figures expressed as percentages in the text may not total 100% or, as applicable, when aggregated, may not be the arithmetic aggregation of the percentages that precede them.

***Use of Estimates***

The preparation of financial statements in conformity with U.S. GAAP, requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, revenue and expenses, classification of the expenses, assets and liabilities and the disclosure of contingent assets and liabilities as of and during the reported period. On an ongoing basis, management evaluates its estimates. Management bases its estimates and assumptions on historical experience when available and on various factors, including expected business and operational changes, sensitivity and volatility associated with the assumption that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of the assets and liabilities that are not readily apparent from other sources. In certain circumstances, management must apply significant judgment in these processes. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management selects an amount that falls within that range of reasonable estimates. Although, the Company regularly assesses these estimates, actual results may differ materially from those estimates and changes in estimates are recorded in the period they become known.

Significant estimates and judgments reflected in these consolidated financial statements include, but are not limited to: accrued expenses, other long-term liabilities, a liability related to settlement royalties, revenues, including various rebates, returns and reserves related to product sales, inventories, classification of expenses between cost of goods sold, R&D and selling, general and administrative, long-term assets, including the Company's right-of-use assets and goodwill.

***Cash, Cash Equivalents and Restricted Cash***

In determining cash, cash equivalents and restricted cash, the Company considers only those highly liquid investments, readily convertible to cash within 90 days from the date of purchase to be cash equivalents. As of December 31, 2024, cash and cash equivalents primarily included cash on hand.

Restricted cash represents amounts required to secure the outstanding letter of credit in connection with the Company's office and laboratory space in Cambridge, Massachusetts, or the Cambridge Lease. Restricted cash is included in "other long-term assets" in the consolidated balance sheets.

The following table reconciles cash, cash equivalents and restricted cash reported within the Company's consolidated balance sheets to the total amounts reported in the consolidated statements of cash flows:

| | December 31, | |
|---|---|---|
| *Reconciliation of cash, cash equivalents and restricted cash (in thousands)* | **2024** | **2023** |
| Cash and cash equivalents | $ 51,870 | $ 42,925 |
| Restricted cash included in other long-term assets | 1,680 | 1,654 |
| Total cash, cash equivalents and restricted cash | $ 53,550 | $ 44,579 |

***Fair Value of Financial Instruments***

Fair value is defined as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities required to be recorded at fair value, management considers the principal or most advantageous market in which it would transact and considers assumptions that market participants would use when pricing the asset or liability. ASC Topic 820, *Fair Value Measurement*, establishes a fair value hierarchy that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. To the extent the valuation is based on models or inputs that are less observable in the market, the determination of fair values requires more judgment. A financial instrument categorization within the fair value hierarchy is based upon the lowest level of input that is significant to the fair value measurement. The three levels of inputs that may be used to measure fair value are:

- **Level 1** – unadjusted quoted prices in active markets for identical assets or liabilities to the reporting entity at the measurement date.
- **Level 2** – quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly, for substantially the full term of the asset or liability.

- **Level 3** – unobservable inputs for the asset or liability used to measure fair value to the extent that observable inputs are not available, thereby allowing for situations in which there is little, if any, market activity for the asset or liability at the measurement date.

***Accounts Receivable***

The Company's accounts receivable represent amounts due to the Company from product sales and from its collaboration, license and other agreements. Reimbursable costs that have not been invoiced as of the balance sheet date are recorded as unbilled accounts receivable. Accounts receivable arising from product sales primarily represent amounts due from the Company's customers, net of allowances for customer discounts and chargebacks. The Company deducts trade allowances for prompt payment, among other certain discounts or chargebacks, from its accounts receivable based on its experience that the Company's customers will earn these discounts and fees.

***Concentrations of Risk and Off-Balance Sheet Risk***

*Credit Risk*

Cash, cash equivalents and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains cash accounts principally at two financial institutions in the U.S., which at times, may exceed the Federal Deposit Insurance Corporation's limits. The Company has not experienced any losses from cash balances in excess of the insurance limit. The Company's management does not believe the Company is exposed to significant credit risk at this time due to the financial condition of the financial institutions where its cash is held.

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding receivables and the overall quality and age of those invoices not specifically reviewed as well as historical payment patterns and existing economic factors. The Company believes that credit risks associated with its customers and collaboration partners are not significant. The Company's allowance for credit losses was $1.2 million and $1.0 million as of December 31, 2024 and 2023, respectively.

The following table summarizes the activity related to the Company's allowance for credit losses (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Beginning balance | $ 1,029 | $ 1,106 |
| Provision for bad debts | 877 | (77) |
| Recoveries/(write-offs) | (695) | — |
| Ending balance | $ 1,212 | $ 1,029 |

Gross revenues and accounts receivable from each of the Company's customers or collaboration partners who individually accounted for 10% or more of total gross revenues and/or 10% or more of total gross accounts receivable consisted of the following:

| | % of Total Gross Revenues | |
|---|---|---|
| | Years Ended December 31, | |
| **Customer** | **2024** | **2023** |
| Fresenius Medical Care Rx | 48% | 40% |
| Cencora, Inc., formerly known as AmerisourceBergen Drug Corporation | 19% | 21% |
| McKesson Corporation | 12% | 11% |
| Cardinal Health, Inc. | * | 10% |

| | % of Gross Accounts Receivable | |
|---|---|---|
| | December 31, | |
| Customer | 2024 | 2023 |
| Fresenius Medical Care Rx | 42% | 31% |
| Cencora, Inc., formerly known as AmerisourceBergen Drug Corporation | 13% | 25% |
| DaVita | 16% | * |
| Cardinal Health, Inc. | * | 16% |
| McKesson Corporation | * | 12% |

**Percentage less than 10% threshold.*

*Off-Balance Sheet Accounts*

The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangement. See Note 9, *Leases,* for further details.

*Manufacturing and Distribution Risk.*

The Company is dependent on third-party manufacturers, logistics companies and distributors to supply products for commercial activities associated with its product and product candidates, as applicable. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to the Company's product and product candidate activities. These activities, including the commercialization of Auryxia and Vafseo, could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs or distribution of finished product to the market.

***Inventories, including Pre-Launch Inventories***

The Company values its inventories at the lower-of-actual cost or net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials, manufacturing services and overhead, on a first-in, first-out basis. Inventory expected to be utilized beyond one year is recorded in inventories, long-term on the consolidated balance sheets.

Prior to obtaining regulatory approval for an investigational product candidate, the Company expenses costs relating to production of pre-launch inventory as R&D expense in its consolidated statements of operations and comprehensive loss in the period incurred. After regulatory approval has been received, the Company capitalizes such inventory costs. Products used in clinical trials are expensed as R&D expense in the statement of operations and comprehensive loss.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess or obsolete inventory to its net realizable value in the period in which the impairment is identified through cost of product and other revenue in the consolidated statements of operations and comprehensive loss.

Additionally, the Company's product is subject to strict quality control and monitoring that is performed throughout the manufacturing process, including release of work-in-process to finished goods. In the event that certain batches or units of product do not meet quality specifications, the Company will record a write-down of any potential unmarketable inventory to its estimated net realizable value and record the expense as cost of product and other revenue in the consolidated statements of operations and comprehensive loss.

The Company prepays for certain manufacturing costs, including raw materials and drug substance, to its CMOs which are included in prepaid expenses and other current assets on the consolidated balance sheets.

***Property and Equipment***

Property and equipment are recorded at cost, less accumulated depreciation. Expenditures for repairs and maintenance are expensed as incurred. Depreciation expense is recognized using the straight-line method over the estimated useful lives, which are typically:

| Asset Category | Estimated Useful Life |
|---|---|
| Computer equipment and software | 3 years |
| Furniture and fixtures | 5 years - 7 years |
| Laboratory and other equipment | 7 years |
| Leasehold improvements | Shorter of the useful life or remaining lease term |

Maintenance and repairs to an asset that do not improve or extend its life are charged to operations. When assets are retired or otherwise disposed of, the assets and related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the Company's consolidated statements of operations and comprehensive loss.

***Intangible Asset***

The Company maintained a definite-lived intangible asset related to developed product rights for Auryxia. The intangible asset was initially recorded at fair value and was stated net of accumulated amortization. The Company amortized its intangible asset that had a finite life using the straight-line method over the estimated useful life of six years. The Company's intangible asset was fully amortized as of December 31, 2024.

***Goodwill***

Goodwill reflects the excess purchase price over the fair value of the net tangible and intangible assets acquired in a business combination.

Goodwill is evaluated for impairment on an annual basis, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist. The Company compares the fair value of its reporting unit to its carrying value. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of its reporting unit, the Company would record an impairment loss equal to the difference. The Company operates in one operating segment which the Company considers to be the only reporting unit.

***Impairment of Long-Lived Assets and Intangible Asset Subject to Amortization***

Long-lived assets primarily include property and equipment, right of use assets and an intangible asset. The Company evaluates its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of such asset groups may not be recoverable. The recoverability of asset groups to be held and used is measured by a comparison of the carrying amount of an asset group to the future undiscounted net cash flows expected to be generated by the asset group. If such asset groups are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset group exceeds the fair value of the asset group.

The Company did not recognize any impairment losses on long-lived assets for the years ended December 31, 2024 and 2023, respectively.

***Leases***

The Company made an accounting policy election not to recognize leases with an initial term of twelve months or less within its consolidated balance sheets and to recognize those lease payments as an expense on a straight-line basis in its consolidated statements of operations and comprehensive loss. The Company also made the accounting policy election not to separate the non-lease components from the lease components for its building leases and, rather, account for each non-lease component and lease component as a single component.

The Company determines if an arrangement is a lease at inception. An arrangement is determined to contain a lease if the contract conveys the right to control the use of an identified property, plant or equipment for a period of time in exchange for consideration. If the Company can benefit from the various underlying assets of a lease on their own or together with other resources that are readily available, or if the various underlying assets are neither highly dependent on nor highly interrelated with other underlying assets in the arrangement, they are considered to be a separate lease component. In the event multiple underlying assets are identified, the lease consideration is allocated to the various components based on each of the component’s relative fair value.

Operating lease assets represent the Company’s right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the leasing arrangement. The right-of-use asset and operating lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. The Company uses the implicit rate when readily determinable and uses an estimate of its incremental borrowing rate when the implicit rate is not readily determinable based upon the available information at the commencement date of lease inception. The incremental borrowing rate is determined using a credit rating scoring model to estimate the Company’s credit rating, adjusted for collateralization. The calculation of the right-of-use asset includes any lease payments made and excludes any lease incentives. If a lease includes an option to extend or terminate the lease, the Company reflects the option in the lease term if it is reasonably certain the Company will exercise the option.

The Company’s operating leases are reflected in operating right-of-use assets, accrued expenses and other current liabilities and long-term operating lease liabilities in its consolidated balance sheets.

***Liability Related to Sale of Future Royalties***

The Company accounts for the liability related to sale of future royalties as a debt financing, amortized under the effective interest rate method over the estimated life of the related expected royalty stream. The liability related to sale of future royalties and the debt amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. The Company will periodically assess the expected royalty payments. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. In the event the Company's estimates of future royalties are less than the proceeds from the sale of future royalties, the Company will not recognize related non-cash interest expense. Non-cash royalty revenue is reflected as royalty revenue within license, collaboration and other revenue, and non-cash amortization of debt is reflected as interest expense in the consolidated statements of operations and comprehensive loss. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for more information.

***Working Capital Fund Liability (Previously Referred to as Refund Liability to Customer)***

The Company accounts for the Working Capital Fund liability as a debt arrangement, which is recorded at net present value. When the funds were received, the Company recorded an initial discount on the Working Capital Fund liability and a corresponding deferred gain to the Working Capital Fund liability. The discount on the Working Capital Fund liability is being amortized to interest expense on the consolidated statement of operations and comprehensive loss and the deferred gain is being amortized to other income on the consolidated statement of operations and comprehensive loss over the expected term of the arrangement. On a quarterly basis, the Company reassesses the effective rate and will adjust the rate prospectively, if needed. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for more information.

***Liability Related to Settlement Royalties***

The Company accounts for the liability related to settlement royalties as a liability, amortized using the effective interest method over the term of the arrangement. The liability related to settlement royalties and the amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for more information.

***Warrant Liability***

The Company accounts for the warrant liability under ASC 815, *Derivatives and Hedging*, as it could potentially require net cash settlement outside of the Company's control. The warrant liability is measured at fair value each period with changes in fair value presented within the consolidated statements of operations and comprehensive loss. See Note 7, *Indebtedness*, for more information.

***Excess Firm Purchase Commitment Liability***

At each reporting period, the Company assesses whether there are excess firm non-cancelable purchase commitment liabilities, resulting from supply agreements with third-party CMOs. The determination of excess firm purchase commitment liabilities requires judgment, including consideration of many factors, such as estimates of future product demand, current and future market conditions, impact of the Company's loss of exclusivity, expiration and utilization of drug substance under firm purchase commitments, and contractual minimums. Any changes in the firm purchase commitment liability are recorded in cost of product and other revenue in the consolidated statements of operations and comprehensive loss.

***Revenue Recognition***

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when, or as, the performance obligation is satisfied.

The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year. Additionally, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that the Company otherwise would have recognized is one year or less.

*Product Revenue, Net*

The Company recognizes product revenues on sales of Auryxia primarily attributable to a limited number of customers, including dialysis organization, wholesale distributors and certain specialty pharmacy providers, in the U.S., which accounts for the largest portion of the Company's total revenue. These customers resell the Company's product to health care providers and patients. In addition to distribution agreements with customers, the Company enters into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of the Company's product. The Company's payment terms are consistent with prevailing practice in the respective markets in which the Company does business. Most of the Company's customers make payments based on contract terms, which are not affected by contingent events that could impact the transaction price. Payment terms fall within the one-year guidance for the practical expedient, which allows the Company to forgo adjustment of the contractual payment amount of consideration for the effects of a significant financing component.

The Company recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time, typically upon receipt of the product by the Company's customer. The Company expenses incremental costs of obtaining a contract, such as sales commissions, as and when incurred, if the expected amortization period of the asset that it would have recognized is one year or less. Sales commissions are recorded in selling, general and administrative expense in the statements of operations and comprehensive loss.

Revenue from product sales is recorded at the net sales price, or Transaction Price, which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances offered within contracts between the Company and its customers, health care providers, payors and other indirect customers relating to the Company's sales of its products. When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns.

The amount of variable consideration that is included in the Transaction Price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. The reserves are classified as reductions to accounts receivable, net of payable, if the trade discount and/or allowance will be credited to the customer or accrued expenses and other current liabilities or other long-term liabilities, if payable to a third-party in the consolidated balance sheets.

*Trade Discounts and Allowances*—The Company generally provides customers with prompt pay discounts and pays fees for distribution services, such as fees for certain data that customers provide to the Company. Trade discounts and allowances are recorded as a reduction of revenue within the consolidated statements of operations and comprehensive loss in the period the related product revenue is recognized. The Company estimates that, based on its experience, its customers will earn these discounts and fees, and the Company will deduct the full amount of these discounts and fees from its gross product revenues and accounts receivable at the time such revenues are recognized.

*Product Returns*—Consistent with industry practice, subject to certain caps for certain customers, the Company generally offers customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer or is subject to a recall. This right of return generally lapses once the product is provided to a patient or generally, if the bottle has been opened. The Company estimates the amount of its product sales that may be returned and records this estimate as a reduction of revenue in the period the related

product revenue is recognized. The Company currently estimates product return reserve using its own historical return information.

*Provider Chargebacks and Discounts*—Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's resale of the product. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed but for which the Company has not yet issued a credit.

*Commercial and Medicare Part D Rebates*—The Company contracts with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates the rebates for commercial and Medicare Part D payors based upon (i) its contracts with the payors and (ii) information obtained from its customers and other third parties regarding the payor mix. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of an accrued liability.

*Other Government Rebates*—The Company is subject to discount obligations under state Medicaid programs and other government programs. The Company estimates its Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities in the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

*Other Incentives*—The Company offers a voluntary patient co-pay assistance program, which provides financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period plus an estimate of the amount the Company expects to pay based on historical utilization rates for the product that has been recognized as revenue but is estimated to be remaining in in the distribution channel at the end of each reporting period.

*License, Collaboration and Other Revenues*

The Company enters into license and collaboration agreements within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include the following: (i) non-refundable, up front licenses fees associated with the licensing of intellectual property; (ii) development, regulatory and commercial milestone payments; (iii) drug product the Company supplies in connection with certain license and collaboration agreements and (iv) royalties earned on net sales of licensed products.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company implements the five-step model noted above. As part of the accounting for these arrangements, the Company develops assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. A deliverable represents a separate performance obligation if both of the following criteria are met: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer, and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

*Licenses of Intellectual Property*

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

*Milestone Payments*

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to assess the milestone as probable of being achieved. There is considerable judgement involved in determining whether a milestone is probable of being reached at each specific reporting period. Milestone payments that are not within the control of the Company or the customer, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration, license and other revenue in the period of adjustment.

*Drug Product Supply*

Collaboration and license arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as a separate performance obligation. If the Company is entitled to additional payments when the licensee exercises these options, any payments are recorded in license, collaboration and other revenues when the licensee obtains control of the goods, which is generally upon delivery.

*Royalties*

The Company will recognize sales-based royalties, including milestone payments based on the level of net sales, at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

*Collaborative Arrangements*

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, *Collaborative Arrangements,* or ASC 808. Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities are recorded as collaborative arrangements. The Company considers the guidance in ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*, in determining the appropriate treatment for the transactions between the Company and its collaborative partners and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. To the extent product revenue is generated from the collaboration, the Company recognizes its share of the net sales on a gross basis if the Company is deemed to be the principal in the transactions with customers, or on a net basis if the Company is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

***Cost of Goods Sold***

Cost of goods sold, or COGS, includes costs closely correlated or directly related to the costs to manufacture commercial products, including costs paid to the Company's contract manufacturing organizations, or CMOs, as well as indirect costs. Direct and indirect costs include fees for packaging, shipping, insurance and quality assurance, idle capacity charges, routine testing costs, routine ongoing efforts to improve existing commercial products, reserves for excess inventory, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, including scrap, changes in

firm purchase commitment liability and royalties due to the licensor of Auryxia related to U.S. and Japan product sales recognized during the period. In addition, COGS includes the amortization of development product rights for the Auryxia intangible asset. The Company also includes personnel-related costs, including salaries and bonuses, employee benefits and stock-based compensation attributable to employees in particular functions and associated directly with the manufacturing of our commercial products.

Further, the Company includes in COGS costs to manufacture drug product provided to customers for which it has a license agreement. Cost of goods sold for a newly launched product may not include the full cost of manufacturing until the initial pre-launch inventory is depleted, and additional inventory is manufactured and sold.

Until the Company received regulatory approval for Vafseo in the U.S. in March 2024, the Company recorded expenses incurred for the manufacture of pre-launch inventory that would support a U.S. launch as R&D expense. The costs associated with the pre-launch inventory for the Medice Territory were expensed to R&D through April 2023 when marketing authorization was received.

***Research and Development Expenses***

R&D costs are expensed as incurred. Internal R&D expenses are comprised of costs incurred in providing R&D activities, including salaries and bonuses, employee benefits, stock-based compensation for personnel engaged in R&D activities. In addition, they include facility costs, including the laboratory and an allocation of office space for utilization by R&D staff, depreciation expense on the laboratory equipment as well as other direct costs such as lab supplies and equipment.

External R&D costs include development of potential new manufacturing processes and methods for both commercial and non-commercial products, conceptual formulation and design of possible product and process alternatives, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support and materials and supplies used in support of the clinical and preclinical programs and costs paid to clinical resource organizations, or CRO, including investigative sites that conduct the Company's clinical trials.

Non-refundable advance payments for goods and services are recorded in prepaid and other current assets in the consolidated balance sheets and expensed when the activity is performed or when the goods are received. In addition, the costs associated with pre-launch inventory, including the cost of raw materials, costs paid to contract manufacturers for inventory manufacturing, freight and custom charges for Vafseo were expensed as R&D prior to regulatory approval.

***Selling, General and Administrative Expenses***

Selling, general and administrative, or SG&A, expenses consist primarily of compensation for personnel, including stock-based compensation related to commercial, marketing, executive, finance and accounting, information technology, corporate and business development and human resource functions. Other SG&A expenses include costs for marketing initiatives for the Company's commercial products, market research and analysis on the Company's commercial products and potential product candidates, conferences and trade shows, travel expenses, professional services fees (including legal, patent, accounting, audit, tax, and consulting fees), insurance costs, general corporate expenses and allocated facilities-related expenses, including rent and maintenance of facilities. Costs associated with advertising are expensed in the period incurred and are included in selling, general and administrative expenses. For the years ended December 31, 2024 and 2023, advertising expenses totaled $4.6 million and $1.0 million, respectively.

***Patent Costs***

All patent-related costs incurred in connection with the filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Such amounts incurred are classified as SG&A expenses in the accompanying consolidated statements of operations and comprehensive loss.

***Stock-Based Compensation***

The Company’s stock-based compensation program allows for grants of common stock options, restricted stock awards, performance-based restricted stock units, or PSUs, stock appreciation rights, or SARs and restricted stock units. Grants are awarded to employees and non-employees, including directors.

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees and non-employees, including modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. The Company estimates the fair value of options granted using the Black-Scholes option pricing model, or Black-Scholes. The Company uses the market price at the time of grant to determine the fair value of restricted stock awards and performance-based restricted stock awards.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Prior to 2017, due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company had based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility was calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the Securities and Exchange Commission, or SEC, Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The Company recognizes forfeitures as they occur.

The Company's stock-based awards are subject to either service or performance-based vesting conditions. Compensation expense related to awards to employees and non-employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. Compensation expense related to awards to employees and non-employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

***Income Taxes***

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2024 and 2023 are classified as non-current within the income tax provision. See Note 15, *Income Taxes*, for further information.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of December 31, 2024 and 2023, the Company does not have any significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

***Net Loss per Share***

Basic net loss per share is calculated by dividing net loss by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, common stock options, stock appreciation rights, warrants and RSUs as well as restricted stock, if the Company was to issue any, are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented. Diluted net income per share is calculated by dividing the net income by the weighted-average common shares outstanding for the period, including any dilutive effect from outstanding options, warrants, restricted stock and RSUs using the treasury stock method.

***Segment Information***

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or CODM, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company operates its business in a single segment and as one reporting unit, which is how its chief operating decision maker (who is the Company's president and chief executive officer) reviews financial performance and allocates resources. The Company views its operations as and manages its business in one operating segment.

***New Accounting Pronouncements - Recently Adopted***

In November 2023, the FASB issued ASU 2023-07, *Improvements to Reportable Segment Disclosures*. ASU 2023-07 requires disclosure of significant segment expenses that are regularly provided to the CODM and included within the segment measure of profit or loss, an amount and description of its composition for other segment items to reconcile to segment profit or loss, and the title and position of the entity's CODM. ASU 2023-07 is applied retrospectively and is effective for annual reporting periods in fiscal years beginning after December 15, 2023, and interim reporting periods in fiscal years beginning after December 31, 2024. See Note 17, *Segment Information*, for further information.

***New Accounting Pronouncements - Not Yet Adopted***

In December 2023, the FASB issued ASU 2023-09, *Income Taxes* (Topic 740): *Improvements to Income Tax Disclosures*. ASU 2023-09 requires public companies to annually (i) disclose specific categories in the rate reconciliation and (ii) provide additional information for reconciling items that meet a quantitative threshold (if the effect of those reconciling items is equal to or greater than 5 percent of the amount computed by multiplying pretax income or loss by the applicable statutory income tax rate). ASU 2023-09 will be effective for the annual reporting periods in fiscal years beginning after December 15, 2024. The Company is currently evaluating ASU 2023-09 and does not expect it to have a material effect on the Company's consolidated financial statements.

In November 2024, the FASB issued an accounting standards update, ASU 2024-03, which requires new tabular disclosures in the notes to consolidated financial statements, disaggregating certain cost and expense categories within relevant captions on the consolidated statements of operations and comprehensive loss. The prescribed cost and expense categories requiring disaggregated disclosures include purchases of inventory, employee compensation, depreciation and intangible asset amortization, along with certain other expense disclosures already required by U.S. GAAP that would need to be integrated within the new tabular disaggregated expense disclosures. Additionally, the amendments also require the disclosure of total selling expenses and an entity's definition of those expenses. ASU 2024-03 will be effective for annual reporting periods in fiscal years beginning after December 15, 2026, and interim reporting periods in fiscal years beginning after December 31, 2027. Early adoption is permitted and the amendments should be applied on a prospective basis. Retrospective application is permitted. The Company is currently reviewing the impact that the adoption of ASU 2024-03 may have on its expense disclosures in the notes to the consolidated financial statements.

## 3. FAIR VALUE MEASUREMENTS

The tables below present certain assets and liabilities measured at fair value categorized by the level of input used in the valuation of each asset and liability (in thousands):

| | December 31, 2024 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Long-term liability:** | | | | |
| Warrant liability | $ — | $ 5,176 | — | $ 5,176 |

| | December 31, 2023 | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| **Cash equivalents:** | | | | |
| Money market funds | $ 1,504 | — | — | $ 1,504 |

*Warrant liability* – The warrant liability is classified within Level 2 of the fair value hierarchy because it is valued using inputs which are observable either directly or indirectly. The fair value was calculated using the Black-Scholes option pricing model using the following key inputs: volatility, risk-free rate, dividend yield and expected term. As of December 31, 2023, the Company did not have a warrant liability.

*Cash and cash equivalents* —Money market funds included within cash and cash equivalents are classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices in active markets. As of December 31, 2024, the Company did not have any money market funds included in cash equivalents.

**4. INVENTORIES**

Inventories consists of the following (in thousands):

| | December 31, | |
|---|---|---|
| Inventories, current: | 2024 | 2023 |
| Work-in-process | $ 12,031 | $ 4,297 |
| Finished goods | 4,212 | 11,394 |
| Inventories, current | $ 16,243 | $ 15,691 |
| Long-term inventories included in other long-term assets: | | |
| Raw materials | 381 | 1,143 |
| Work-in-process | 34,572 | 8,260 |
| Inventories, long-term | 34,953 | 9,403 |
| Total inventories | $ 51,196 | $ 25,094 |

Inventory written down for Auryxia as a result of excess, obsolescence, scrap or other reasons charged to cost of product and other revenue in the consolidated statements of operations and comprehensive loss totaled approximately $4.2 million and $1.6 million during the years ended December 31, 2024 and 2023, respectively. For the years ended December 31, 2024 and 2023, the Company realized $12.3 million and $4.3 million, respectively, of lower cost of product and other revenue due to the Company's ability to commercially sell inventory previously written down to zero, its then net realizable value.

Prior to the FDA's approval of Vafseo on March 27, 2024, all costs for the manufacture of product to support clinical development and commercial launch, including pre-launch inventory, were expensed as incurred. Pre-launch inventory manufactured prior to the FDA approval of Vafseo will be used in commercial production until it is depleted. As of December 31, 2024 and 2023, the Company had cumulatively expensed $28.4 million in pre-launch inventory costs for Vafseo intended for the U.S. launch.

**5. INTANGIBLE ASSET AND GOODWILL**

*Intangible Asset*

Intangible asset, net of accumulated amortization, prior impairments and adjustments as of December 31, 2024 and 2023 consisted of the following (in thousands):

| | December 31, 2024 | | | December 31, 2023 | |
|---|---|---|---|---|---|
| **Intangible asset:** | **Gross Carrying Value** | **Accumulated Amortization** | **Net Book Value** | **Net Book Value** | **Estimated Useful Life** |
| Developed product rights for Auryxia | $ 214,705 | $ (214,705) | $ — | $ 36,042 | 6 years |

The Company recorded $36.0 million in amortization expense during each of the years ended December 31, 2024 and 2023 related to the developed product rights for Auryxia. As of December 31, 2024, the intangible asset is fully amortized.

*Goodwill*

As of December 31, 2024 and 2023, the Company had goodwill of $59.0 million recorded in connection with the December 2018 merger with Keryx Biopharmaceuticals, Inc., or Keryx. The Company has not identified any goodwill impairment to date.

**6. ADDITIONAL BALANCE SHEET DETAIL**

Prepaid expenses and other current assets are as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Prepaid manufacturing | 4,029 | 14,489 |
| Other | 7,321 | 5,754 |
| Total prepaid expenses and other current assets | 11,350 | 20,243 |

Prepaid manufacturing expenses include advance payments to contract manufacturing organizations, or CMOs, for active pharmaceutical ingredient or drug substance. Such amounts are reclassified to work-in-process inventory upon the quality release of the batches and transfer of title to the Company from the CMO. Prior to receiving regulatory approval for Vafseo,

such amounts were expensed to R&D upon the quality release of the batches and transfer of title to the Company from the CMO. See Note 4, *Inventories*, for further information on inventories, including pre-launch inventory.

Other long-term assets are as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Long-term inventories | $ 34,953 | $ 9,403 |
| Restricted cash | 1,680 | 1,654 |
| Other | 744 | 1,366 |
| Total other long-term assets | $ 37,377 | $ 12,423 |

See Note 4, *Inventories*, for further information on long-term inventories.

Accrued expenses and other current liabilities are as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Product revenue allowances | $ 15,727 | $ 22,940 |
| Product return reserves, current portion | 5,295 | 5,420 |
| Compensation and related benefits | 9,194 | 8,216 |
| Operating lease liabilities, current portion | 5,400 | 4,491 |
| Royalties due to Panion & BF Biotech, Inc. | 3,543 | 3,989 |
| Liability related to sale of future royalties, current portion | 2,039 | 2,048 |
| Professional fees | 1,452 | 1,909 |
| Accrued manufacturing costs | 1,468 | 5,555 |
| BioVectra, Inc. termination fees, current portion | 7,204 | 7,500 |
| Settlement royalties liability, current portion | 5,924 | — |
| Clinical trial costs | 1,885 | 328 |
| Restructuring costs, current portion | 489 | 737 |
| Other | 3,840 | 4,602 |
| Total accrued expenses and other current liabilities | $ 63,460 | $ 67,735 |

## 7. INDEBTEDNESS

***Entry into BlackRock Loan Facility***

On January 29, 2024, or the Closing Date, the Company entered into the Agreement for the Provision of a Loan Facility, or the BlackRock Credit Agreement, with Kreos Capital VII (UK) Limited, or Kreos, which are funds and accounts managed by BlackRock Inc., collectively, BlackRock, and provides for a senior secured term loan facility in the aggregate principal amount of up to $55.0 million, or the Term Loan Facility. The Term Loan Facility was available in three tranches: (i) Tranche A — $37.0 million was funded on the Closing Date and used to repay the Pharmakon Term Loans; (ii) Tranche B — $8.0 million was funded on April 19, 2024, or the Tranche B Closing Date, and (ii) Tranche C — $10.0 million was funded on February 3, 2025, or the Tranche C Closing Date, collectively the Term Loans.

On February 3, 2025, the Company and Kreos entered into a Second Amendment to the Agreement for the Provision of a Loan Facility, or the Second Amendment, which, among other things, extended the expiry date of Tranche C from December 31, 2024 to the Tranche C Closing Date, or the Extended Tranche C. Tranche C was available subject to receipt of a certain amount of cumulative gross cash proceeds after the Closing Date in the form of equity or equity linked securities in one or more series of transactions. The terms of the Extended Tranche C are substantially similar to the terms of the original Tranche C, however, interest will accrue on the Extended Tranche C as if it was advanced on December 31, 2024. See Note 18, *Subsequent Events*, for further details on the Second Amendment.

On the Closing Date, the Company received $34.5 million on Tranche A, after deducting debt issuance costs, fees and expenses. On the Tranche B Closing Date, the Company received $7.5 million, after deducting debt issuance costs, fees and expenses. On the Tranche C Closing Date, the Company received $9.3 million, after deducting debt issuance costs, interest, fees and expenses.

The BlackRock Term Loan Facility had an initial maturity date of March 31, 2025, which was automatically extended to January 29, 2028, or the BlackRock Maturity Date, after the Company received FDA approval for Vafseo. The Company is required to make interest-only payments until December 31, 2026, or the BlackRock Interest Only Period, after which the Company will begin paying equal monthly principal on the first calendar day of each month. In the event of certain prespecified events, the repayment schedule will be accelerated.

The Term Loan Facility will accrue interest at a floating annual rate equal to the sum of (i) term Secured Overnight Financing Rate, or SOFR, for a tenor of one month (subject to a floor of 4.25% per annum) plus (ii) a margin of 6.75% per annum (subject to an overall cap of 15.00% per annum on the all-in interest rate). As of December 31, 2024, the Company's interest rate was 11.09%. During the year ended December 31, 2024, the Company recognized interest expense of $7.1 million.

During the continuance of any payment event of default under the BlackRock Credit Agreement, the interest rate on such overdue sum will automatically increase by an additional 3.0% per annum, and may be subject to an additional late fee of 2.0% of such overdue sum. The Term Loan Facility also includes transaction fees ranging from 1.00% to 1.25% of the draw down amount as well exit fees of 0.75% of the amount funded to the relevant tranche.

If the Company prepays the outstanding loan prior to maturity, it will be required to pay a prepayment fee ranging from 1.0% to 4.0% of the amount prepaid. If prepayment is made during the first year, the Company also is required to pay the amount of otherwise due interest payments for the twelve-month period following prepayment.

As of December 31, 2024, future principal payments under the BlackRock Credit Agreement are as follows (in thousands):

| Years ended December 31, | Amounts |
|---|---|
| 2025 | — |
| 2026 | — |
| 2027 | 41,363 |
| 2028 | 1,589 |
| Total before unamortized discount and issuance costs | 42,952 |
| Less: unamortized discount and issuance costs | (4,259) |
| Total term loans | $ 38,693 |

The BlackRock Term Loan Facility is secured by substantially all of the existing and after-acquired assets of the Company, including intellectual property. The BlackRock Credit Agreement requires the Company to (i) maintain a minimum aggregate cash balance of $15.0 million in one or more controlled accounts or (ii) trailing twelve-month revenue of $150.0 million, both of which are measured monthly. The BlackRock Credit Agreement contains certain representations and warranties, affirmative and negative covenants that limit the Company's ability to engage in specified types of transactions and other provisions typical within a credit agreement. If an event of default occurs and is continuing under the BlackRock Credit Agreement, BlackRock is entitled to take enforcement action, including acceleration of amounts due and it could limit the Company's ability to make certain payments under the Vifor Termination Agreement (as defined below).

On July 10, 2024, in connection with the Vifor Termination and Settlement Agreement, or the Vifor Termination Agreement, the Company and Kreos entered into a First Amendment to the BlackRock Credit Agreement, or the BlackRock Credit Amendment, which amended certain provisions of the BlackRock Credit Agreement. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for further information on the Vifor Termination Agreement.

***Warrant***

On the Closing Date, Kreos Capital VII Aggregator SCSp, an affiliate of Kreos, or the Warrant Holder, received a warrant to purchase 3,076,923 shares of the Company’s common stock, at an exercise price per share of $1.30, or the Initial Warrant. On the Tranche C Closing Date, the Company issued the Warrant Holder additional warrants to purchase 1,153,846 shares of the Company’s common stock at an exercise price per share of $1.30, or the Tranche C Warrant. Each warrant is exercisable for eight years from the date of issuance. See Note 18, *Subsequent Events*, for further details on the Tranche C Warrant.

The Initial Warrant is liability classified under ASC 815, *Derivatives and Hedging*, as it could potentially require net cash settlement outside of the Company’s control. The Initial Warrant is measured at fair value each period with changes in fair value presented within the consolidated statements of operations and comprehensive loss. The fair value of the warrant liability was $5.2 million as of December 31, 2024. See Note 3, *Fair Value of Financial Instruments*, for information on the fair value determination.

***Other Agreements Accounted for as Debt***

The Company has a liability related to settlement royalties and a Working Capital Fund liability with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, and a liability related to the sale of future royalties, which are accounted for as debt arrangements. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for further information.

***Pharmakon Term Loan (Extinguished January 29, 2024)***

On November 11, 2019, the Company, with Keryx as guarantor, entered into a loan agreement, or the Pharmakon Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, and a Guaranty and Security Agreement with the Collateral Agent. BioPharma Credit PLC subsequently transferred its interest in the loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent and the lenders are collectively referred to as Pharmakon. The Pharmakon Loan Agreement, as amended, consisted of a secured term loan facility in an aggregate amount of up to $100.0 million, or Pharmakon Term Loans, which was made available under two tranches: (i) Tranche A — $80.0 million and (ii) Tranche B — $20.0 million. On November 25, 2019, the Company drew $77.3 million on Tranche A, net of fees and expenses of $2.7 million. On December 10, 2020, the Company drew $20.0 million on Tranche B, net of immaterial lender expenses and issuance costs.

On the Closing Date, using the proceeds from the BlackRock Credit Agreement, the Company paid the then outstanding principal balance on the Pharmakon Term Loans of $35.0 million, plus the outstanding interest and a prepayment fee of $0.2 million. During the year ended December 31, 2024, the Company recorded a debt extinguishment loss of $0.5 million.

The Pharmakon Term Loans, as amended, bore interest through maturity at a variable rate based on the three month SOFR plus a SOFR adjustment of 0.30% plus 7.50%. The SOFR interest rate was capped at 3.35% through October 31, 2023, the date of the Fourth Amendment to the Pharmakon Loan Agreement, or Fourth Amendment. The Company recognized immaterial interest expense and $6.0 million of interest expense related to the Pharmakon Loan Agreement during the years ended December 31, 2024 and 2023, respectively.

**8. LIABILITY RELATED TO SETTLEMENT ROYALTIES, WORKING CAPITAL FUND LIABILITY AND LIABILITY RELATED TO SALE OF FUTURE ROYALTIES**

***Vifor License Agreement***

*Summary of Agreement*

On February 18, 2022, the Company entered into a Second Amended and Restated License Agreement, or the Vifor License Agreement, with CSL Vifor, which amended and restated the License Agreement dated as of May 12, 2017, or the Original License Agreement. The Vifor License Agreement granted CSL Vifor an exclusive license to sell Vafseo to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by the Company, to independent dialysis organizations that were members of certain group purchasing organizations and certain non-retail specialty pharmacies, collectively, the Supply Group, in the U.S.

The Vifor License Agreement was structured as a profit share arrangement between the Company and CSL Vifor in which the Company would receive approximately 66% of the profit, net of certain pre-specified costs. In addition, CSL Vifor made an upfront payment to the Company of $25.0 million in February 2022 in connection with the amendment and restatement of the Vifor License Agreement, which was previously recorded as long-term deferred revenue in the consolidated balance sheets.

*Investment Agreements*

In connection with the Original License Agreement, in May 2017, the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or 2017 Shares, to CSL Vifor at a price per share of $14.00 for a total of $50.0 million.

In February 2022, in connection with the Vifor License Agreement, the Company sold an aggregate of 4,000,000 shares of its common stock, or 2022 Shares, to CSL Vifor at a price per share of $5.00 for a total of $20.0 million.

The $18.3 million, which represented the premiums over the closing stock price, or $4.7 million for the 2017 Shares and $13.6 million for the 2022 Shares, was previously recorded as long-term deferred revenue in the consolidated balance sheets as it represented consideration related to the Vifor License Agreement.

The 2017 Shares and 2022 Shares are subject to standstill agreement and are subject to voting agreements. The 2017 Shares and 2022 Shares have not been registered pursuant to the Securities Act of 1933, as amended, or the Securities Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder as the transaction did not involve any public offering within the meaning of Section 4(a)(2) of the Securities Act.

*Vifor Termination Agreement*

On July 10, 2024, the Company and CSL Vifor entered into the Vifor Termination Agreement, pursuant to which the Company and CSL Vifor agreed, among other things, to terminate, effective immediately, the Vifor License Agreement.

Pursuant to the terms of the Vifor Termination Agreement, the Company will pay CSL Vifor decreasing quarterly tiered royalty payments ranging from a high single-digit percentage of the Company's net sales of Vafseo up to $450.0 million to mid-single digit percentage of the Company's net sales of Vafseo above $450.0 million, in each case, in the U.S. during a calendar year, or the Settlement Royalty Payments. The Settlement Royalty Payments will commence upon the first sale of Vafseo by the Company, its affiliates or third-party licensees to a third party for use in the U.S., and will continue until the later of the (i) expiration of the last-to-expire valid claim listed in the FDA Orange Book that would be infringed by the making, using, selling or importing of Vafseo in the U.S. or (ii) the expiration of marketing or regulatory exclusivity for Vafseo in the U.S., or the Settlement Royalty Term. Beginning on July 1, 2027 and throughout the Settlement Royalty Term, the Company has the option to make a one-time payment to CSL Vifor, or the Royalty Buy-Down Option, upon which the Settlement Royalty Payments will be adjusted as of the date of exercise of the Royalty Buy-Down Option such that the Company will then only pay CSL Vifor quarterly royalty payments based on a mid-single digit percentage of the Company's net sales of Vafseo up to $450.0 million in the U.S. during a calendar year in lieu of the above Settlement Royalty Payments. If the Company exercises the Royalty Buy-Down Option, the WCF Royalty Payments, as described below, will continue as described above.

The WCF Royalty Payments, as described below, the Settlement Royalty Payments and the Royalty Buy-Down Option are in consideration for the termination of the Vifor License Agreement and all obligations thereunder, and the covenants and agreements set forth in the Vifor Termination Agreement, including the settlement and release of all disputes and claims arising from the Vifor License Agreement.

At inception, the Company evaluated the elements of the Vifor License Agreement in accordance with the provisions of ASC 606, *Revenue from Contracts with Customers,* and concluded that CSL Vifor, was a customer. Furthermore, the Company identified one performance obligation under the Vifor License Agreement, which was the non-sublicensable, non-transferrable license under certain of the Company's intellectual property to (i) sell Vafseo solely to the Supply Group, (ii) sell Vafseo to Designated Wholesalers solely for resale to members of the Supply Group, (iii) conduct medical affairs with respect to Vafseo in the U.S. in the field during the term of the Vifor License Agreement and (iv) use the Akebia Trademark solely in connection with the sale of Vafseo. The transaction price of $43.3 million comprised of the $25.0 million upfront payment and the premiums paid by CSL Vifor for the 2017 Shares and 2022 Shares of $4.7 million and $13.6 million, respectively, was constrained at inception and recorded as long-term deferred revenue due to certain conditions in which the Company would be required to repay the consideration received from CSL Vifor.

As a result of the Vifor Termination Agreement, the Company reassessed whether the Vifor License Agreement still met the criteria to be considered a contract within the scope of ASC 606 and concluded that the arrangement should not be considered a revenue contract with a customer under ASC 606 as CSL Vifor no longer met the definition of a customer. Furthermore, the Company determined that the consideration received from CSL Vifor of $43.3 million should be classified as debt. Accordingly, the Company recorded the $43.3 million as a liability and is amortizing such amount using the effective interest method over the Settlement Royalty Term. The liability related to settlement royalties and the amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize the related non-cash interest expense on a prospective basis. On a quarterly basis, the Company reassesses the expected royalty payments.

The annual effective interest rate as of December 31, 2024 was 41.0% which is reflected as interest expense in the consolidated statements of operations and comprehensive loss. The Company recognized interest expense of $9.3 million for the year ended December 31, 2024. As of December 31, 2024 and 2023, the balances related to the settlement royalties liability were as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Current portion (included in accrued expenses and other current liabilities) | $ 5,924 | $ — |
| Long-term portion | 46,697 | — |
| Total settlement royalties liability | $ 52,621 | $ — |

***Working Capital Fund Liability (Previously Referred to as Refund Liability to Customer)***

Pursuant to the Vifor License Agreement, CSL Vifor contributed $40.0 million to a working capital fund, or Working Capital Fund, established to partially fund the Company's costs of purchasing Vafseo from its contract manufacturers.

The Working Capital Fund is considered a debt arrangement with zero coupon interest and the Company imputes interest on the Working Capital Fund liability at a rate of 15.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield and the expected repayment period. On March 18, 2022, when the $40.0 million was received from CSL Vifor, the Company recorded an initial discount on the Working Capital Fund liability and a corresponding deferred gain to the Working Capital Fund liability in the consolidated balance sheet.

On May 3, 2024, the Company and CSL Vifor entered into Amendment #1 to the Vifor License Agreement, or the Amendment. Pursuant to the Amendment, and as modified by the Vifor Termination Agreement, the Company and CSL Vifor agreed to modify the method of repayment of the Working Capital Fund such that the Working Capital Fund will be repaid through quarterly tiered royalty payments ranging from 8% to 14% of the Company's net sales of Vafseo in the U.S., or the WCF Royalty Payments. The WCF Royalty Payments will commence on July 1, 2025, and will continue until the earlier of (i) the cumulative total of the WCF Royalty Payments equals $40.0 million, or (ii) May 31, 2028, or the WCF Royalty Term. The WCF Royalty Payments are subject to minimum true-up milestones of $10.0 million, $20.0 million and $40.0 million, or the WCF Royalty True-Up Payments, on each of May 31, 2026, May 31, 2027 and May 31, 2028, respectively, or the WCF Royalty True-Up Dates. If the cumulative total of the WCF Royalty Payments paid to CSL Vifor on any given WCF Royalty True-Up Date is less than the respective WCF Royalty True-Up Payment, the Company will pay CSL Vifor a one-time payment equal to the difference between the WCF Royalty True-Up Payment and the cumulative total of the WCF Royalty Payments paid by the Company through such WCF Royalty True-Up Date. The Company determined that the terms of the Amendment are not substantially different than the terms of the Vifor License Agreement, and therefore the Amendment was accounted for as a modification. The Company concluded that the 15% discount rate remains appropriate. On a quarterly basis, the Company reassesses the effective rate and will adjust the rate prospectively, if needed.

The discount on the Working Capital Fund liability is being amortized to interest expense using the effective interest method over the WCF Royalty Term. The deferred gain is being amortized to interest income on a straight-line basis over the WCF Royalty Term. The amortization of the discount was $3.8 million and $3.1 million for the years ended December 31, 2024 and 2023, respectively. The amortization of the deferred gain was $3.6 million and $4.0 million for the years ended December 31, 2024 and 2023, respectively.

As of December 31, 2024 and 2023, the balances related to the Working Capital Fund liability were as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Current portion | $ 2,274 | $ — |
| Long-term portion | 38,013 | 40,093 |
| Total Working Capital Fund liability | $ 40,287 | $ 40,093 |

***Liability Related to Sale of Future Royalties***

In February 2021, the Company entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which the Company sold to HCR its right to receive royalties and sales milestones for Vafseo in Japan and certain other Asian countries, such countries collectively, the MTPC Territory, and such payments collectively the Royalty Interest Payments, in each case, payable to the Company under the Company's Collaboration Agreement, or the MTPC Agreement, with Mitsubishi Tanabe Pharma Corporation, or MTPC. The Royalty Interest Payments are subject to an annual maximum "cap" of $13.0 million, after which the Company will receive 85% of the Royalty Interest Payments for the remainder of that year. The Royalty Interest Payments are also subject to an aggregate maximum "cap" of $150.0 million, after which the Royalty Interest Payments will revert back to the Company.

The Company retains the right to receive all potential future regulatory milestones for Vafseo under the MTPC Agreement. The Royalty Agreement will terminate on the earlier of the date on which HCR has received (i) the last Royalty Interest Payment or (ii) payment by the Company of an amount equal to the Aggregate Cap minus the aggregate amount of all Royalty Interest Payments actually received by HCR.

At the transaction date, the Company recognized the proceeds received from HCR of $44.8 million (net of certain transaction expenses) as a liability and is amortizing it using the effective interest method over the life of the arrangement. The liability related to sale of future royalties and the debt amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize related non-cash interest expense on a

prospective basis. In the event the Company's estimates of future royalties are less than the proceeds from the sale of future royalties, the Company will not recognize related non-cash interest expense. On a quarterly basis, the Company assesses the expected royalty payments. The annual effective interest rate as of December 31, 2024 was 0% and, therefore the Company did not recognize any non-cash interest expense in the consolidated statements of operations and comprehensive loss. As a result of the Company's ongoing involvement in the cash flows related to the royalties and sales milestones in the MTPC Territory, the Company will continue to account for the royalties received as non-cash royalty revenue which is reflected within license, collaboration and other revenue in the consolidated statements of operations and comprehensive loss.

During each of the years ended December 31, 2024 and 2023, the Company paid $2.0 million of royalties to HCR. As of December 31, 2024 and 2023, the balances related to the liability related to the sale of future royalties were as follows (in thousands):

| | December 31, | |
|---|---|---|
| **Description** | **2024** | **2023** |
| Current portion (included in accrued expenses and other current liabilities) | $ 2,039 | $ 2,048 |
| Long-term portion | 52,066 | 54,013 |
| Total liability related to sale of future royalties | $ 54,105 | $ 56,061 |

The Royalty Agreement requires the Company to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, and the Company's intellectual property. The Royalty Agreement also contains certain representations and warranties, covenants, indemnification obligations, events of default and other provisions that are customary for a royalty monetization transaction of this nature. In addition, the Company granted HCR a precautionary security interest in connection with the Royalty Interest Payments.

## 9. LEASES

***Cambridge Leases***

Under the Cambridge Lease, the Company leases approximately 65,167 square feet of office, storage and laboratory space in Cambridge, Massachusetts. The term of the Cambridge Lease with respect to the 59,216 square feet of office and storage space expires on September 11, 2026, with one five-year extension option available. The term of the Cambridge Lease with respect to the 5,951 square feet of the laboratory space expires on September 11, 2026, with one two-year extension option available. In addition to rent, the Company is required to pay additional amounts for taxes, insurance, maintenance, and other operating expenses.

The Cambridge Lease is non-cancelable and is classified as an operating lease. The renewal options with respect to the office, storage and the lab space of the Cambridge Lease were not included in the calculation of the right-of-use asset and operating lease liability as the renewals are not reasonably certain. The Cambridge Lease does not contain residual value guarantees. The components of lease right-of-use assets and lease liabilities are included in the consolidated balance sheets. Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, the Company used its incremental borrowing rate when measuring operating lease liabilities. In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.65% to 6.94%, which were based on the remaining lease term at either the date of adoption of ASC 842, *Leases*, or the effective date of any subsequent lease term extensions. As of December 31, 2024, the remaining lease term for the Cambridge Leases was 1.70 years.

Operating lease costs were $5.0 million and $5.7 million for the years ended December 31, 2024 and 2023, respectively. Cash paid for amounts included in the measurement of operating lease liabilities were $5.7 million and $5.9 million for the years ended December 31, 2024 and 2023, respectively. The security deposit in connection with the Cambridge Lease is $1.7 million in the form of a letter of credit, which is included as restricted cash in other long-term assets in the Company's consolidated balance sheet as of December 31, 2024 and 2023.

***Sublease and Former Boston Lease***

Previously, the Company leased 27,924 square feet of office space in Boston, Massachusetts, or the Boston Lease, under a non-cancelable operating lease that was set to expire in July 2031. The Company subleased the entire Boston Lease, effective October 2019 through February 2023. The Company recorded no rental income and $0.3 million in rental income as other income in the consolidated statements of operations and comprehensive loss during the years ended December 31, 2024 and 2023, respectively.

In May 2023, pursuant to a Lease Assignment Agreement, or the Lease Assignment Agreement, the Company assigned all of its rights, title, and interest in, to, and under the Boston Lease to LG Chem Life Sciences Innovation Center, Inc., or LG Chem, and made a payment to LG Chem of $1.3 million. As of May 2023, LG Chem assumed all of the rights and obligations of the

Company under the Boston Lease and the Company has no further obligations for rent or other payments under the Boston Lease. In accordance with ASC 842, *Leases*, the Company wrote off the right-of-use asset and lease liability associated with the Boston Lease, and recognized the difference between the right-of-use asset and the lease liability offset by the $1.3 million payment as a loss on lease termination in the consolidated statements of operations and comprehensive loss of $0.5 million during the year ended December 31, 2023.

***Future Lease Commitments***

Future commitments under non-cancelable Cambridge Leases are as follows (in thousands):

| | Operating Leases |
|---|---|
| 2025 | $ 5,819 |
| 2026 | 3,613 |
| Total lease commitments | $ 9,432 |
| Less: present value adjustment | (485) |
| Current and long-term operating lease liabilities | $ 8,947 |

**10. COMMITMENTS AND CONTINGENCIES**

***Manufacturing and Unconditional Purchase Commitment Agreements***

*Siegfried Manufacturing*

The Company's contractual obligations include a commercial supply agreement with Siegfried Evionnaz, or Siegfried, to supply commercial drug substance for Auryxia. The Company and Siegfried entered into a Master Manufacturing Services and Supply Agreement, most recently amended in February 2023, or the Siegfried Agreement, under which the Company has agreed to purchase a minimum quantity of drug substance of Auryxia, annually at a predetermined price. As of December 31, 2024, the Company had a minimum total commitment of approximately $15.0 million through the end of 2026.

The term of the Siegfried Agreement expires on December 31, 2026. The Siegfried Agreement provides the Company and Siegfried with certain early termination rights.

The Company regularly reviews its estimate of the excess firm purchase commitment liability which relates to the amount of minimum purchase commitments under the Siegfried Agreement that exceed the current forecast, including review of assumptions of expected future demand and expiry of inventory. The excess firm purchase commitment liability was $3.6 million and $1.5 million as of December 31, 2024 and 2023, respectively. During the years ended December 31, 2024 and 2023, the Company recorded $2.1 million and $1.5 million, respectively, to costs of product and other revenue related to the change in the excess firm purchase commitment liability.

*Patheon Manufacturing*

In March 2020, the Company entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement, under which Patheon will manufacture Vafseo drug product for commercial use under a volume-based pricing structure through June 30, 2025, renewing annually unless either party gives the other party eighteen months' prior written notice. Under the Patheon Agreement, the Company agreed to purchase from Patheon a certain percentage of the estimated global demand for Vafseo drug product based on certain quarterly and annual forecasts provided by the Company. As of December 31, 2024, the Company has committed to purchase $1.1 million of Vafseo drug product from Patheon through the end of 2026, however, as estimated global demand fluctuates, the Company may have additional future obligations under the Patheon Agreement.

*WuXi STA Manufacturing*

In April 2020, the Company entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, or, as amended, the WuXi STA DS Agreement. Under the WuXi STA DS Agreement, WuXi STA will manufacture Vafseo drug substance for commercial use under a volume-based pricing structure through April 2, 2029. Pursuant to the WuXi STA DS Agreement, the Company has agreed to purchase a certain percentage of the global demand for Vafseo drug substance from WuXi STA. As of December 31, 2024, the Company has committed to purchase $4.6 million of Vafseo drug substance from WuXi STA through the first half of 2025, however, as estimated global demand fluctuates, the Company may have additional future obligations under the WuXi STA DS Agreement.

On February 10, 2021, the Company entered into a Supply Agreement with WuXi STA, which was amended on October 15, 2024, or the WuXi STA DP Agreement, under which WuXi STA will manufacture and supply Vafseo drug product for commercial purposes under a volume-based pricing structure through January 1, 2032. The Vafseo drug product price is reviewed annually by the Company and WuXi STA. The Company also reimburses WuXi STA for certain reasonable expenses.

Pursuant to the WuXi STA DP Agreement, the Company has agreed to purchase a certain percentage of global demand for Vafseo drug product from WuXi STA. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of the Company and WuXi STA with at least eighteen months' prior written notice. The WuXi STA DP Agreement allows the Company to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions. As of December 31, 2024, the Company has committed to purchase $0.9 million of Vafseo drug product from WuXi STA through the first half of 2025, however, as estimated global demand fluctuates, the Company may have additional future obligations under the WuXi STA DP Agreement.

*Esteve - Assigned Supply Agreement*

On April 9, 2019, the Company and Esteve Química, S.A., or Esteve, entered into a Supply Agreement, or the Esteve Agreement, which included the terms and conditions under which Esteve would manufacture Vafseo drug substance for commercial use under a volume-based pricing structure. On December 16, 2022, the Company, MTPC, and Esteve executed the Esteve Assignment Agreement, pursuant to which the Esteve Agreement was assigned to MTPC. The Esteve Assignment Agreement transferred the rights and obligations of the Esteve Agreement to MTPC, specifically including the obligations under certain purchase orders issued by the Company and accepted by Esteve.

Although the Esteve Agreement was assigned to MTPC in December 2022, the Company and Esteve have agreed to negotiate the terms of a new commercial supply relationship. As of December 31, 2024, the Company has committed to purchase $7.6 million of Vafseo drug substance from Esteve through the end of 2025.

*BioVectra - Former Manufacturing and Unconditional Purchase Commitments*

Under the Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra, the Company agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices as well as reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of Auryxia drug substance.

On December 22, 2022, the Company and BioVectra entered into a termination agreement, under which the parties agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between the parties in connection with the manufacture and supply, by BioVectra to the Company, of Auryxia drug substance. In the termination agreement, the Company and BioVectra released one another from all existing and future claims and liabilities and the return of certain materials and documents. In addition, the Company agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million and (ii) six quarterly payments of $2.5 million commencing in April 2024, totaling $15.0 million. The upfront payment of $17.5 million was made during the quarter ended December 31, 2022 and was recorded in cost of product and other revenue. In accordance with ASC 420, *Exit or Disposal Cost Obligations*, the Company recognized a liability and corresponding expense for the remaining termination fees based on estimated fair value as of December 22, 2022. The Company imputed interest on the liability for the remaining termination fees at a rate of 17.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield and expected repayment period of the remaining termination fees. The Company recorded an initial discount on the remaining termination fees in the consolidated balance sheet on the date of the termination. This resulted in the recording of a liability and corresponding charge to cost of goods sold of $11.2 million during the quarter ended December 31, 2022. The discount on the liability balance is being amortized to interest expense using the effective interest rate method over the term of the liability. The amortization of the discount was $1.6 million and $1.9 million for the years ended December 31, 2024 and 2023, respectively.

***License Agreements***

*Panion License Agreement*

On April 17, 2019, the Company and Panion & BF Biotech, Inc., or Panion, entered into a second amended and restated license agreement, or Panion Amended License Agreement, which amended and restated in full the license agreement between the Company and Panion. The Panion Amended License Agreement provides the Company with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding certain Asian-Pacific countries, or the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Company-owned patents covering the rights to sublicense (with the Company's written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Under the Panion Amended License Agreement, Panion is eligible to receive from the Company or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in the Company's licensed territories. The Company is eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion's licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of the Company's and Panion's obligations to pay royalties thereunder. In addition, the Company may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in the Company's licensed territory, in either case upon ninety days' notice. The Company and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, until the second anniversary of the expiration of the obligation of the Company or Panion, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country.

The Panion Amended License Agreement includes customary terms relating to, among others, indemnification, confidentiality, remedies, and representations and warranties. In addition, the Panion Amended License Agreement provides that each of the Company and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the years ended December 31, 2024 and 2023, the Company incurred approximately $9.1 million and $10.0 million, respectively, in royalty payments due to Panion relating to the Company's sales of Auryxia in the U.S. and JT and Torii's net sales of Riona in Japan.

*Cyclerion Agreement*

In June 2021, the Company entered into a license agreement, or Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, under which the Company obtained an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase stimulator.

Under the terms of the Cyclerion Agreement, the Company made an upfront payment of $3.0 million to Cyclerion, which was paid during the second quarter of 2021. Substantially all of the fair value of the assets acquired in conjunction with the Cyclerion Agreement was concentrated in the acquired license. As a result, the Company accounted for this transaction as an asset acquisition under ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*. The $3.0 million upfront payment was charged to research and development expense at acquisition in June of 2021, as it relates to a development stage compound with no alternative future use.

In December 2024, the Company and Cyclerion entered into Amendment #1 to the License Agreement, or the Cyclerion Amendment, pursuant to which the Company agreed to pay Cyclerion (i) $1.25 million, which was paid in December 2024, and (ii) $0.5 million on or before September 30, 2025. In addition, the parties agreed to the reduction of certain development milestones and the increase of certain royalty rates on net sales and sublicense income. During the year ended December 31, 2024, the Company recorded the $1.25 million payment and $0.5 million future payment to research and development expense in accordance with ASC 730, Research and Development, as praliciguat remains a development stage compound with no alternative future use. Furthermore, the only contingency as it relates to the $0.5 million payment due on or before September 30, 2025 is the passage of time.

Under the Cyclerion Agreement, as amended, Cyclerion is eligible to receive up to an aggregate of $198.5 million from the Company in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a mid-single-digit percentage to twenty percent of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product and (iii) ten years from first commercial sale of such product. The Company may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

***Other Third Party Contracts***

The Company contracts with various organizations to conduct R&D activities with remaining contract costs to the Company of approximately $48.0 million at December 31, 2024. The scope of the services under these R&D contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

***Litigation and Related Matters***

The Company is involved from time to time in various legal proceedings arising in the normal course of business. The Company provides disclosure when a loss in excess of any reserve is reasonably possible, and if estimable, the Company discloses the potential loss or range of possible loss. Significant judgment is required to assess the likelihood of various potential outcomes and the quantification of loss in those scenarios. Changes in the Company's estimates could have a material impact and are recorded as litigation progresses and new information comes to light. Although the outcomes of potential legal proceedings are inherently difficult to predict, the Company does not expect the resolution of current legal proceedings to have a material adverse effect on its financial position, results of operations or cash flows of the Company.

***Guarantees and Indemnifications***

As permitted under Delaware law, the Company may indemnify its officers, directors and employees for certain events or occurrences that happen by reason of their relationship with, or position held at, the Company. The Company may also be subject to indemnification obligations by law with respect to the actions of its employees under certain circumstances and in certain jurisdictions. The Company maintains director and officer liability insurance coverage that is intended to cover a portion of amounts that may be due with respect to indemnification after a deductible is met. Further, the Company is a party to a variety of agreements in the ordinary course of business under which it may be obligated to indemnify third parties with respect to certain matters. For the years ended December 31, 2024 and 2023, the Company did not experience any losses related to these indemnification obligations, and no claims were outstanding as of December 31, 2024. The Company does not have any claims related to these indemnification obligations and consequently concluded that the fair value of these obligations is negligible and no related accruals were recorded.

**11. PRODUCT REVENUE AND RESERVES FOR VARIABLE CONSIDERATION**

Until the Vafseo U.S. launch in January 2025, the Company's only source of product revenue has been from the U.S. sales of Auryxia. Total net product revenue was $152.2 million and $170.3 million for the years ended December 31, 2024 and 2023, respectively. Product revenue allowance and reserve categories were as follows:

| *(in thousands)* | Chargebacks and Discounts | Rebates, Fees and other Deductions | Returns | Total |
|---|---|---|---|---|
| Balance at December 31, 2022 | $ 1,259 | $ 26,252 | $ 10,923 | $ 38,434 |
| Current provisions related to sales in current year | 11,138 | 79,648 | 6,181 | 96,967 |
| Adjustments related to prior year sales | (304) | (1,506) | 1,648 | (162) |
| Credits/payments made | (10,486) | (81,403) | (11,836) | (103,725) |
| Balance at December 31, 2023 | $ 1,607 | $ 22,991 | $ 6,916 | $ 31,514 |
| Current provisions related to sales in current year | 9,225 | 44,914 | 4,862 | 59,001 |
| Adjustments related to prior year sales | (94) | (2,056) | (540) | (2,690) |
| Credits/payments made | (9,302) | (50,123) | (4,796) | (64,221) |
| Balance at December 31, 2024 | $ 1,436 | $ 15,726 | $ 6,442 | $ 23,604 |

Chargebacks, discounts and estimated product returns are recorded as a reduction of revenue in the period the related product revenue is recognized in the consolidated statements of operations and comprehensive loss. Chargebacks are recorded as a reduction to accounts receivable while discounts, rebates, fees and other deductions are recorded with a corresponding increase to accrued expenses and other current liabilities or accounts payable in the consolidated balance sheets. Estimated product returns on product sales that are not expected to be returned within one year are recorded as other long-term liabilities in the consolidated balance sheets.

Accounts receivable, net related to product sales was approximately $32.4 million and $35.9 million as of December 31, 2024 and 2023, respectively.

**12. LICENSE, COLLABORATION AND OTHER REVENUE**

The Company recognized the following revenues from its license, collaboration and other revenue agreements (in thousands):

| Entity | Description | Years Ended December 31, 2024 | 2023 |
|---|---|---|---|
| Medice | License and Product Supply of Vafseo in EU | $ 22 | $ 10,968 |
| MTPC | License and Product Supply of Vafseo in Japan | 2,612 | 5,735 |
| JT and Torii | License and royalties related to the sale of Riona in Japan | 5,366 | 5,394 |
| Otsuka | Terminated U.S. and International Agreements | — | 2,225 |
| Total License, Collaboration and Other Revenue | | $ 8,000 | $ 24,322 |

The following table presents changes in the Company's contract assets and liabilities related to license, collaboration and other revenue agreements (in thousands):

| | Twelve Months Ended December 31, 2024 | | | |
|---|---|---|---|---|
| | Balance at Beginning of Period | Additions | Deductions | Balance at End of Period |
| **Contract assets:** | | | | |
| Accounts receivable[1] | $ 3,333 | $ 8,562 | $ (9,885) | $ 2,010 |
| **Contract liability:** | | | | |
| Deferred revenue (long-term)[2] | $ 43,296 | $ — | $ (43,296) | $ — |

| | Twelve Months Ended December 31, 2023 | | | |
|---|---|---|---|---|
| | Balance at Beginning of Period | Additions | Deductions | Balance at End of Period |
| **Contract assets:** | | | | |
| Accounts receivable[1] | $ 1,901 | $ 10,088 | $ (8,656) | $ 3,333 |
| Prepaid expenses and other current assets | $ 781 | $ — | $ (781) | $ — |
| **Contract liabilities:** | | | | |
| Deferred revenue (current and long-term) | $ 47,034 | $ — | $ (3,738) | $ 43,296 |

(1) Excludes accounts receivable from product sales of Auryxia which are included in the accompanying consolidated balance sheets as of December 31, 2024 and 2023.

(2) See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for further information.

During the years ended December 31, 2024 and 2023, the Company recognized the following revenues as a result of changes in the contract asset and contract liability balances in the respective periods (in thousands):

| Revenue Recognized in the Period from: | Years Ended December 31, 2024 | 2023 |
|---|---|---|
| Deferred revenue - beginning of the period | $ — | $ 3,738 |
| Performance obligations satisfied in previous periods | $ — | $ — |

***Medice License Agreement***

On May 24, 2023, or Medice Effective Date, the Company and MEDICE Arzneimittel Pütter GmbH & Co. KG, or Medice, entered into a License Agreement, or the Medice License Agreement, pursuant to which the Company granted to Medice an exclusive license to develop and commercialize Vafseo for the treatment of anemia in adult patients with chronic kidney disease in the European Economic Area, the UK, Switzerland and Australia, or the Medice Territory.

Under the Medice License Agreement, the Company received an up-front payment of $10.0 million and is eligible to receive the following payments:

(i) commercial milestone payments up to an aggregate of $100.0 million, and

(ii) tiered royalties ranging from 10% to 30% of Medice's annual net sales of Vafseo in the Medice Territory, subject to reduction in certain circumstances.

The royalties will expire on a country-by-country basis upon the latest to occur of (a) the date of expiration of the last-to-expire valid claim of any Company, Medice or joint patent that covers Vafseo in such country in the Medice Territory, (b) the date of expiration of data or regulatory exclusivity for Vafseo in such country in the Medice Territory and (c) the date that is twelve years from first commercial sale of Vafseo in such country in the Medice Territory.

Under the Medice License Agreement, the Company retains the right to develop Vafseo for non-dialysis patients with anemia due to CKD in the Medice Territory. If the Company develops Vafseo for non-dialysis patients and Vafseo receives marketing approval in the Medice Territory, Medice will commercialize Vafseo for both indications in the Medice Territory. In this instance, the Company would receive 70% of the net product margin of any sales of Vafseo in the non-dialysis patient population, unless Medice requests to share the cost of the development necessary to gain approval to market Vafseo for non-dialysis patients in the Medice Territory and the parties agree on alternative financial terms. If the Company develops Vafseo for non-dialysis patients, the Company has determined that the activities under the Medice License Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the success of the activities. Accordingly, if the Company develops Vafseo for non-dialysis patients the Company will account for the joint activities in accordance with ASC No. 808, *Collaborative Arrangements*, or ASC 808. Additionally, the Company has determined that in the context of the development of Vafseo for non-dialysis patients, Medice does not represent a customer as contemplated by ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*. As a result, the activities conducted pursuant to development activities for Vafseo for non-dialysis patients will be accounted for as a component of the related expense in the period incurred.

The Medice License Agreement expires on the date of expiration of all payment obligations due thereunder with respect to Vafseo in the last country in the Medice Territory, unless earlier terminated in accordance with the terms of the Medice License Agreement. Either party may, subject to a cure period, terminate the Medice License Agreement in the event of the other party's uncured material breach. Medice has the right to terminate the Medice License Agreement in its entirety for convenience upon twelve months' prior written notice delivered on or after the date that is twelve months after the Medice Effective Date.

The Company evaluated the elements of the Medice License Agreement in accordance with the provisions of ASC 606 and concluded Medice is a customer. The Company identified one performance obligation in connection with its obligations under the Medice License Agreement, which is the license, or License Performance Obligation. The transaction price at inception was comprised of the up-front payment of $10.0 million, of which the Company received $8.6 million during the quarter ended June 30, 2023. The remaining $1.4 million was withheld by the German Federal Tax Office and is included in prepaid expenses and other current assets as of December 31, 2024 and other long-term assets as of December 31, 2023 in the consolidated balance sheet.

Pursuant to the terms of the Medice License Agreement, the up-front payment of $10.0 million is non-refundable and non-creditable against any other amount due to the Company and was allocated to the License Performance Obligation, which was satisfied as of the Medice Effective Date. As such, the Company recognized the $10.0 million up-front payment as license, collaboration and other revenue in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2023.

In accordance with ASC 606, the Company will recognize sales-based royalties and milestone payments at the later of when the performance obligation is satisfied or the related sales occur. During the years ended December 31, 2024 and 2023, the Company recognized immaterial revenue from Medice royalties and no revenue from Medice royalties, respectively. As of December 31, 2024, there were immaterial contract assets, and no accounts receivable, payables or deferred revenue in connection with the Medice License Agreement.

*Medice Letter Agreement*

On December 6, 2023, the Company and Medice entered into a letter agreement, or the Medice Letter Agreement, pursuant to which the Company agreed to sell to Medice a partial batch of Vafseo in order to achieve packaging validation for the Medice Territory. The Company previously recognized revenue under this arrangement when risk of loss passed to Medice and delivery occurred. During the year ended December 31, 2023, the Company recognized $1.0 million in collaboration, license and other revenue under the Medice Letter Agreement. As of December 31, 2024, there were no accounts receivable, contract assets, payables or deferred revenue recorded in connection with the Medice Letter Agreement.

*Supply of Drug Product to Medice*

On September 13, 2024, the Company and Medice entered into a supply agreement, or the Medice Supply Agreement, under which the Company will supply Vafseo drug product to Medice for commercial and developmental use in the Medice Territory. The Company recognizes revenue under this arrangement when risk of loss passes to Medice, delivery has occurred, and Medice has accepted the product. The Company did not recognize any revenue under the Medice Supply Agreement during the years ended December 31, 2024 or 2023.

***MTPC Collaboration Agreement***

On December 11, 2015, the Company and MTPC entered into the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to Vafseo in the MTPC Territory, which was amended effective as of December 2, 2022. In addition, the Company supplies Vafseo to MTPC for both clinical and commercial use in the MTPC Territory. In February 2021, the Company entered into the Royalty Agreement with HCR, whereby the Company sold its right to receive royalties and sales milestones under the MTPC Agreement, subject to certain caps and other terms and conditions. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties,* for more information.

Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: expiration of the last-to-expire patent covering Vafseo in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of Vafseo in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

Under the MTPC Agreement, MTPC is required to make certain milestone payments to the Company aggregating up to approximately $225.0 million upon the achievement of specified development, regulatory and commercial events. The Company has received $10.0 million in development milestone payments. Of the $40.0 million in regulatory milestone payments the Company is eligible for, the Company received $10.0 million in relation to the Japanese NDA filing in the third quarter of 2019 and $15.0 million following regulatory approval of Vafseo in Japan in the third quarter of 2020. The Company is also entitled to receive up to $175.0 million in commercial milestone payments associated with aggregate sales of all products. In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC made a $20.0 million upfront payment as well as a $20.5 million payment for Phase 2 studies in Japanese patients completed by the Company and reimbursed by MTPC. Additionally, the Company is entitled to receive tiered royalty payments ranging from 13% to 20% of annual net sales of Vafseo in the MTPC Territory, subject to reduction in certain circumstances.

The Company evaluated the elements of the MTPC Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, MTPC, is a customer. The Company identified two performance obligations in connection with its material promises under the MTPC Agreement as follows: (i) License, Research and Clinical Supply Performance Obligation and (ii) Rights to Future Know-How Performance Obligation.

The transaction price was comprised of: (i) the up-front payment of $20.0 million, (ii) the cost for the Phase 2 studies of $20.5 million, (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies, (iv) $10.0 million in development milestones received, (v) $25.0 million in regulatory milestones received and (vi) $6.9 million in royalties from net sales of Vafseo. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. As of December 31, 2024, all development milestones and $25.0 million in regulatory milestones have been achieved. No other regulatory milestones or commercial milestones have been assessed as probable and have been fully constrained until the period in which they are achieved.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it is immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License, Research and Clinical Supply Performance Obligation and allocated the entire transaction price to this performance obligation.

Revenue for the License, Research and Clinical Supply Performance Obligation for the MTPC Agreement is being recognized using a proportional performance method, for which all deliverables have been completed. The Company recognizes any revenue from MTPC royalties in the period in which the sales occur. The Company recognized $1.9 million and $2.0 million of revenue for royalties from the net sales of Vafseo during the years ended December 31, 2024 and 2023, respectively. As noted above, in February 2021, the Company entered into the Royalty Agreement, whereby the Company sold its right to receive these royalties and sales milestones under the MTPC Agreement, subject to certain caps and other conditions. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for more information. The revenue is classified as collaboration, license and other revenue in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2024, there were no accounts receivable, payables or deferred revenue and $0.5 million in contract assets recorded in connection with the MTPC Agreement.

*Supply of Drug Product to MTPC*

On July 15, 2020, the Company and MTPC entered into a supply agreement, or the MTPC Supply Agreement, under which the Company supplies Vafseo drug product to MTPC for commercial use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement. The term of the MTPC Supply Agreement extends throughout the term of the MTPC Agreement, and the termination provisions of the MTPC Agreement govern termination of the MTPC Supply Agreement. The Company does not recognize revenue under this arrangement until risk of loss on the drug product passes to MTPC and delivery has occurred and MTPC has accepted the product.

On December 16, 2022, the Company, MTPC and Esteve Química, S.A., or Esteve, executed an Assignment of Supply Agreement, or Esteve Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve, or the Esteve Agreement, was assigned to MTPC. The Esteve Assignment Agreement transferred the rights and obligations of the Company under the Esteve Agreement to MTPC. The Company has no further obligation to take delivery of, or pay for, product delivered by Esteve except as disclosed in Note 10, Commitments and Contingencies.

During the years ended December 31, 2024 and 2023, the Company recognized $0.7 million and $3.7 million of revenue, respectively, under the MTPC Supply Agreement. As of December 31, 2024, there were no accounts receivable, deferred revenue or other current liabilities relating to the MTPC Supply Agreement.

***JT and Torii Sublicense Agreement***

The Company has an Amended and Restated Sublicense Agreement, which was amended in June 2013, with JT and Torii, or JT and Torii Sublicense Agreement, under which JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate hydrate in Japan. JT and Torii are responsible for the future development and commercialization costs in Japan.

The Company is eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that the Company must pay to Panion on JT and Torii's net sales of Riona under the Panion License Agreement subject to certain reductions upon expiration or termination of the Amended and Restated License Agreement between the Company and Panion, pursuant to which Company in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development and commercialization of ferric citrate. The Company is entitled to receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones.

The sublicense under the JT and Torii Sublicense Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the JT and Torii Sublicense Agreement with or without cause upon at least six months' prior written notice to the Company. Additionally, either party may terminate the JT and Torii Sublicense Agreement for cause upon 60 days’ prior written notice after the breach of any uncured material provision of the JT and Torii Sublicense Agreement, or after certain insolvency events.

The Company evaluated the elements of the JT and Torii Sublicense Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, JT and Torii, is a customer. The Company identified two performance obligations in connection with its obligations under the JT and Torii Sublicense Agreement: (i) License and Supply Performance Obligation and (ii) Rights to Future Know-How Performance Obligation. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License and Supply Performance Obligation and allocated the entire transaction price to this performance obligation. Additionally, as of the consummation of the Merger, the services associated with the License and Supply Performance Obligation were completed and JT and Torii had secured their own source to manufacture ferric citrate hydrate. As such, any initial license fees as well as any development-based milestones and manufacturing fee revenue were received and recognized prior to the Merger. The Company determined that the remaining consideration that may be payable to the Company under the terms of the sublicense agreement are either quarterly royalties on net sales or payments due upon the achievement of sales-based milestones. In accordance with ASC 606, the Company recognizes sales-based royalties and milestone payments based on the level of sales, when the related sales occur as these amounts have been determined to relate predominantly to the license granted to JT and Torii and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur.

During each of the years ended December 31, 2024 and 2023, the Company recognized license revenue of $5.4 million related to royalties earned on net sales of Riona in Japan. The Company records the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of Riona, in the same period as the royalty revenue from JT and Torii is recorded. As of December 31, 2024, there was $1.5 million in accounts receivables relating to the JT and Torii Sublicense Agreement.

***Prior Collaboration and License Agreements***

***U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.***

On December 18, 2016, the Company entered into a collaboration and license agreement, or Otsuka U.S. Agreement, with Otsuka Pharmaceutical Co. Ltd, or Otsuka. The collaboration was focused on the development and commercialization of Vafseo in the U.S.

On May 12, 2022, the Company received notice from Otsuka that Otsuka had elected to terminate the Otsuka U.S. Agreement and the April 25, 2017 collaboration and license agreement with Otsuka, or Otsuka International Agreement. On June 30, 2022, the Company and Otsuka entered into the Termination and Settlement Agreement, or Otsuka Termination Agreement, pursuant to which, among other things, the Company and Otsuka agreed to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement as of June 30, 2022.

During the year ended December 31, 2023, the Company recognized $2.2 million in collaboration, license and other revenue in connection with the Packaging Validation Transfer Agreement entered into with Otsuka on April 20, 2023. Under the Packaging Validation Transfer Agreement, the parties agreed that responsibility for all remaining packaging validation activities would be transferred from Otsuka to the Company in consideration of payments made by Otsuka to the Company. The Company evaluated the agreement under ASC 606 and concluded it was closely tied to the prior collaboration, license and other revenue agreements and under ASC 606 recognized collaboration, license and other revenue during the year ended December 31, 2023.

**13. CAPITAL STOCK**

***Authorized and Outstanding Capital Stock***

As of December 31, 2024, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value $0.00001 per share, of which 224,848,992 and 194,582,539 shares were issued and outstanding at December 31, 2024 and 2023, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which no shares were issued and outstanding at December 31, 2024 and 2023.

***At-the-Market Facility***

On April 7, 2022, the Company entered into an at-the-market, or ATM, sales agreement, or the Original Sales Agreement, with Jefferies LLC, or Jefferies, as the Company's sales agent, under which the Company could offer and sell from time to time up to $26.0 million of shares of the Company's common stock at current market prices. During the year ended December 31, 2023, the Company sold 6,189,974 shares of common stock under this program for gross proceeds of $6.8 million ($6.7 million, net of offering expenses). During the year ended December 31, 2024, the Company sold 13,261,311 shares of its common stock under this program with gross proceeds of $19.2 million, ($18.7 million, net of offering expenses). The Company paid the Agent commissions for its services of acting as agent of up to 3.0% of the gross proceeds from the sale of the common stock pursuant to the ATM.

On September 3, 2024, in connection with the filing of a new shelf registration statement on Form S-3, the Company filed a prospectus related to the Company's amended and restated sales agreement (which amended and restated the Original Sales Agreement), with Jefferies, as the Company's sales agent, pursuant to which the Company is able to offer and sell up to $75.0 million of its common stock at current market prices from time to time. Since September 12, 2024 (the date the Company's shelf registration statement on Form S-3 went effective) through December 31, 2024, the Company sold 14,271,631 shares of its common stock under this program with gross proceeds of $24.3 million ($23.8 million, net of offering expenses).

***Unregistered Common Stock***

In connection with the Vifor License Agreement, CSL Vifor owns 7,571,429 shares of common stock that are unregistered under the Securities Act. See Note 8, *Liability Related to Settlement Royalties, Working Capital Fund Liability and Liability Related to Sale of Future Royalties*, for more information.

***Warrants to Purchase Common Stock***

In connection with the BlackRock Credit Agreement, described in more detail in Note 7, *Indebtedness*, the Company issued a warrant to purchase 3,076,923 shares of the Company's common stock, at an exercise price per share of $1.30, and upon the borrowing of Tranche C in February 2025, the Company issued additional warrants to purchase 1,153,846 shares of the Company's common stock at an exercise price per share of $1.30. Each warrant is exercisable for eight years from the date of issuance. The warrants and the common stock issuable upon the exercise of such warrants were not registered under the Securities Act of 1933. Accordingly, the holder thereof may only sell common stock issued upon exercise of such warrants pursuant to an effective registration statement under the Securities Act covering the resale of those shares, an exemption

under Rule 144 under the Securities Act or another applicable exemption under the Securities Act. See Note 18, *Subsequent Events*, for further details on the Tranche C Warrant.

## 14. STOCK-BASED COMPENSATION AND EMPLOYEE RETIREMENT PLANS

***Stock-Based Compensation Plans***

The Company incurred stock-based compensation expenses of $7.8 million and $9.3 million for the years ended December 31, 2024 and 2023, respectively.

***Equity Incentive Plans***

The following table contains information about the Company's equity incentive plans:

| | | | December 31, 2024 | | December 31, 2023 | |
|---|---|---|---|---|---|---|
| Title of Plan | Group Eligible | Type of Award Granted (or to be Granted) | Awards Outstanding | Additional Awards Available for Grant | Awards Outstanding | Additional Awards Available for Grant |
| Keryx Equity Plans[1][2] | Employees, directors and consultants | Common stock options and RSUs | 163,765 | — | 232,203 | — |
| Akebia Therapeutics, Inc. 2014 Incentive Plan, as amended [2] [3] (the 2014 Plan) *(replaces 2008 Plan)* | Employees, directors, consultants and advisors | Common stock options, RSUs, SARs and performance awards | 11,559,708 | — | 15,311,501 | — |
| Akebia Therapeutics, Inc. 2023 Stock Incentive Plan[3] (the 2023 Plan) *(replaces 2014 Plan)* | Employees, officers, directors, consultants and advisors | Common stock options, SARs, restricted stock, unrestricted stock, RSUs, performance awards, other share-based awards and dividend equivalents | 10,390,642 | 11,340,648 | 1,712,400 | 17,382,722 |

(1) The Keryx Equity Plans consist of the Keryx Biopharmaceuticals, Inc. 1999 Share Option Plan, Keryx Biopharmaceuticals, Inc., as amended, the 2004 Long-Term Incentive Plan, as amended, the Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan, the Keryx Biopharmaceuticals Inc. Amended and Restated 2013 Incentive Plan and the Keryx Biopharmaceuticals, Inc. 2018 Equity Incentive Plan.

(2) New awards are no longer being granted under these plans.

(3) This table includes the following inducement awards that are subject to the terms and conditions of the applicable plan but were granted as inducement awards consistent with Nasdaq Listing Rule 5635(c)(4) and not under the applicable plan: 1,151,127 options outstanding under the 2014 Plan and 2,534,775 options outstanding under the 2023 Plan as of December 31, 2024 and 1,616,019 options outstanding under the 2014 Plan and 794,000 options outstanding under the 2023 Plan as of December 31, 2023.

*Common Stock Options and Stock Appreciation Rights*

During the year ended December 31, 2024, the Company granted 3,117,500 options to employees and 315,000 options to directors under the 2023 Plan. Options and SARs granted by the Company generally vest over periods of between 12 and 48 months, subject, in each case, to the individual's continued service through the applicable vesting date. Options and SARs generally vest either 100% on the first anniversary of the grant date or in installments of (i) 25% at the one year anniversary and (ii) 12 equal quarterly installments beginning after the one year anniversary of the grant date, subject to the individual's continuous service with the Company. Options and SARs generally expire ten years after the date of grant.

The Company also maintains an inducement award program with a share pool that is separate from the Company's equity plans under which inducement awards may be granted consistent with Nasdaq Listing Rule 5635(c)(4). During the year ended December 31, 2024, the Company granted 1,911,550 options to purchase shares of the Company's common stock to new hires as inducements to such employees entering into employment with the Company, of which 1,904,550 options remained outstanding at December 31, 2024.

The Company grants annual service-based stock options to employees and directors and SARs to certain executives under the 2023 Plan and previously granted options under the 2014 Plan. In addition, the Company issues common stock options to directors, new hires and occasionally to other employees not in connection with the annual grant process.

Finally, the Company grants performance-based stock options which generally vest in connection with the achievement of specified commercial, regulatory and corporate milestones. The performance-based stock options also generally feature a time-based vesting component. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of options granted and recognized over time based on the probability of meeting such commercial, regulatory and corporate milestones.

The combined stock option activity for the year ended December 31, 2024, is as follows:

| | Stock Options | Weighted-Average Exercise Price | Weighted-Average Contractual Life (years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding, December 31, 2023 | 13,312,835 | $ 4.20 | 7.27 years | $ 2,680 |
| Granted | 5,344,050 | $ 1.57 | | |
| Exercised | (444,239) | $ 0.87 | | |
| Expired | (865,478) | $ 10.03 | | |
| Canceled and forfeited | (662,843) | $ 3.09 | | |
| Outstanding at December 31, 2024 | 16,684,325 | $ 3.19 | 7.17 years | $ 6,797 |
| Exercisable at December 31, 2024 | 8,636,721 | $ 4.80 | 5.72 years | $ 2,885 |
| Vested and expected to vest at December 31, 2024 | 16,684,325 | $ 3.19 | 7.17 years | $ 6,797 |

The intrinsic value of options exercised during the year ended December 31, 2024 was $0.4 million. There was immaterial intrinsic value of options exercised during the year ended December 31, 2023, as the value of options exercised in 2023 was immaterial. The fair value of options that vested during the years ended December 31, 2024 and 2023 was $3.7 million and $6.4 million, respectively. As of December 31, 2024, there was approximately $7.7 million of unrecognized compensation cost related to common stock options outstanding under the Company's 2023 Plan or the 2014 Plan or made pursuant to the Company's inducement award program, which is expected to be recognized over a weighted average period of 2.67 years.

*Restricted Stock Units*

Generally, RSUs, granted by the Company vest in one of the following ways: (i) 100% of each RSU grant vests on the first anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, (iii) 50% of each RSU grant vests on the first anniversary and 25% of each RSU grant vests every six months after the one year anniversary of the grant date, or (iv) one third of each RSU grant vests on the first anniversary of the grant date and the remaining two thirds vests in eight substantially equal quarterly installments beginning after the one year anniversary, subject, in each case, to the individual's continued service through the applicable vesting date. The grant-date fair value of the RSUs is recognized as expense on a straight-line basis. The Company determines the fair value of the RSUs based on the closing price of the common stock on the date of the grants.

The Company also periodically grants performance-based restricted stock units, or PSUs, to employees under the 2023 Plan and previously granted PSUs under the 2014 Plan. The PSUs granted by the Company generally vest in connection with the achievement of specified commercial, regulatory and corporate milestones. The PSUs also generally feature a time-based vesting component. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted and recognized over time based on the probability of meeting such commercial, regulatory and corporate milestones.

RSU and PSU activity is as follows:

| | 2014 Plan | | 2023 Plan | |
|---|---|---|---|---|
| | Number of Shares | Weighted Average Grant Date Fair Value | Number of Shares | Weighted Average Grant Date Fair Value |
| Unvested as of December 31, 2023 | 3,339,869 | $1.30 | 603,400 | $1.48 |
| Granted | — | $0.00 | 3,993,400 | $1.59 |
| Vested | (1,742,807) | $1.58 | (356,733) | $1.36 |
| Forfeited and canceled | (275,639) | $1.29 | (131,700) | $1.68 |
| Unvested as of December 31, 2024 | 1,321,423 | $0.95 | 4,108,367 | $1.59 |

The total fair value of RSUs and PSUs that vested during 2024 and 2023 (measured on the date of vesting) was $3.2 million and $8.4 million, respectively. As of December 31, 2024, there was approximately $5.1 million of unrecognized compensation cost related to RSUs and PSUs, which is expected to be recognized over a weighted average period of 1.91 years.

***Employee Stock Purchase Plan***

On June 6, 2019, the Company's stockholders approved the Amended and Restated 2014 Employee Stock Purchase Plan, or ESPP. Under the ESPP substantially all employees may voluntarily enroll to purchase shares of the Company's common stock

through payroll deductions at a price equal to 85% of the lower of the fair market values of the stock as of the beginning or the end of the six-month offering period. An employee's payroll deductions under the ESPP are limited to 15% of the employee's compensation, and an employee may not purchase more than $25,000 worth of stock during any calendar year. In addition, an employee may not purchase more than 1,500 shares in any six-month offering period. As of December 31, 2024 and 2023, a total of 4,448,069 and 4,637,801 shares of the Company's common stock were available for future issuance under the ESPP, respectively. The Company issued 189,732 shares during the year ended December 31, 2024.

***Stock-Based Compensation Expense***

The Black-Scholes option pricing model is used to estimate the fair value of the common stock options. The weighted-average assumptions used in calculating the fair values of the rights to acquire stock under the 2023 Plan, the 2014 Plan and inducement awards were as follows:

| | Years ended December 31, | | | | | |
|---|---|---|---|---|---|---|
| **Common Stock Options** | **2024** | | | **2023** | | |
| Risk-free interest rate | 3.60% | - | 4.66% | 3.54% | - | 4.81% |
| Expected volatility | 109.98% | - | 119.81% | 100.97% | - | 111.71% |
| Expected term (years) | 5.51 | - | 6.25 | 5.51 | - | 6.25 |
| Expected dividend yield | | —% | | | —% | |
| Weighted average grant date fair value | | $1.36 | | | $0.69 | |

The Company has classified stock-based compensation in its consolidated statements of operations and comprehensive loss as follows (in thousands):

| | Years ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Cost of goods sold | $ 399 | $ 267 |
| Research and development | 1,498 | 1,964 |
| Selling, general and administrative | 5,840 | 6,456 |
| Restructuring | 38 | 630 |
| Total | $ 7,775 | $ 9,317 |

Stock-based compensation by type of award was as follows (in thousands):

| | Years ended December 31, | |
|---|---|---|
| | **2024** | **2023** |
| Stock options | $ 4,036 | $ 5,310 |
| Restricted stock units | 3,655 | 3,637 |
| Performance RSUs | — | 297 |
| Employee stock purchase plan | 84 | 73 |
| Total | $ 7,775 | $ 9,317 |

***Employee Retirement Plan***

In 2008, the Company established a retirement plan, or the Plan, authorized by Section 401(k) of the Internal Revenue Code, or IRC. In accordance with the Plan, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following their date of employment. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary and contributions in the amount of approximately $1.7 million were made during each of the years ended December 31, 2024 and 2023.

**15. INCOME TAXES**

The Company’s income tax provision was computed based on the federal statutory rate and the state statutory rates, net of the related federal benefit. There was no current or deferred income tax expense or benefit for the years ended December 31, 2024 and 2023 due to the Company’s net losses and increases in its valuation allowance against its deferred tax assets.

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2024 and 2023:

| | Years Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Federal tax at statutory rate | 21.0 % | 21.0 % |
| State and local tax at statutory rate | 0.6 | 2.7 |
| Research and development tax credits | 1.9 | 0.3 |
| Change in valuation allowance | (32.5) | (9.1) |
| Other permanent differences | (1.7) | (2.0) |
| Stock option cancellations | (1.8) | (3.7) |
| Stock option shortfalls | — | (1.7) |
| Effect of rate changes | 13.5 | (7.7) |
| Provision to return adjustment | (1.0) | (0.3) |
| Other | — | 0.5 |
| Effective tax rate | — % | — % |

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets. Accordingly, the Company has recorded a valuation allowance against the Company's otherwise recognizable net deferred tax assets. The Company continues to maintain the underlying tax benefits to offset future taxable income and to monitor the need for a valuation allowance based on the profitability of its future operations. The valuation allowance increased by approximately $22.5 million and $4.7 million during the years ended December 31, 2024 and 2023, respectively. Significant components of the Company's deferred tax assets and liabilities are as follows (in thousands):

| | December 31, | |
|---|---|---|
| | 2024 | 2023 |
| **Deferred tax assets:** | | |
| Accrued expenses and other current liabilities | $ 1,757 | $ 1,411 |
| Deferred revenue | 13,222 | 9,534 |
| Sale of royalty | 13,595 | 12,346 |
| Stock-based compensation | 6,238 | 6,183 |
| R&D credits | 6,152 | 4,843 |
| Capitalized R&D costs | 21,270 | 18,295 |
| Other non-current liabilities | 2,515 | 3,434 |
| Net operating loss carryforward | 291,723 | 288,939 |
| ASC 842 lease liability | 2,248 | 2,959 |
| Inventories reserve | 841 | 4,537 |
| Return reserve | 1,500 | 1,624 |
| Working Capital Fund liability | 10,123 | 8,829 |
| Intangible assets | 2,040 | — |
| Other | 17,954 | 14,036 |
| Total deferred tax assets | 391,178 | 376,970 |
| Less valuation allowance | (387,803) | (365,330) |
| Total deferred tax assets, net of valuation allowance | 3,375 | 11,640 |
| **Deferred tax liabilities:** | | |
| Intangible assets | — | (6,868) |
| 481(a) adjustments | (1,271) | (1,924) |
| ROU asset (ASC 842) | (2,065) | (2,734) |
| Other | (39) | (114) |
| Total deferred tax liabilities | (3,375) | (11,640) |
| Net deferred tax liability | $ — | $ — |

As of December 31, 2024 and 2023, the Company had approximately $1,245.8 million and $1,230.4 million, respectively, of federal net operating losses, or NOLs, carry-forwards which expire through 2037. Included in the $1,245.8 million of federal NOLs are losses of $663.7 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. Additionally, at December 31, 2024 and 2023, the Company had approximately $584.3 million and $590.8 million, respectively, of state NOL carry-forwards, which expire through 2044. The Company also has approximately $4.0 million of federal research and development tax credit carryforwards which expire through 2040 and $2.7 million of state R&D tax credit carryforwards which expire through 2038.

Under the provisions of the IRC, the NOLs and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOLs and tax credit carryforwards may become subject to an annual limitation under IRC Sections 382 and 383 if there is more than a 50% change in ownership of the stockholders that own 5% or more of the Company's outstanding stock over a three-year period. The Company completed an evaluation of its ownership changes and concluded that an ownership change did occur on December 12, 2018 for both Akebia and Keryx in connection with the Merger. As a consequence of this ownership change, the Company's NOLs and tax credit carryforwards allocable to the tax periods preceding the ownership change became subject to limitation under Section 382 of the IRC. The Company reduced its associated deferred tax assets by $44.9 million as a result of the limitation. The Company completed an evaluation of its ownership changes as of March 31, 2022 and concluded that an ownership change had not occur since the previous evaluation done through December 12, 2018. The Company may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside the Company's control. As a result, the Company's ability to utilize these attributes to offset taxable income may be subject to limitations.

The Company has not conducted a full study of its research and development credit carryforwards. A study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts will be presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheet or statement of operations at this time, if an adjustment were required.

The Company files income tax returns in the U.S. federal and various state and local jurisdictions. For federal and state income tax purposes, the 2022, 2021 and 2020 tax years remain open for examination under the normal three-year statute of limitations. The statute of limitations for income tax audits in the U.S. will commence upon utilization of NOLs and will expire three years from the filing of the tax return the loss was utilized on.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits for the years ending December 31, 2024 and 2023 are as follows (in thousands):

| | |
|---|---|
| Balance at December 31, 2022 | $ 2,697 |
| Reductions based on tax positions of current years | (2,697) |
| Balance at December 31, 2023 | — |
| Reductions based on tax positions of current years | — |
| Balance at December 31, 2024 | $ — |

The Company does not believe there will be a material change in its unrecognized tax positions over the next twelve months. All of the unrecognized tax benefits, if recognized, would be offset by the valuation allowance.

**16. NET LOSS PER SHARE**

Potentially dilutive securities, warrants, common stock options, RSUs and SARs have been excluded from the calculation of diluted net loss per share as their effects would be anti-dilutive. For periods in which the Company reports a net loss, the weighted average number of shares outstanding used to calculate both basic and diluted net loss per share were the same. The shares in the table below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, due to their anti-dilutive effect:

| | Years Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Warrants | 3,076,923 | — |
| Outstanding common stock options | 16,049,012 | 12,690,624 |
| Unvested restricted stock units | 5,429,790 | 3,930,167 |
| Stock appreciation rights | 635,313 | 635,313 |
| Total | 25,191,038 | 17,256,104 |

(1) On the Tranche C Closing Date, the Company became obligated to issue to the Warrant Holder additional warrants to purchase 1,153,846 shares of the common stock which are excluded from this table.

**17. Segment Information**

The Company operates as one operating segment focused on developing and commercializing innovative therapeutics primarily in the U.S. The accounting policies of the segment are the same as those described in the summary of significant accounting policies.

The determination of a single business segment is consistent with the consolidated financial information regularly reviewed by the chief executive officer, who is the Company's CODM, in assessing segment performance and deciding how to allocate resources on a consolidated basis.

The CODM makes decisions on resource allocation, assesses performance of the business, and monitors budget versus actual results using income from operations. Net income is also a measure that is considered in monitoring budget versus actual results. The measure of segment assets is reported on the consolidated balance sheets as total consolidated assets.

The following table presents information about reported segment revenues, segment profit and significant segment expenses for the years ended December 31, 2024 and 2023:

| | Years Ended December 31, | |
|---|---|---|
| | 2024 | 2023 |
| Revenues | $ 160,180 | $ 194,623 |
| Less: | | |
| Direct cost of product and other revenue | 15,970 | 26,525 |
| Panion royalty | 9,097 | 10,048 |
| Excess firm purchase commitment charge | 2,068 | 1,533 |
| Amortization of intangible asset | 36,042 | 36,042 |
| Research and development | 37,652 | 63,079 |
| Selling, general and administrative | 106,545 | 100,233 |
| License | 3,220 | 3,237 |
| Restructuring | 58 | 181 |
| Loss from operations | (50,472) | (46,256) |
| | | |
| Other income (expense) | | |
| Interest expense | (18,185) | (6,032) |
| Other (expense) income | 94 | 887 |
| Change in fair value of warrant liability | (330) | — |
| Loss on extinguishment of debt | (517) | — |
| Loss on termination of lease | — | (524) |
| Net loss before income taxes | $ (69,410) | $ (51,925) |
| **Net loss** | $ (69,410) | $ (51,925) |

**18. SUBSEQUENT EVENTS**

The Company has evaluated events and transactions occurring after the balance sheet date through the filing date of this Form 10-K with the Securities and Exchange Commission, to ensure that the audited consolidated financial statements include appropriate disclosure of events both recognized in the accompanying consolidated financial statements as of December 31, 2024, and events which occurred subsequently but were not recognized in the consolidated financial statements. The Company has concluded that no subsequent events have occurred that require disclosure other than the following:

*Second Amendment to the BlackRock Credit Agreement*

On February 3, 2025, the Company and Kreos entered into the Second Amendment, which amends certain provisions of the BlackRock Credit Agreement. The Term Loan Facility provided the Company access to three tranches: (i) an initial tranche of $37.0 million, which was funded on January 29, 2024, (ii) an additional tranche of $8.0 million, which was funded on April 19, 2024, and (iii) a final tranche of $10.0 million, which was available in a single draw through an expiry date of December 31, 2024, or the Prior Tranche C Loan. As a result of the Second Amendment, the Prior Tranche C Loan expiry date was extended until February 3, 2025, or the Extended Tranche C Loan. The terms of the Extended Tranche C Loan are substantially similar to the terms of the Prior Tranche C Loan, however, interest will accrue on the Extended Tranche C Loan as if it was advanced on December 31, 2024.

On the Tranche C Closing Date, the Company received $9.3 million, after deducting debt issuance costs, feeds and expenses.

On February 3, 2025, in connection with the drawdown of the Extended Tranche C Loan, in accordance with the warrant agreement, dated as of January 29, 2024, between the Company and the Warrant Holder, the Company issued a warrant to the Warrant Holder to purchase 1,153,846 shares of the Company's common stock, at an exercise price per share of $1.30. The warrant is exercisable for eight years from the date of issuance.

See Note 7, *Indebtedness*, for further information on the BlackRock Credit Agreement.

**Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

**Item 9A. Controls and Procedures**

***Management's Evaluation of our Disclosure Controls and Procedures***

"Disclosure controls and procedures", as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the U.S. Securities and Exchange Commission, or the SEC, rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in company reports filed or submitted under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

As required by Rules 13a-15 and 15d-15 under the Exchange Act, our management, with the participation of our principal executive officer and principal financial officer, carried out an evaluation of our disclosure controls and procedures as of December 31, 2024. Based upon their evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2024, our disclosure controls and procedures were not effective because of a material weakness in the design of our internal control over financial reporting related to our accounting for inventories and inventory related transactions which is described in more detail below.

**Management's Annual Report on Internal Control Over Financial Reporting**

Our management, with the participation of our principal executive officer and principal financial officer, is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive officer and principal financial officer and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

Our management conducted the assessment of the effectiveness of our internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013.

As a result of this assessment, our management has concluded that the material weakness in our internal control over financial reporting relating to our inventory process as reported in our Annual Report on Form 10-K for the year ended December 31, 2023 was not fully remediated as of December 31, 2024 and that our internal control over financial reporting as of December 31, 2024 was not effective as described below.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

**Material Weakness - Inventory**

During 2024 we strengthened our controls and remediated three of the five components of the previously reported material weakness related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the verification that the existence of all inventories subject to physical inventory counts were accurately counted.

To remediate the above components of the material weakness we:

i) Designed and implemented new controls throughout 2024,

ii) Hired accounting personnel with U.S. GAAP experience specific to inventory accounting and

iii) Enhanced our monitoring and oversight controls related to physical inventory counts.

However, as of December 31, 2024, our management concluded that despite the above, we did not maintain effective controls over inventory. Specifically, we did not effectively document controls that operated with a sufficient level of precision to evaluate the completeness, accuracy and reasonableness of the product sales forecast, which is used in the evaluation of excess inventory, including the calculation of excess firm purchase commitments and the classification of current and non-current inventory, or the Remaining Control Deficiencies.

The Remaining Control Deficiencies resulted in certain immaterial accounting errors, which have been corrected prior to the issuance of the annual consolidated financial statements for the year ended December 31, 2024. However, because the material weakness creates a reasonable possibility that a material misstatement to our financial statements would not be prevented or detected on a timely basis, our management concluded that as of December 31, 2024, the internal control over financial reporting was not effective.

**Remediation Efforts of the Material Weakness - Inventories**

Our management has taken and plans to continue to take actions to remediate the Remaining Control Deficiencies in our internal control over financial reporting.

We have begun the following remediation plan: increasing the level of precision of our review controls that support the completeness, accuracy and reasonableness of the sales forecast used to support our inventory evaluations, including the identification and consideration of contrary evidence that could detect a potential error in the sales forecast.

As management continues to evaluate and work to improve our internal control over financial reporting, management may determine it is necessary to take additional measures to address the material weakness. Until the controls have been operating for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively, the material weakness described above will continue to exist.

Ernst & Young LLP, the independent registered public accounting firm that audited the consolidated financial statements included in this Annual Report on Form 10-K, has issued an attestation report on the effectiveness of internal control over financial reporting as of December 31, 2024, included below.

***Changes in Internal Control over Financial Reporting***

Except for the remediation efforts as noted above, there have been no changes in our internal control over financial reporting during the quarter ended December 31, 2024, as defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

***Limitations of Effectiveness of Controls and Procedures***

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

**Report of Independent Registered Public Accounting Firm**

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

**Opinion on Internal Control Over Financial Reporting**

We have audited Akebia Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, because of the effect of the material weakness described below on the achievement of the objectives of the control criteria, Akebia Therapeutics, Inc. (the "Company") has not maintained effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment. The Company did not maintain effective review controls that operated with a sufficient level of precision to evaluate the completeness, accuracy and reasonableness of the product sales forecast, which is used in the evaluation of excess inventory, including the calculation of excess firm purchase commitments, and the classification of current and non-current inventory.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' (deficit) equity and cash flows for each of the two years in the period ended December 31, 2024, and the related notes. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2024 consolidated financial statements, and this report does not affect our report dated March 13, 2025, which expressed an unqualified opinion thereon.

**Basis for Opinion**

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

**Definition and Limitations of Internal Control Over Financial Reporting**

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 13, 2025

**Item 9B. Other Information**

**Rule 10b5-1 - Director and Officer Trading Arrangements**

From time to time, the Company's directors and officers (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, engage in open-market transactions with respect to Company securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in Company securities by directors and officers are required to be made in accordance with the Company's insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in the Company's securities in a manner that avoids concerns about initiating transactions while in possession of material nonpublic information.

The following table describes, for the fourth quarter of 2024, each trading arrangement for the sale or purchase of Company securities adopted or terminated by our directors and officers that is either (1) a contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) (a "Rule 10b5-1 trading arrangement") or (2) a "non-Rule 10b5-1 trading arrangement" (as defined in Item 408(c) of Regulation S-K):

| Name (Title) | Action Taken (Date of Action) | Type of Trading Arrangement | Nature of Trading Arrangement | Duration of Trading Arrangement | Aggregate Number of Securities |
|---|---|---|---|---|---|
| **Richard C. Malabre (Senior Vice President, Chief Accounting Officer)** | December 12, 2024 | Rule 10b5-1 Non-Discretionary Option Exercise and Stock Sale Plan | Sale | Until March 17, 2026 | Up to an aggregate of 85,002 shares |

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

## PART III

**Item 10. Director, Executive Officers and Corporate Governance**

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 11. Executive Compensation**

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and, other than the information required by Item 402(v) of Regulation S-K, is incorporated herein by reference.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 14. Principal Accountant Fees and Services**

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

**PART IV**

**Item 15. Exhibits and Financial Statement Schedules**

(a) Documents filed as part of this Annual Report on Form 10-K.

(b) Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' (Deficit) Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the consolidated financial statements and related footnotes.

(3) Exhibits

The Exhibits listed below are filed as part of this Annual Report on Form 10-K.

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 2.1** | Agreement and Plan of Merger, dated as of June 28, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc., and Keryx Biopharmaceuticals, Inc. | 8-K | 001-36352 | 2.1 | June 28, 2018 |
| 2.2 | First Amendment to Agreement and Plan of Merger, dated as of October 1, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc. and Keryx Biopharmaceuticals, Inc. | 8-K | 001-36352 | 2.1 | October 1, 2018 |
| 3.1 | Ninth Amended and Restated Certificate of Incorporation | 8-K | 001-36352 | 3.1 | March 28, 2014 |
| 3.2 | Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Akebia Therapeutics, Inc. | 8-K | 001-36352 | 3.1 | June 9, 2020 |
| 3.3 | Second Amended and Restated Bylaws of Akebia Therapeutics, Inc. | 8-K | 001-36352 | 3.1 | April 28, 2023 |
| 4.1 | Form of Common Stock Certificate | S-1/A | 333-193969 | 4.1 | March 4, 2014 |
| 4.2 | Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 | 10-K | 001-36352 | 4.4 | March 4, 2015 |
| 4.3# | Amendment No. 1 to Fourth Amended and Restated Investors' Rights Agreement, dated June 28, 2017 | 10-K | 001-36352 | 4.5 | March 12, 2018 |
| 4.4# | Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 | 10-Q | 001-36352 | 4.1 | August 8, 2017 |
| 4.5! | Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated February 18, 2022 | 10-K | 001-36352 | 4.5 | March 1, 2022 |
| 4.6 | Description of Registrant's Securities | 10-K | 001-36352 | 4.6 | February 25, 2021 |
| 4.7 | Form of Warrant | 10-K | 001-36352 | 4.7 | March 14, 2024 |
| 10.1† | Form of Director and Officer Indemnification Agreement | 10-K | 001-36352 | 10.1 | March 12, 2018 |
| 10.2 | Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 | S-1 | 333-193969 | 10.2 | February 14, 2014 |
| 10.3 | First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014 | 10-K | 001-36352 | 10.3 | March 4, 2015 |
| 10.4 | Second Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated November 23, 2015 | 10-K | 001-36352 | 10.4 | March 14, 2016 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.5 | Third Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated July 25, 2016 | 10-Q | 001-36352 | 10.1 | November 9, 2016 |
| 10.6 | Fourth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc., dated May 1, 2017 | 10-K | 001-36352 | 10.6 | March 12, 2018 |
| 10.7 | Fifth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated April 9, 2018 | 10-Q | 001-36352 | 10.1 | August 8, 2018 |
| 10.8 | Sixth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated November 30, 2020 | 10-K | 001-36352 | 10.8 | February 25, 2021 |
| 10.9 | Seventh Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated May 6, 2024. | 10-Q | 001-36352 | 10.1 | August 8, 2024 |
| 10.10† | Amended and Restated 2008 Equity Incentive Plan | S-1 | 333-193969 | 10.5 | February 14, 2014 |
| 10.11† | Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan | S-1 | 333-193969 | 10.6 | February 14, 2014 |
| 10.12† | Executive Employment Agreement with John P. Butler, dated September 16, 2013 | S-1 | 333-193969 | 10.7 | February 14, 2014 |
| 10.13† | Form of Non-Statutory Stock Option Agreement for Officers under 2014 Incentive Plan | S-1/A | 333-193969 | 10.24 | March 4, 2014 |
| 10.14† | Form of Non-Statutory Stock Option Agreement for Non-Employee Directors under 2014 Incentive Plan | S-1/A | 333-193969 | 10.25 | March 4, 2014 |
| 10.15† | Amended and Restated Non-Employee Director Compensation Program, effective April 27, 2023 | 10-Q | 001-36352 | 10.1 | May 8, 2023 |
| 10.16† | Second Amended and Restated Non-Employee Director Compensation Program, effective June 6, 2023 | 10-Q | 001-36352 | 10.8 | August 28, 2023 |
| 10.17† | Third Amended and Restated Non-Employee Director Compensation Program, effective January 1, 2024 | 10-K | 001-36352 | 10.21 | March 14, 2024 |
| 10.18†* | Fourth Amended and Restated Non-Employee Director Compensation Program, effective January 27, 2025 | | | | |
| 10.19† | Form of Executive Severance Agreement for Officers | S-1/A | 333-193969 | 10.27 | March 4, 2014 |
| 10.20† | 2014 Incentive Plan | S-1 | 333-193969 | 10.29 | March 4, 2014 |
| 10.21† | Amendment No. 1 to the Akebia Therapeutics, Inc. 2014 Incentive Plan | S-8 | 333-229366 | 4.4 | January 25, 2019 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.22† | Amended and Restated 2014 Employee Stock Purchase Plan | DEF 14A | 001-36352 | Appendix A | April 26, 2019 |
| 10.23† | Amended and Restated Cash Incentive Plan, effective January 19, 2022 | 10-K | 001-36352 | 10.28 | March 1, 2022 |
| 10.24† | Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan | 10-K | 001-36352 | 10.18 | March 12, 2018 |
| 10.25† | Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan | 10-K | 001-36352 | 10.29 | March 26, 2019 |
| 10.26† | Form of Officer Inducement Award Non-Statutory Stock Option Agreement | S-8 | 333-222728 | 4.4 | January 26, 2018 |
| 10.27† | Form of Inducement Award Non-Statutory Stock Option Agreement for Non-Officers | S-8 | 333-222728 | 4.5 | January 26, 2018 |
| 10.28† | Form of Officer Performance-Based Stock Option Award, under the Company's 2014 Incentive Plan, as amended | 10-Q | 001-36352 | 10.1 | November 4, 2021 |
| 10.29† | Form of Officer Performance-Based Stock Restricted Stock Unit Award, under the Company's 2014 Incentive Plan, as amended | 10-Q | 001-36352 | 10.2 | November 4, 2021 |
| 10.30† | Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (Retention Awards) | 10-Q | 001-36352 | 10.6 | August 4, 2022 |
| 10.31† | Form of Officer Non-Statutory Stock Option Agreement under 2014 Incentive Plan (Retention Awards) | 10-Q | 001-36352 | 10.7 | August 4, 2022 |
| 10.32†! | Form of Officer Cash Bonus Letter Agreement | 10-Q | 001-36352 | 10.3 | November 4, 2021 |
| 10.33† | Form of Officer Stock Appreciation Rights Award Agreement under 2014 Incentive Plan | 10-Q | 001-36352 | 10.3 | May 8, 2023 |
| 10.34† | Akebia Therapeutics, Inc. 2023 Stock Incentive Plan | S-8 | 333-272453 | 99.1 | June 6, 2023 |
| 10.35† | Form of Non-Employee Director Stock Option Agreement under 2023 Stock Incentive Plan | 10-Q | 001-36352 | 10.10 | August 28, 2023 |
| 10.36† | Form of Non-Employee Director Restricted Stock Unit Agreement under 2023 Stock Incentive Plan | 10-Q | 001-36352 | 10.12 | August 28, 2023 |
| 10.37† | Form of Officer Stock Option Agreement under 2023 Stock Incentive Plan | 10-Q | 001-36352 | 10.11 | August 28, 2023 |
| 10.38† | Form of Officer Restricted Stock Unit Agreement under 2023 Stock Incentive Plan | 10-Q | 001-36352 | 10.13 | August 28, 2023 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.39† | Form of Officer Inducement Award Stock Option Agreement under 2023 Stock Incentive Plan | 10-Q | 001-36352 | 10.14 | August 28, 2023 |
| 10.40† | Form of Officer Executive Severance Agreement (Reflecting Clawback Policy) | 10-K | 001-36352 | 10.43 | March 14, 2024 |
| 10.41† | Form of Officer Cash Bonus Agreement (Reflecting Clawback Policy) | 10-K | 001-36352 | 10.44 | March 14, 2024 |
| 10.42† | Form of Officer Stock Option Agreement under 2023 Stock Incentive Plan (Reflecting Clawback Policy) | 10-K | 001-36352 | 10.45 | March 14, 2024 |
| 10.43† | Form of Officer Restricted Stock Unit Agreement under 2023 Stock Incentive Plan (Reflecting Clawback Policy) | 10-K | 001-36352 | 10.46 | March 14, 2024 |
| 10.44† | Form of Officer Inducement Award Stock Option Agreement under 2023 Stock Incentive Plan (Reflecting Clawback Policy) | 10-K | 001-36352 | 10.47 | March 14, 2024 |
| 10.45† | Form of Non-Officer Inducement Award Stock Option Agreement under 2023 Stock Incentive Plan | S-8 | 333-284590 | 99.2 | January 30, 2025 |
| 10.46† | Keryx Biopharmaceuticals, Inc. 1999 Stock Option Plan | 10-Q | 001-30929 | 10.2 | March 21, 2003 |
| 10.47† | Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan | DEF 14A | 000-30929 | Annex C | April 29, 2004 |
| 10.48† | Amendment to the Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan dated April 11, 2006 | 10-Q | 000-30929 | 10.1 | August 9, 2006 |
| 10.49† | Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan | DEF 14A | 000-30929 | Annex D | April 30, 2007 |
| 10.50† | Keryx Biopharmaceuticals, Inc. Amended and Restated 2013 Incentive Plan | 8-K | 000-30929 | 10.1 | May 27, 2016 |
| 10.51† | Keryx Biopharmaceuticals, Inc. 2018 Equity Incentive Plan | S-8 | 333-226005 | 99.1 | June 29, 2018 |
| 10.52† | Form of Indemnification Agreement between Keryx Biopharmaceuticals, Inc. and its Directors and Officers | 10-Q | 000-30929 | 10.1 | November 9, 2016 |
| 10.53† | Form of Employee Agreement (Confidentiality, Non-Competition, Non-Solicitation and Development Agreement) applicable to Officers | 10-K | 001-36352 | 10.56 | March 26, 2019 |
| 10.54† | Keryx Biopharmaceuticals, Inc. Fourth Amended and Restated Directors Equity Compensation Plan | 8-K | 000-30929 | 10.2 | May 27, 2016 |
| 10.55† | Keryx Biopharmaceuticals, Inc. Third Amended and Restated Directors Equity Compensation Plan | 10-Q | 000-30929 | 10.1 | August 7, 2014 |
| 10.56† | Keryx Biopharmaceuticals, Inc. Director Non-Statutory Stock Option Award Terms and Conditions under the Third Amended and Restated Directors Equity Compensation Plan | 10-K | 001-36352 | 10.59 | March 26, 2019 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.57† | Form of Officer Retention Letter Agreement | 10-Q | 001-36352 | 10.6 | May 9, 2022 |
| 10.58†! | Form of Retention and Separation Agreement for Michel Dahan and Nicole R. Hadas | 10-Q | 001-36352 | 10.7 | May 9, 2022 |
| 10.59†! | Form of Amendment to Retention and Separation Agreement for Michel Dahan and Nicole R. Hadas | 10-Q | 001-36352 | 10.2 | November 3, 2022 |
| 10.60†! | Form of May 2023 Amendment to Retention and Separation Agreement for Michel Dahan and Nicole R. Hadas | 10-Q | 001-36352 | 10.4 | August 28, 2023 |
| 10.61†! | July 2023 Amendment to Retention and Separation Agreement for Michel Dahan | 10-Q | 001-36352 | 10.5 | August 28, 2023 |
| 10.62†! | July 2023 Amendment to Retention and Separation Agreement for Nicole R. Hadas | 10-Q | 001-36352 | 10.6 | August 28, 2023 |
| 10.63†! | October 2023 Amendment to Retention and Separation Agreement for Nicole R. Hadas | 10-Q | 001-36352 | 10.3 | November 8, 2023 |
| 10.64†! | February 2024 Amendment to Retention and Separation Agreement for Nicole R. Hadas | 10-K | 001-36352 | 10.66 | March 14, 2024 |
| 10.65†! | February 2024 Amendment to Retention and Separation Agreement for Michel Dahan | 10-K | 001-36352 | 10.67 | March 14, 2024 |
| 10.66† | Separation Agreement with David Spellman, dated June 9, 2023 and Amendment to Separation Agreement dated July 6, 2023 | 10-Q | 001-36352 | 10.7 | August 28, 2023 |
| 10.67† | Separation Agreement with Ellen Snow, dated March 15, 2024 | 10-Q | 001-36352 | 10.11 | May 9, 2024 |
| 10.68! | Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015 | 10-K | 001-36352 | 10.49 | March 1, 2022 |
| 10.69# | Letter Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated September 26, 2017 | 10-Q | 001-36352 | 10.1 | November 8, 2017 |
| 10.70! | Amendment No. 1 to Collaboration Agreement, dated December 2, 2022, by and between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation | 10-K | 001-36352 | 10.53 | March 10, 2022 |
| 10.71! | Second Amended and Restated License Agreement, dated February 18, 2022, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd. | 10-K | 001-36352 | 10.54 | March 1, 2022 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.72! | Amendment #1 to Second Amended and Restated License Agreement, dated May 3, 2024, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd. | 10-Q | 001-36352 | 10.3 | August 8, 2024 |
| 10.73! | Termination and Settlement Agreement, dated July 10, 2024, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd. | 10-Q | 001-36352 | 10.4 | August 8, 2024 |
| 10.74 | Amended and Restated Open Market Sale Agreement, dated September 3, 2024, by and between Akebia Therapeutics, Inc. and Jefferies LLC | S-3 | 333-281903 | 1.2 | September 3, 2025 |
| 10.75! | Second Amended and Restated License Agreement dated April 17, 2019, by and between Akebia Therapeutics, Inc. and Panion & BF Biotech, Inc. | 10-Q | 001-36352 | 10.1 | August 8, 2019 |
| 10.76# | Amended and Restated Sub-License Agreement, dated June 8, 2009, as amended by the First Amendment thereto, dated June 12, 2013, by and between Keryx Biopharmaceuticals, Inc., Japan Tobacco, Inc. and Torii Pharmaceutical Co., Ltd | 10-Q | 000-30929 | 10.1 | November 7, 2017 |
| 10.77! | Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates, dated September 27, 2016, and related Product Agreement dated September 27, 2016, and related Product Agreement dated October 12, 2016 | 10-K | 001-36352 | 10.58 | March 1, 2022 |
| 10.78*! | Product Agreement, dated August 29, 2017, by and between Keryx Biopharmaceuticals, Inc. and Patheon Inc. (an affiliate of Patheon Manufacturing Services LLC) related to the Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates dated November 12, 2016 | | | | |
| 10.79# | Master Manufacturing Services and Supply Agreement, dated December 20, 2017, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA | 10-K | 000-30929 | 10.13 | February 21, 2018 |
| 10.80 | Amendment No. 1 to Master Manufacturing Services and Supply Agreement, dated as of December 21, 2020, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. | 10-K | 001-36352 | 10.57 | February 25, 2021 |
| 10.81 | Amendment No. 2 to Master Manufacturing Services and Supply Agreement, dated as of January 29, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. | 10-K | 001-36352 | 10.58 | February 25, 2021 |
| 10.82! | Amendment No. 3 to Master Manufacturing Services and Supply Agreement, dated as of February 11, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. | 10-K | 001-36352 | 10.59 | February 25, 2021 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.83 | Amendment No. 4 to Master Manufacturing Services and Supply Agreement, dated as of December 17, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. | 10-K | 001-36352 | 10.64 | March 1, 2022 |
| 10.84! | Amendment No. 5 to Master Manufacturing Services and Supply Agreement, dated February 28, 2023, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA | 10-Q | 001-36352 | 10.2 | May 8, 2023 |
| 10.85# | Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated October 16, 2014 and First Amendment to Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated April 14, 2015 | 10-K | 001-36352 | 10.60 | March 26, 2019 |
| 10.86! | Termination and Settlement Agreement, dated December 22, 2022, by and between Keryx Biopharmaceuticals, Inc. and BioVectra Inc. | 10-K | 001-36352 | 10.70 | March 10, 2023 |
| 10.87! | Loan Agreement, dated November 11, 2019, by and among Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc., Biopharma Credit plc and Biopharma Credit Investments V (Master) LP | 10-K | 001-36352 | 10.62 | March 12, 2020 |
| 10.88! | First Amendment and Waiver, dated February 18, 2022, by and among Akebia Therapeutics, Inc., Biopharma Credit plc, BPCR Limited Partnership and Biopharma Credit Investments V (Master) LP | 10-K | 001-36352 | 10.69 | March 1, 2022 |
| 10.89! | Second Amendment and Waiver, dated July 15, 2022, by and among Akebia Therapeutics, Inc., Biopharma Credit plc, BPCR Limited Partnership and Biopharma Credit Investments V (Master) LP | 10-Q | 001-36352 | 10.9 | August 4, 2022 |
| 10.90! | Third Amendment to Loan Agreement, dated as of June 30, 2023, by and among Akebia Therapeutics, Inc., Biopharma Credit plc, BPCR Limited Partnership and Biopharma Credit Investments V (Master) LP | 10-Q | 001-36352 | 10.2 | August 28, 2023 |
| 10.91! | Fourth Amendment to Loan Agreement dated as of October 31, 2023, by and among Akebia Therapeutics, Inc., BioPharma Credit PLC, BPCR Limited Partnership, and BioPharma Credit Investments V (Master) LP | 10-K | 001-36352 | 10.93 | March 14, 2024 |
| 10.92! | Guaranty and Security Agreement, dated November 25, 2019, by and between Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc. and Biopharma Credit plc | 10-K | 001-36352 | 10.63 | March 12, 2022 |
| 10.93! | Supply Agreement, dated as of March 11, 2020, by and between Akebia Therapeutics, Inc. and Patheon, Inc. | 10-Q | 001-36352 | 10.1 | May 5, 2020 |
| 10.94! | Supply Agreement, dated as of April 2, 2020, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited | 10-Q | 001-36352 | 10.2 | August 10, 2020 |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 10.95! | Amendment #1 to Supply Agreement, dated as of April 15, 2021, by and between Akebia Therapeutics, Inc, and STA Pharmaceutical Hong Kong Limited | 10-Q | 001-36352 | 10.1 | August 5, 2021 |
| 10.96! | Amendment #2 to the Supply Agreement, dated as of April 15, 2024, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited | 10-Q | 001-36352 | 10.2 | August 8, 2024 |
| 10.97! | Supply Agreement, dated February 10, 2021, by and between the Company and STA Pharmaceutical Hong Kong Limited | 10-Q | 001-36352 | 10.4 | May 10, 2021 |
| 10.98! | Amendment #1 to Supply Agreement, dated October 15, 2024, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited | 10-Q | 001-36352 | 10.5 | November 7, 2024 |
| 10.99! | Royalty Interest Acquisition Agreement, dated February 25, 2021, by and between the Company and HealthCare Royalty Partners IV, L.P. | 10-Q | 001-36352 | 10.5 | May 10, 2021 |
| 10.100! | License Agreement, dated December 22, 2022, by and among Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc. and Averoa SAS | 10-K | 001-36352 | 10.81 | March 10, 2023 |
| 10.101 | Amendment #1 to License Agreement, dated August 30, 2024, by and among Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc. and Averoa SAS | 10-Q | 001-36352 | 10.4 | November 7, 2024 |
| 10.102! | License Agreement, dated May 24, 2023, by and between the Company and MEDICE Arzneimittel Pütter GmbH & Co. KG | 10-Q | 001-36352 | 10.1 | August 28, 2023 |
| 10.103! | Agreement for the Provision of a Loan Facility dated January 29, 2024 between the Company and Kreos Capital VII (UK) Limited | 10-K | 001-36352 | 10.102 | March 14, 2024 |
| 10.104! | Amendment #1 to Agreement for the Provision of a Loan Facility, dated July 10, 2024, by and between Akebia Therapeutics, Inc. and Kreos Capital VII (UK) Limited | 10-Q | 001-36352 | 10.5 | August 8, 2024 |
| 10.105!* | Second Amendment to Agreement for the Provision of a Loan Facility, dated February 3, 2025, by and between Akebia Therapeutics, Inc. and Kreos Capital VII (UK) Limited | | | | |
| 10.106 | Warrant Agreement dated January 29, 2024 by and between the Company and Kreos Capital VII Aggregator SCSp | 10-K | 001-36352 | 10.103 | March 14, 2024 |
| 19.1* | Akebia Therapeutics, Inc. Insider Trading Compliance Policy | | | | |
| 21.1 | List of Subsidiaries | 10-K | 001-36352 | 21.1 | February 25, 2021 |
| 23.1* | Consent of Ernst & Young LLP | | | | |

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| | | Schedule/ Form | File No. | Exhibit | Filed Date/ Period End Date |
| 31.1* | Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended | | | | |
| 31.2* | Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended | | | | |
| 32.1* | Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350 | | | | |
| 97.1† | Akebia Therapeutics, Inc. Dodd-Frank Compensation Recovery Policy | 10-K | 001-36352 | 97.1 | March 14, 2024 |
| 101.INS* | Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document) | | | | |
| 101.SCH* | Inline XBRL Taxonomy Extension Schema Document | | | | |
| 101.CAL* | Inline XBRL Taxonomy Extension Calculation Linkbase Document | | | | |
| 101.DEF* | Inline XBRL Taxonomy Extension Definition Linkbase Document | | | | |
| 101.LAB* | Inline XBRL Taxonomy Extension Labels Linkbase Document | | | | |
| 101.PRE* | Inline XBRL Taxonomy Extension Presentation Linkbase Document | | | | |
| 104 | Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101) | | | | |

* Filed, or submitted electronically, herewith

† Indicates management contract or compensatory plan

# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment

! Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

** The schedules to the Agreement and Plan of Merger have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish copies of such schedules to the Securities and Exchange Commission upon request by the Commission

**Item 16. Form 10-K Summary**

None.

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

**AKEBIA THERAPEUTICS, INC.**

| | | |
|---|---|---|
| Date: March 13, 2025 | By: | /s/ John P. Butler |
| | | John P. Butler |
| | | *President and Chief Executive Officer* |

Pursuant to the requirements of the Securities Exchange Act of 1934, this report was signed by the following persons on behalf of the registrant and in the capacities and on the date indicated.

| | | |
|---|---|---|
| Date: March 13, 2025 | By: | /s/ John P. Butler<br>John P. Butler<br>*Director, President and Chief Executive Officer (Principal Executive Officer)* |
| Date: March 13, 2025 | By: | /s/ Erik J. Ostrowski<br>Erik J. Ostrowski<br>*Senior Vice President, Chief Financial Officer and Chief Business Officer (Principal Financial Officer)* |
| Date: March 13, 2025 | | /s/ Richard C. Malabre<br>Richard C. Malabre<br>*Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)* |
| Date: March 13, 2025 | By: | /s/ Adrian Adams<br>Adrian Adams<br>*Chairperson and Director* |
| Date: March 13, 2025 | By: | /s/ Ron Frieson<br>Ron Frieson<br>*Director* |
| Date: March 13, 2025 | By: | /s/ Steven C. Gilman<br>Steven C. Gilman<br>*Director* |
| Date: March 13, 2025 | By: | /s/ Michael Rogers<br>Michael Rogers<br>*Director* |
| Date: March 13, 2025 | By: | /s/ Cynthia Smith<br>Cynthia Smith<br>*Director* |
| Date: March 13, 2025 | By: | /s/ Myles Wolf<br>Myles Wolf<br>*Director* |
| Date: March 13, 2025 | By: | /s/ LeAnne M. Zumwalt<br>LeAnne M. Zumwalt<br>*Director* |

# AKEBIA THERAPEUTICS, INC.
# FOURTH AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION PROGRAM

**Effective January 27, 2025**

Non-employee members of the Board of Directors (the "***Board***") of Akebia Therapeutics, Inc. (the "***Company***") shall be eligible to receive cash and equity compensation as set forth in this Fourth Amended and Restated Non-Employee Director Compensation Program (this "***Program***"). The cash and equity compensation described in this Program shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a "***Non-Employee Director***") who is eligible to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Program shall remain in effect until it is revised or rescinded by further action of the Board. This Program shall be reviewed by the Board periodically and may be amended, modified or terminated by the Board at any time in its sole discretion and nothing herein should be construed as a guarantee to any Non-Employee Director of any particular level of cash or equity compensation. The terms and conditions of this Program shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors. This Program shall become effective on the date set forth above (the "***Effective Date***").

1. Cash Compensation.

(a) Annual Retainers. Each Non-Employee Director shall be eligible to receive an annual retainer of $50,000 for service on the Board.

(b) Additional Annual Retainers. In addition to the annual retainer payable pursuant to Section 1(a) above, a Non-Employee Director shall be eligible to receive the following annual retainers:

(i) Chairperson of the Board. A Non-Employee Director serving as Chairperson of the Board shall be eligible to receive an additional annual retainer of $35,000 for such service; provided, that, in the event that a Non-Employee Director is one of two concurrently serving Chairpersons of the Board, the additional annual retainer payable to such Non-Employee Director pursuant to this Section 1(b)(i) shall be $17,500.

(ii) Audit Committee. A Non-Employee Director serving as Chairperson of the Audit Committee of the Board (the "***Audit Committee***") shall be eligible to receive an additional annual retainer of $20,000 for such service. A Non-Employee Director serving as a member of the Audit Committee (other than the Chairperson of the Audit Committee) shall be eligible to receive an additional annual retainer of $10,000 for such service.

(iii) Compensation Committee. A Non-Employee Director serving as Chairperson of the Compensation Committee of the Board (the "***Compensation Committee***") shall be eligible to receive an additional annual retainer of $15,000 for such service. A Non-Employee Director serving as a member of the Compensation Committee (other than the Chairperson of the Compensation Committee) shall be eligible to receive an additional annual retainer of $7,500 for such service.

(iv) Nominating and Corporate Governance Committee. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee of the Board (the "***NCG Committee***") shall be eligible to receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the NCG Committee (other than the Chairperson of the NCG Committee) shall be eligible to receive an additional annual retainer of $5,000 for such service.

(v) Research and Development Committee. A Non-Employee Director serving as Chairperson of the Research and Development Committee of the Board (the "***R&D Committee***") shall be eligible to receive an additional annual retainer of $10,000 for such service. A Non-Employee Director serving as a member of the R&D Committee (other than the Chairperson of the R&D Committee) shall be eligible to receive an additional annual retainer of $5,000 for such service.

(c) Payment of Retainers. The annual retainers described in Sections 1(a) and 1(b) shall be earned on a quarterly basis based on a calendar quarter and shall be paid in cash by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section 1(b), for an entire calendar quarter, the retainer paid to such Non-Employee Director shall be prorated for the portion of such calendar quarter actually served as a Non-Employee Director, or in such position, as applicable.

2. Equity Compensation. Non-Employee Directors shall be granted the equity awards described below. Each award described below shall be granted under and shall be subject to the terms and provisions of the Company's 2023 Stock Incentive Plan, as amended, or any other successor Company equity incentive plan under which awards are permitted to be made to Non-Employee Directors (the "***Equity Plan***") and (i) for option awards, a non-qualified stock option award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable, and (ii) for restricted stock unit awards, a restricted stock unit award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable. All applicable terms of the Equity Plan apply to this Program as if fully set forth herein. For the avoidance of doubt, if there is any conflict between the terms of the Equity Plan (including the applicable award agreements thereunder) and this Program, the Equity Plan (including the applicable award agreements thereunder) shall control.

(a) Initial Awards. Each Non-Employee Director who is initially elected or appointed to the Board after the Effective Date shall be eligible to receive, on the date of such initial election or appointment, an option to purchase 214,400 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(a) shall be referred to as "***Initial Awards***." No Non-Employee Director shall be granted more than one Initial Award.

(b) Subsequent Awards. A Non-Employee Director who (i) has been serving on the Board for at least six months as of the date of any annual meeting of the Company's stockholders after the Effective Date and (ii) will continue to serve as a Non-Employee Director immediately following such meeting, shall be automatically granted, on the date of such annual meeting, an option to purchase 53,600 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan) and 35,700 restricted stock units of the Company. The option awards described in this Section 2(b) shall be referred to as "***Subsequent Options***", the restricted stock unit awards described in this Section 2(b) shall be referred to as "***Subsequent RSUs***", and the Subsequent Options and Subsequent RSUs shall together be referred to as the "***Subsequent Awards***." For the avoidance of doubt, a Non-Employee Director elected for the first time to the Board at an annual meeting of the Company's stockholders shall only receive an Initial Award in connection with such election, and shall not receive any Subsequent Awards on the date of such meeting as well.

(c) Termination of Service of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their service with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section 2(a) above, but to the extent that they are otherwise eligible, will be eligible to receive, after termination from service with the Company and any parent or subsidiary of the Company, Subsequent Awards as described in Section 2(b) above.

(d) Terms of Awards Granted to Non-Employee Directors.

(i) Purchase Price. The per share exercise price of each option granted to a Non-Employee Director shall equal the fair market value (as determined pursuant to the Equity Plan) of a share of the Company's common stock on the date the option is granted.

(ii) Vesting. Each Initial Award shall vest and become exercisable in accordance with the following schedule, subject to the Non-Employee Director remaining in continuous employment or other service relationship with the Company ("***Service***") through each such vesting date: 33 1/3% of the Initial Award shall vest on the one-year anniversary of the date of grant and 66 2/3% shall vest ratably on the first day of each calendar quarter between the one-year anniversary of the date of grant and the third anniversary of the date of grant. Each Subsequent Option shall vest and become exercisable in full on the first anniversary of the date of grant (or, if earlier, immediately prior to the first annual meeting of the Company's stockholders occurring after the date of grant), subject to the Non-Employee Director remaining in continuous Service through such vesting date. Each Subsequent RSU shall vest in full on the first anniversary of the date of grant (or, if earlier, immediately prior to the first annual meeting

of the Company's stockholders occurring after the date of grant), subject to the Non-Employee Director remaining in continuous Service through such vesting date. Each Initial Award and Subsequent Award that is then-outstanding shall vest and become exercisable in full upon a change in control of the Company or termination of the Non-Employee Director's Service due to the Non-Employee Director's death or Disability. For purposes of the Program, "***Disability***" means Executive's inability by reason of physical or mental impairment to perform his/her job duties for a period exceeding twelve (12) consecutive weeks.

(iii) Term. The term of each option granted to a Non-Employee Director shall be ten (10) years from the date the option is granted.

3. Non-Employee Director Compensation Limit. Notwithstanding anything herein to the contrary, the cash compensation and equity compensation that each Non-Employee Director is entitled to receive under this Program shall be subject to any limits set forth in the applicable Equity Plan with respect to limits on awards to Non-Employee Directors.

4. Reimbursements. The Company shall reimburse each Non-Employee Director for all reasonable, documented, out-of-pocket travel and other business expenses incurred by such Non-Employee Director in the performance of such Non-Employee Director's duties to the Company in accordance with the Company's applicable expense reimbursement policies and procedures, as in effect from time to time. To the extent that any reimbursement under this Program provides for a deferral of compensation under Section 409A of the Internal Revenue Code of 1986, as amended: (a) the amount eligible for reimbursement in one calendar year may not affect the amount eligible for reimbursement in any other calendar year; (b) the right to reimbursement is not subject to liquidation or exchange for another benefit; and (c) any such reimbursement of an expense must be made on or before the last day of the calendar year following the calendar year in which the expense was incurred.

**Exhibit 10.78**

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

**WHITBY PRODUCT AGREEMENT (Ferric Citrate IR Tablets)**

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated **September 27, 2016** between Patheon Manufacturing Services LLC and Keryx BioPharmaceuticals, Inc. (the "**Master Agreement**"), and is entered into **August 29, 2017** (the "**Effective Date**"), between Patheon Inc., a Canadian corporation, having a place of business at [**] ("**Patheon")** and Keryx BioPharmaceuticals, Inc., a corporation existing under the laws of Delaware, having a principal place of business at One Marina Park Drive, 12th Floor, Boston, MA 02210 ("**Client**").

The terms and conditions of the Master Agreement are incorporated herein except to the extent this Product Agreement expressly references the specific provision in the Master Agreement to be modified by this Product Agreement. All capitalized terms that are used but not defined in this Product Agreement will have the respective meanings given to them in the Master Agreement.

The Schedules to this Product Agreement are incorporated into and will be construed in accordance with the terms of this Product Agreement.

1. **Product List and Specifications:** (See Schedule A attached hereto)
2. **Minimum Order Quantity, Annual Volume, and Price:** (See Schedule B attached hereto)
3. **Annual Stability Testing and Validation Activities (if applicable):** (See Schedule C attached hereto)
4. **Active Materials, Active Materials Credit Value, and Maximum Credit Value:** (See Schedule D attached hereto)
5. **Client Supply Chain Inventory Documentation Requirements:** (See Schedule E attached hereto)
6. **Yearly Forecasted Volume:** Not applicable
7. **Territory:** USA, Europe, Canada
8. **Manufacturing Site**: [**]
9. **Governing Law:** New York per the Master Agreement
10. **Inflation Index:** PPI
11. **Currency:**$ USD
12. **Initial Set Exchange Rate:** 1:1.3401 (USD:CAD)
13. **Initial Product Term:** From the Effective Date until December 31, 2024.

14. **Notices:**
[**]

15. **Other Modifications to the Master Agreement:** None

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Product Agreement as of the Effective Date set forth above.

**PATHEON, INC.**

By: */s/ Don Liscombe*

Name: Don Liscombe

Title: VP & General Manager

**KERYX BIOPHARMACEUTICALS, INC.**

By: */s/ Gregory P. Madison*

Name: Gregory P. Madison

Title: President & CEO

## SCHEDULE A

## PRODUCT LIST AND SPECIFICATIONS

**Product List**

Auryxia (Ferric Citrate IR Tablets) [**]

**Specifications**

[**]

## SCHEDULE B

## MINIMUM ORDER QUANTITY. ANNUAL VOLUME, AND PRICE

[**]

## SCHEDULE C

## ANNUAL STABILITY TESTING AND VALIDATION ACTIVITIES

**Stability Testing**

Patheon and Client will agree in writing on any stability testing to be performed by Patheon on the Products. This agreement will specify the commercial and Product stability protocols applicable to the stability testing and the fees payable by Client for this testing.

[**]

## SCHEDULE D

## ACTIVE MATERIALS

| ACTIVE MATERIALS | SUPPLIER |
|---|---|
| Ferric Citrate | [**] |

## ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

| PRODUCT | ACTIVE MATERIALS | ACTIVE MATERIALS CREDIT VALUE |
|---|---|---|
| Auryxia (Ferric Citrate IR Tablets) | Ferric Citrate | [**] |

## MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Master Agreement in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

| PRODUCT | MAXIMUM CREDIT VALUE |
|---|---|
| Auryxia (Ferric Citrate IR Tablets) | [**] per Year to Patheon under this Product Agreement. |

## YIELD TOLERANCE

[**]

## SCHEDULE E

**Client Supply Chain Inventory Documentation Requirements**

[**]

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential.
Double asterisks denote omissions.

SECOND AMENDMENT TO AGREEMENT FOR THE PROVISION OF A LOAN FACILITY

This **SECOND AMENDMENT TO AGREEMENT FOR THE PROVISION OF A LOAN FACILITY** (the "**Amendment**"), dated as of February 3, 2025 (the "**Amendment Effective Date**"), is made by and between **KREOS CAPITAL VII (UK) LIMITED**, a company incorporated in England and Wales under registration number 13611522 whose registered office is at 8 Sackville Street, London, WS1 3DG, as a Lender (the "**Lender**" and "**Lender Representative**", which expression shall include its permitted successors and permitted assigns), and **AKEBIA THERAPEUTICS, INC.**, a Delaware corporation (the "**Borrower**" and "**Borrower Representative**"), and amends that certain AGREEMENT FOR THE PROVISION OF A LOAN FACILITY dated as of January 29, 2024 (as amended by that certain First Amendment to Agreement for the Provision of a Loan Facility, dated as of July 10, 2024, the "**Existing Loan Agreement**") by and between the Lender Representative and the Borrower Representative and the other parties thereto from time to time. The Existing Loan Agreement as amended by this Amendment is hereinafter referred to as the "**Loan Agreement**". Capitalized terms used in this Amendment without definition shall have the meanings ascribed to such terms in the Loan Agreement.

**WHEREAS**, the Borrower Representative and the Lender Representative are party to the Existing Loan Agreement which provides for, among other things, (A) a Loan under Tranche C to be made to the Borrower Representative on the terms and conditions contained in the Existing Loan Agreement, including that the Expiry Date of Tranche C was December 31, 2024 (the "**Original Expiry Date**") and (B) a Transaction Fee in respect of Tranche C in an amount equal to [**]% of the aggregate committed amount of Tranche C, [**]% of which was paid on the Closing Date and the remaining [**]% of which (such remaining amount, the "**Tranche C Funding Fee**") is payable on the earliest to occur of (i) the date Tranche C is funded, (ii) the date that the commitments in respect of Tranche C are terminated or cancelled and (iii) the date on which the availability period of Tranche C terminates;

**WHEREAS**, the Borrower Representative has requested the Lender Representative to amend the Loan Agreement to provide for an extension of the Expiry Date for Tranche C to February 3, 2025; and

**WHEREAS**, the Lender Representative has agreed to provide such extension on the terms and subject to the conditions hereof.

**NOW THEREFORE**, for good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, the Borrower Representative and the Lender Representative hereby agree as follows:

1. Amendments.
    a. The Existing Loan Agreement is hereby amended by deleting "December 31, 2024" appearing next to "Tranche C" in the Expiry Date portion of the Loan Facility Terms, and replacing it with "February 3, 2025."
    b. The Existing Loan Agreement is hereby amended by deleting Clause 6.2 and replacing it with the following:
        "Interest on the principal amount of each Tranche from time to time shall accrue from day to day at a rate of Adjusted Term SOFR plus six point seven five per cent (6.75% per annum) (the "**Applicable Interest Rate**"), from the applicable Drawdown Date until the repayment in full of such Loan; provided that the all-in interest rate shall not exceed 15.00% per annum. Notwithstanding the foregoing, to the extent a Loan is funded by the Lender to the Borrower under Tranche C (such Loan, the "**Tranche C Loan**"), interest on the Tranche C Loan shall accrue commencing on December 31, 2024 (notwithstanding that such Tranche C Loan will not be advanced until on or about February 3, 2025), as if such Tranche C Loan were advanced on December 31, 2024, and accordingly, the first interest payment in respect of the Tranche C Loan (which shall be

comprised of the accrued and unpaid interest from December 31, 2024 through (but excluding) the Drawdown Date for such Tranche C Loan) shall be paid by Borrower at the time of the disbursement of such Tranche C Loan, by way of deduction by the Lender Representative from the principal amount advanced; such interest payment is intended to compensate Lender Representative for delayed funding, and shall not constitute a penalty. Interest on the Loan and each part thereof shall be paid to the Lender Representative on each Monthly Repayment Date in the Contractual Currency in the amounts to be specified in the Repayment Schedule."

c. Notwithstanding anything in the Existing Loan Agreement or the Loan Agreement to the contrary (including Section 3.2.1 or Section 3.5.3(i) thereof), the Lender hereby agrees that the executed Drawdown Notice in respect of Tranche C may be delivered to the Lender [**] prior to the date of funding of Tranche C.

d. The parties hereto hereby agree that the Tranche C Funding Fee shall be due and payable on the Drawdown Date for the Tranche C Loan (and for the avoidance of doubt and notwithstanding anything in the Existing Loan Agreement or the Loan Agreement to the contrary, no Default or Event of Default resulted from the Tranche C Funding Fee not being paid by the Borrower on the Original Expiry Date).

e. All references in the Loan Documents to the Loan Agreement shall henceforth include references to the Existing Loan Agreement, as modified and amended by this Amendment, and as may, from time to time, be further amended, modified, extended, renewed, and/or increased.

f. Any and all of the terms and provisions of the Loan Documents are hereby amended and modified wherever necessary, even though not specifically addressed herein, so as to conform to the amendments and modifications set forth herein.

2. Conditions Precedent. This Amendment shall not be effective unless and until:

a. Lender Representative receives fully executed counterparts of this Amendment signed by Borrower Representative;

b. Borrower Representative shall have delivered, or caused to be delivered, in each case, in form and substance reasonably satisfactory to Lender Representative:

i. to Kreos Capital VII Aggregator SCSp, a duly executed Tranche C Warrant (as defined in the Warrant Agreement, dated as of January 29, 2024, by and among the Borrower and Kreos Capital VII Aggregator SCSp); and

ii. to Lender Representative, a duly executed Drawdown Notice for the Tranche C Loan in the principal amount of $10,000,000, as required by the Loan Agreement;

c. Immediately after giving effect to this Amendment, the representations and warranties in Section 4 of this Amendment shall be true and correct in all material respects (without duplication of any materiality qualifiers therein) as of the Amendment Effective Date with the same effect as though made as of such date (except to the extent that such representations and warranties

specifically refer to an earlier date, in which case they are true and correct in all material respects (without duplication of any materiality qualifiers therein) as of such earlier date);

d. Immediately after giving effect to this Amendment, no Default or Event of Default exists; and

e. Borrower Representative shall have paid all fees, costs and expenses required to be paid by it under the Loan Documents as of the Amendment Effective Date (including all fees, charges and disbursements of counsel to Lender Representative in connection with this Amendment) to the extent invoiced on or before [**] prior to the Amendment Effective Date.

3. Ratifications. Borrower Representative (a) ratifies and confirms all provisions of the Loan Documents as amended by this Amendment; (b) ratifies and confirms that all guaranties and liens granted to the Lender Representative under the Loan Documents are not released, reduced, or otherwise adversely affected by this Amendment and continue to guarantee and secure, as applicable, full payment and performance of all present and future obligations under the Loan Documents; and (c) subject to the Perfection Exceptions and any other exceptions, thresholds, limitations and deadlines contained in the other Loan Documents, agrees to perform such acts and duly authorize, execute, acknowledge, deliver, file, and record such additional documents, and certificates as the Lender Representative may request in order to create, perfect, preserve, and protect those guaranties, assurances, and Security Interests.

4. Representations. Borrower Representative hereby represents and warrants to the Lender Representative that as of the date of this Amendment:

a. the Borrower Representative has the corporate capacity, and has taken all corporate action and obtained all corporate consents, necessary for it to execute this Amendment and perform its obligations hereunder;

b. this Amendment will, upon execution and delivery thereof by all parties hereto, constitute the Borrower Representative's legal, valid and binding obligation enforceable against the Borrower Representative in accordance with its terms, subject to the effects of bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and other similar laws relating to or affecting creditors' rights generally, and general equitable principles (whether considered in a proceeding in equity or at law);

c. the execution and delivery of this Amendment by the Borrower Representative does not violate (i) any applicable material law or other material legal or regulatory requirement or (ii) its organizational documents;

d. all representations and warranties in the Loan Documents are true and correct in all material respects (without duplication of any materiality qualifiers therein) as of the Amendment Effective Date with the same effect as though made as of such date (except to the extent that such representations and warranties specifically refer to an earlier date, in which case they are true and correct in all material respects (without duplication of any materiality qualifiers therein) as of such earlier date); and

e. immediately after giving effect to this Amendment, no Default or Event of Default has occurred and is continuing.

5. Continued Effect. Except to the extent amended hereby, all terms, provisions and conditions of the Loan Agreement and the other Loan Documents, and all documents executed in connection therewith, shall continue in full force and effect and shall remain enforceable and binding in accordance with their respective terms. Without limitation of the foregoing or Section 2(e), all unpaid legal fees of Lender Representative in connection with this Amendment and the transactions contemplated hereby shall be paid by the Borrower, to the extent required by and in accordance with the terms of Section 10.3.1 of the Loan Agreement.
6. Post Amendment Effective Date Covenant.
    a. On or before the [**] following the Amendment Effective Date (or such later time period as the Lender Representative may agree in its reasonable discretion), the Borrower Representative shall have delivered a supplemental Perfection Certificate to the Lender Representative.

7. Loan Documents. This Amendment constitutes a Loan Document.
8. Parties. This Amendment binds and inures to the benefit of the Loan Parties and the Lender Representative and their respective permitted successors and permitted assigns.
9. RELEASE. BORROWER REPRESENTATIVE AND EACH LOAN PARTY HEREBY ACKNOWLEDGES AND AGREES THAT, AS OF THE DATE HEREOF, SUBJECT TO APPLICABLE LAW, THE OBLIGATIONS UNDER THE LOAN AGREEMENT AND UNDER THE OTHER LOAN DOCUMENTS ARE ABSOLUTE AND UNCONDITIONAL WITHOUT ANY RIGHT OF RESCISSION, SETOFF, COUNTERCLAIM, DEFENSE, OFFSET, CROSS-COMPLAINT, CLAIM OR DEMAND OF ANY KIND OR NATURE WHATSOEVER THAT CAN BE ASSERTED TO REDUCE OR ELIMINATE ALL OR ANY PART OF ITS LIABILITY TO REPAY SUCH OBLIGATIONS OR TO SEEK AFFIRMATIVE RELIEF OR DAMAGES OF ANY KIND OR NATURE FROM LENDER REPRESENTATIVE. BORROWER REPRESENTATIVE AND EACH LOAN PARTY HEREBY VOLUNTARILY AND KNOWINGLY RELEASES AND FOREVER DISCHARGES LENDER REPRESENTATIVE, AND ITS PREDECESSORS, AGENTS, EMPLOYEES, SUCCESSORS, AND ASSIGNS (COLLECTIVELY, THE "RELEASED PARTIES"), FROM ALL POSSIBLE CLAIMS, DEMANDS, ACTIONS, CAUSES OF ACTION, DAMAGES, COSTS, EXPENSES, AND LIABILITIES WHATSOEVER ARISING FROM OR UNDER THE LOAN DOCUMENTS, AND THE TRANSACTION EVIDENCED THEREBY, [**], FIXED, CONTINGENT, OR CONDITIONAL, AT LAW OR IN EQUITY, ORIGINATING IN WHOLE OR IN PART ON OR PRIOR TO THE DATE HEREOF WHICH BORROWER REPRESENTATIVE AND/OR ANY SUBSIDIARY GUARANTOR MAY NOW OR HEREAFTER HAVE AGAINST THE RELEASED PARTIES, IF ANY, AND IRRESPECTIVE OF WHETHER ANY SUCH CLAIMS ARISE OUT OF CONTRACT, TORT, VIOLATION OF LAW OR REGULATIONS, OR OTHERWISE, INCLUDING, WITHOUT LIMITATION, ANY CONTRACTING FOR, CHARGING, TAKING, RESERVING, COLLECTING, OR RECEIVING INTEREST IN EXCESS OF THE HIGHEST LAWFUL RATE APPLICABLE.

10. Incorporation by Reference. Clauses 2, 15.1, 15.3, 15.15, 15.17, 15.18, 15.21, 15.22, 15.23, 15.24, 15.25 and 15.26 of the Loan Agreement are hereby incorporated by reference ***mutatis mutandis***.

11. Governing Law. THIS AMENDMENT SHALL BE CONSTRUED IN ACCORDANCE WITH AND GOVERNED BY THE LAWS OF THE STATE OF NEW YORK.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be duly executed and delivered as of the day and year first above written.

**BORROWER AND BORROWER REPRESENTATIVE**

**AKEBIA THERAPEUTICS, INC.**

By: /s/ John P. Butler
Name: John P. Butler
Title: President and CEO

**Acknowledged and Agreed**

**SUBSIDIARY GUARANTORS**

**KERYX BIOPHARMACEUTICALS, INC.**

By: /s/ John P. Butler
Name: John P. Butler
Title: President and CEO

**LENDER AND LENDER REPRESENTATIVE**

**KREOS CAPITAL VII (UK) LIMITED**

By: __/s/ Aris Constantinides_____
Name: _Aris Constantinides _____
Title: __Director_____

[Signature Page to Second Amendment]

**Exhibit 19.1**

# Akebia Therapeutics, Inc.
# Insider Trading Compliance Policy

## BACKGROUND

The Board of Directors of Akebia Therapeutics, Inc. ("Akebia" or the "Company") has adopted this Insider Trading Compliance Policy (this "Policy") to:

- document its policies with respect to (i) transactions in the Company's securities and the securities of companies with which the Company does business and (ii) the handling of confidential information about the Company and the companies with which the Company does business;
- promote compliance with applicable securities laws; and
- promote compliance with the Company's obligation to publicly disclose information related to its insider trading policies and procedures and the use of certain trading arrangements by Company insiders.

While the "Prohibitions" of this Policy do not apply to transactions by the Company itself, transactions by the Company will only be made in accordance with applicable U.S. federal securities laws, including those relating to insider trading.

This policy has been designed to prevent insider trading and the appearance of impropriety on the part of the Company's Insiders, to satisfy the Company's obligation to reasonably supervise the activities of Company personnel, to protect the reputation of the Company and to help Company Insiders avoid the severe consequences associated with violations of insider trading laws.

## PERSONS SUBJECT TO THE POLICY

This Policy applies to the following individuals and entities ("Covered Persons"):

- Any director, employee, consultant or contractor of the Company or its subsidiaries ("Insiders");
- Individuals who reside with an Insider, regardless of whether those individuals are family members and any family member of an Insider who does not live in the Insider's household but whose transactions in any Covered Security (as defined below) are directed by the Insider or are subject to the Insider's influence or control; and
- All corporations, limited liability companies, partnerships, trusts or other entities controlled by any of the above Covered Persons included in the prior two bullets, unless the entity has implemented policies or procedures designed to ensure that such person cannot influence transactions by the entity involving Company securities.

An Insider is responsible for ensuring that Covered Transactions (as defined below) comply with this Policy. An Insider is also responsible for ensuring that those subject to this Policy as a result of their relationship with the Insider are informed of, and comply with, this Policy.

The General Counsel, Chief Financial Officer or Board of Directors may also determine that other persons should be subject to this Policy who have access to material nonpublic information of the Company or the companies with which the Company does business.

## COVERED TRANSACTIONS AND SECURITIES

The trading prohibitions in this Policy apply to all transactions in the Company's securities, including common stock, options and other securities the Company may issue from time to time, as well as derivative securities that are not issued by the Company, such as publicly traded options.

The term "transaction" as used in this Policy includes the purchase, sale or gift (which term, as used in this Policy, includes charitable donations) of securities. The trading prohibitions under this Policy also apply to transactions in the securities of companies with which the Company does business, such as the Company's collaboration partners, customers or suppliers, and companies with which the Company may be negotiating major transactions, such as an acquisition, investment, joint venture, collaboration, license or sale. The transactions described in this section are referred to in this Policy as "Covered Transactions," and the securities described in this section are referred to in this Policy as "Covered Securities."

## PROHIBITIONS

*No Trading While In Possession of Material Nonpublic Information.* Covered Persons may not engage in any transaction in the Company's securities, directly or indirectly, if they are aware of any material nonpublic information (defined below) regarding the Company or recommend doing so to someone else. Please note that transactions that may be necessary or justifiable for independent reasons (such as the need to raise money for an emergency expenditure) are no exception. Even the appearance of an improper transaction must be avoided.

*No Tipping.* Covered Persons may not tip or otherwise communicate to someone else any material nonpublic information about the Company if the recipient may use that information to purchase, sell or gift Company securities or tip that information to others.

In addition, no Covered Person who, in the course of service to the Company, learns of material nonpublic information about another company (i) with which the Company does business, such as the Company's collaboration partners, customers or suppliers, or (ii) that is involved in a potential transaction or business relationship with the Company, may purchase, sell or gift that other company's securities until the information becomes public or is no longer material, or tip or otherwise disclose to someone else such information if the recipient may use that information to purchase, sell or gift that other company's securities or tip that information to others.

*Stock Option Exercises.* This Policy's trading restrictions generally do not apply to the exercise of stock options granted by the Company. The trading restrictions do apply, however, to any sale of the underlying stock or to a cashless exercise of the option through a broker, such as Shareworks or Morgan Stanley, as this entails selling a portion of the underlying stock to cover the costs of exercise.

*Restricted Stock Awards/Units.* This Policy's trading restrictions do not apply to the vesting of restricted stock or restricted stock units, or the surrender of shares to the Company or the sale by the Company, on your behalf, in satisfaction of any tax withholding obligations arising from such vesting of restricted stock or restricted stock units, including within a black-out period, as long as such withholding or sale is permitted by the applicable award agreement or is pursuant to a permitted sell-to-cover instruction (as defined below), as applicable. This Policy's trading restrictions do apply, however, to market sales of any shares received through the vesting of restricted stock or restricted stock units not in accordance with a previously provided written instruction from the Insider.

*Employee Stock Purchase Plan.* This Policy's trading restrictions do not apply to (i) periodic purchases under any Company employee stock purchase plan that are made as the result of standing instructions, in a form approved by the Company, (ii) withdrawal from participation in the plan, or (iii) a decision to decrease the level of contribution in the plan. This Policy's trading restrictions do apply, however, to (a) an initial decision to participate in any Company employee stock purchase plan, (b) a decision to increase the level of contribution in a subsequent purchase period, and (c) any sales of shares acquired under the plan.

*Post-Termination Transactions*. If an individual or entity ceases to be a Covered Person at a time when such individual or entity is aware of material nonpublic information concerning the Company, the prohibitions on purchasing, selling and gifting of Company securities in this Policy shall continue to apply until that information has become public or is no longer material.

*Standing or Limit Orders*. Standing or limit orders, except standing or limit orders under an approved 10b5-1 trading plan (described below), create heightened risks for insider trading violations because the individual placing the order retains discretion over the orders after they have been placed. As a result, a standing or limit order could execute when an individual is in possession of material nonpublic information. The Company, therefore, discourages placing standing or limit orders on Covered Securities. If a Covered Person determines that he or she must use a standing or limit order, the order must not be entered into or modified while the Covered Person is aware of material nonpublic information, should be limited to short duration and should otherwise comply with this Policy, including any applicable black-out period and the preclearance procedures described in this Policy.

*Short Sales and Derivative Transactions.* Covered Persons may not engage in short sales (sales of securities that are not then owned) of Covered Securities, including "sales against the box" (a sale with delayed delivery) or purchases or sales of puts, calls or other derivative securities.

*Hedging Transactions.* Covered Persons may not purchase financial instruments (including prepaid variable forward contracts, equity swaps, collars, and exchange funds) or otherwise engage in transactions that hedge or offset, or are designed to hedge or offset, any decrease in the market value of Covered Securities.

*Trading on Margin or Pledging*. Covered Persons may not hold Covered Securities in a margin account or pledge such securities as collateral for a loan.

## EXEMPT TRANSACTIONS

*Company Benefit Plans*. This Policy does not apply to transactions under Company benefit plans, except as noted above.

*Bona Fide Gifts*. The prohibitions on transactions described above in the Section entitled "Prohibitions" do not apply to bona fide gifts of Covered Securities that are approved in advance by the Company.

*Mutual Funds*. If an individual owns shares of a mutual fund that invests in any Covered Securities, there are no restrictions on trading the shares of the mutual fund at any time.

*Change in Form of Ownership*. Transactions that involve merely the change in the form in which you own Covered Securities are permissible under this Policy. For example, you may transfer Covered Securities to an *inter vivos* trust of which you are the sole beneficiary during your lifetime.

*Transactions under 10b5-1 Trading Plans*. Transactions under 10b5-1 trading plans are discussed below.

## 10b5-1 TRADING PLANS

A U.S. Securities and Exchange Commission ("SEC") rule, Rule 10b5-1(c) ("10b5-1"), provides an affirmative defense to insider trading liability if a transaction occurs in compliance with the rule and is pursuant to a binding contract, written plan or specific instruction which satisfies the applicable affirmative defense conditions of Rule 10b5-1(c) (a "10b5-1 trading plan"), including as applicable the requirements applicable to an eligible sell-to-cover transaction as defined in Rule 10b5-1(c)(1)(ii)(D)(3) (a "permitted sell-to-cover instruction"). In general terms, a valid 10b5-1 trading plan is one that removes any control or discretion that a Covered Person has with respect to a transaction or series of transactions to be executed at some future time. Such 10b5-1 trading plan must be (1) in writing and (2) submitted to the Company for review prior to its adoption. Notwithstanding any other restrictions described in this Policy, transactions made

pursuant to a 10b5- 1 trading plan implemented in accordance with this Policy may occur during a black-out period or while a person is in possession of material nonpublic information.

Note that, in addition to the legal requirements to implement a valid 10b5-1 trading plan, directors and employees must also comply with the following Company policies:

1. A director or employee may only enter into a 10b5-1 trading plan outside a black-out period and when the individual is not in possession of any material nonpublic information.

2. A director or employee seeking to implement a 10b5-1 trading plan involving Akebia securities must submit the plan for review by the General Counsel or Chief Financial Officer (or their designees) prior to adoption.

3. Transactions of securities subject to a 10b5-1 trading plan must only be made pursuant to that plan (and not outside of that plan).

4. Any change or modification of a 10b5-1 trading plan, including its termination, must also be submitted for review by the General Counsel or Chief Financial Officer (or their designees).

Ensuring that a 10b5-1 trading plan complies with the requirements of 10b5-1 and the execution of transactions pursuant to the 10b5-1 trading plan are the sole responsibility of the individual initiating the plan, and not the Company, the General Counsel or Chief Financial Officer (or their designees), or any other Company employee. Any Covered Person who is interested in establishing a 10b5-1 trading plan should reach out to the Company's equity team member(s) within the Finance department for assistance.

The Company reserves the right to suspend, discontinue or otherwise prohibit any transaction in the Company's securities, even pursuant to a previously approved 10b5-1 trading plan, if the General Counsel or Chief Financial Officer (or their designees), or the Company's Board of Directors, in its discretion, determines that such action is in the best interests of the Company.

## BLACK-OUT PERIODS

The Company has regularly scheduled quarterly black-out periods and, from time-to-time, implements event-specific black-out periods. During a black-out period, directors, executive officers and other designated employees listed on Appendix A of this Policy are prohibited from engaging in any transactions involving Company securities or securities of other companies that could be related to the purpose of a particular black-out (other than as specified by the Policy). The Company will notify those individuals, entities, and/or Covered Persons who are subject to a black-out period.

*Quarterly Black-out Periods*. Quarterly black-out periods begin at the close of trading of The Nasdaq Capital Market 14 calendar days prior to the close of each fiscal quarter and end two full trading days following the public release of the Company's financial results for such quarter.

*Event-Specific Black-out Periods*. From time to time, the Company may implement an event- specific black-out period because of significant events or developments at the Company that have not yet been disclosed to the public. The existence of an event-specific black-out period will not be announced to the Company as a whole and should not be communicated to any other person.

*Awareness of Material Nonpublic Information when a Black-out Period is Not in Effect*. Even if no black-out period is then in effect, if a Covered Person is aware of material nonpublic information the trading prohibitions in this Policy apply.

*Sales to Cover*. This Policy shall not prohibit the Company, on your behalf, from instructing an agent to sell that number of shares pursuant to a permitted sell-to-cover instruction to satisfy any resulting tax withholding obligations, including within a black-out period.

## PRE-CLEARANCE PROCEDURES

Directors and employees may not engage in any transaction in Company securities without first obtaining pre-clearance of the transaction from the General Counsel or Chief Financial Officer (or their designees). This pre-clearance requirement applies to *all* transactions in Company securities, including a purchase or sale in the open market, the sale of any Company securities received as equity compensation and the transfer of securities of the Company.

A request for pre-clearance must be submitted to the General Counsel or Chief Financial Officer (or their designees) at least two business days in advance of the proposed transaction. The General Counsel or Chief Financial Officer (or their designees) is under no obligation to approve a transaction submitted for pre-clearance and may determine not to permit the transaction in his or her sole discretion. If a person seeks pre-clearance and permission to engage in the transaction is denied, then he or she must refrain from initiating any transaction in Company securities and should not inform any other person of the restriction.

All transactions that are pre-cleared must be effected within three business days of receipt of the pre-clearance unless a specific exemption has been granted by the General Counsel or Chief Financial Officer (or their designees). A pre-cleared transaction (or any portion of a pre-cleared transaction) that has not been effected during the three business day period must be pre-cleared again prior to execution.

When a request for pre-clearance is made, the requestor should carefully consider whether he or she may be aware of any material nonpublic information about the Company, and must describe fully those circumstances to the General Counsel or Chief Financial Officer (or their designees). None of the Company, General Counsel or Chief Financial Officer (or their

designees) or other employees will have any liability for any delay in reviewing or refusal of a request for pre-clearance. Pre-clearance does not relieve an individual of his or her responsibility under applicable securities laws.

The requestor should be prepared, if necessary, to file a Form 4 for the proposed transaction and to comply with SEC Rule 144 and file a Form 144 at the time of any sale.

## DEFINITIONS

*Material Information*. Information is material if there is a substantial likelihood that a reasonable investor would consider it important in deciding whether to buy, hold or sell a security. Any information that could reasonably be expected to affect the price of the security is material. Both positive and negative information can be material. Common examples of material information are:

- Information regarding sales, revenue or earnings, including prescription volumes;
- Projections and financial forecasts of any kind, including future earnings or losses or other financial guidance or changes in estimates;
- Significant business trends and metrics,
- Financial results that are inconsistent with the consensus expectations of the investment community;
- Information concerning upcoming U.S. Food and Drug Administration actions, the European Medicines Agency and other comparable foreign regulatory authorities regarding regulatory submissions or other significant regulatory developments, including a significant product recall;
- Clinical trial data or developments regarding products;
- A pending or proposed merger, acquisition, investment, tender offer, joint venture, licensing arrangement or an acquisition or disposition or divestitures of significant assets;
- A change in management;
- Major events regarding the Company’s securities, including financings, restructurings, the declaration of a stock split or the offering of additional securities or the establishment of a program to repurchase securities of the Company;
- Severe financial liquidity problems;

- Actual or threatened major litigation or government investigations or the resolution or major developments of such litigation or government investigations; or

- New significant contracts, orders, suppliers, customer or financing sources, or the loss of any of them.

This list is illustrative only and is not intended to provide a comprehensive list of circumstances that could give rise to material information, and trading that receives scrutiny will be evaluated after the fact with the benefit of hindsight. Therefore, it is important to err on the safe side and if you have any questions, please reach out to the Company's General Counsel (or his or her designee) before you transact.

*Nonpublic Information.* Nonpublic information is information that is not generally known or available to the public. Information is considered to be available to the public only when it has been released broadly to the marketplace (such as by a press release or an SEC filing) and the investing public has had time to absorb the information fully. As with questions of materiality, if you are not sure whether information is considered public, please reach out to the Company's General Counsel (or his or her designees) before you transact.

## CONFIDENTIALITY

Maintaining the confidentiality of Company information is essential for competitive, security and other business reasons, as well as to comply with applicable securities laws. Covered Persons must treat all information they learn about the Company or the companies with which the Company does business as a result of an Insider's service to or employment by the Company as confidential and proprietary.

The timing and nature of the Company's disclosure of material information to outsiders is subject to legal rules, the breach of which could result in substantial liability to individual directors or employees, the Company and its management. Accordingly, it is important that responses to inquiries regarding the Company from the press, investment analysts or others in the financial community be made on the Company's behalf only through authorized individuals, as expressly identified by the Company.

## CONSEQUENCES OF VIOLATIONS

Pursuant to applicable securities laws, individuals may be subject to a variety of penalties, including disgorgement of any profits, substantial fines and imprisonment, for engaging in insider trading and/or tipping material nonpublic information to an individual who engages in insider trading.

The Company's General Counsel (or his or her designee) is responsible for monitoring compliance and will work with Human Resources to address violations of this Policy. Employees in violation of this Policy will be subject to disciplinary action, which may include ineligibility for future equity awards, suspension or termination of employment.

## PERSONAL RESPONSIBILITY AND COMPANY ASSISTANCE

Compliance with this Policy is of the utmost importance. Covered Persons are responsible for knowing and understanding this Policy, complying with this Policy, and requesting clarification when questions arise. You are prohibited from engaging in any transaction in Akebia securities while aware of material nonpublic information about Akebia whether or not you rely upon or use material nonpublic information in deciding to trade.

If an individual or entity has any questions about this Policy or its application to any proposed transaction, he or she may obtain additional guidance from the Company's General Counsel (or his or her designee). Individuals should not try to resolve uncertainties on their own, as the rules relating to insider trading are often complex and violations carry severe consequences.

## CERTIFICATION REQUIREMENT

All directors, employees and consultants must certify their understanding of, and compliance with, this Policy. The required certification is attached to this Policy.

## Appendix A

During a black-out period, the following designated employees are prohibited from engaging in any transactions involving Company securities or securities of other companies that could be related to the purpose of such black-out period:

- Legal
- Finance
- Sales & Market Access
- Executive Team
- Leadership Team
- Management Team
- Company Administrative Assistants
- Investor Relations
- Business Development
- Board of Directors

## Certification

I certify that I have received, reviewed and understand Akebia Therapeutics, Inc.'s Insider Trading Compliance Policy and undertake, as a condition to my present and continued employment (or, if I am not an employee, affiliation with) Akebia Therapeutics, Inc. and/or any of its subsidiaries, to comply fully with the policies and procedures contained therein.

I understand that the Legal and Compliance Department is available to answer any questions I have regarding the Insider Trading Compliance Policy.

Print Name: _____

Signature: _____

Date: _____

**Exhibit 23.1**

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-196748) pertaining to the Amended and Restated 2008 Equity Incentive Plan, the 2014 Incentive Plan, and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-209469) pertaining to the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(3) Registration Statements (Form S-8 Nos. 333-216475 and 333-222728) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

(4) Registration Statement (Form S-8 No. 333-228772) pertaining to the 2014 Incentive Plan of Akebia Therapeutics, Inc. and the 1999 Share Option Plan, 2004 Long-Term Incentive Plan, 2007 Incentive Plan, Amended and Restated 2013 Incentive Plan, and 2018 Equity Incentive Plan of Keryx Biopharmaceuticals, Inc.,

(5) Registration Statement (Form S-8 No. 333-229366) pertaining to the 2014 Incentive Plan, the 2014 Employee Stock Purchase Plan, and the Inducement Grant Awards (January 2018 – December 2018) of Akebia Therapeutics, Inc.,

(6) Registration Statement (Form S-8 No. 333-233140) pertaining to the Amended and Restated 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(7) Registration Statement (Form S-8 No. 333-236060) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2019 – December 2019) of Akebia Therapeutics, Inc.,

(8) Registration Statement (Form S-8 No. 333-252336) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2020 – December 2020) of Akebia Therapeutics, Inc.,

(9) Registration Statement (Form S-8 No. 333-262392) pertaining to the 2014 Incentive Plan, as amended, and the Inducement Grant Awards (January 2021 – December 2021) of Akebia Therapeutics, Inc.,

(10) Registration Statement (Form S-8 No. 333-269457) pertaining to the 2014 Incentive Plan, as amended, and the Inducement Stock Option Awards (January 2022 – December 2022) of Akebia Therapeutics, Inc.,

(11) Registration Statement (Form S-8 No. 333-272453) pertaining to the 2023 Stock Incentive Plan of Akebia Therapeutics, Inc.,

(12) Registration Statement (Form S-8 No. 333-276770) pertaining to the Inducement Stock Option Awards (January 2023 – December 2023) of Akebia Therapeutics, Inc.,

(13) Registration Statement (Form S-3 No. 333-281903) of Akebia Therapeutics, Inc., and

(14) Registration Statement (Form S-8 No. 333-284590) pertaining to the Inducement Stock Option Awards (January 2024 – December 2024) of Akebia Therapeutics, Inc.;

of our reports dated March 13, 2025, with respect to the consolidated financial statements of Akebia Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Akebia Therapeutics, Inc. included in this Annual Report (Form 10-K) of Akebia Therapeutics, Inc. for the year ended December 31, 2024.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 13, 2025

**Exhibit 31.1**

**CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, John P. Butler, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 13, 2025

By: /s/ John P. Butler
John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

**Exhibit 31.2**

**CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Erik J. Ostrowski, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 13, 2025

By: /s/ Erik J. Ostrowski

Erik J. Ostrowski
Senior Vice President, Chief Financial Officer, Chief Business Officer and Treasurer
(Principal Financial Officer)

**Exhibit 32.1**

**CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. Section 1350)**

In connection with the accompanying Annual Report of Akebia Therapeutics, Inc., or the Company, on Form 10-K for the fiscal year ended December 31, 2024, or the Report, I, John P. Butler, as Chief Executive Officer and President of the Company, and I, Erik J. Ostrowski, as Senior Vice President, Chief Financial Officer, Chief Business Officer and Treasurer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

| | | | |
|---|---|---|---|
| Date: | March 13, 2025 | By: | /s/ John P. Butler<br>John P. Butler<br>President, Chief Executive Officer and Director<br>(Principal Executive Officer) |
| Date: | March 13, 2025 | By: | /s/ Erik J. Ostrowski<br>Erik J. Ostrowski<br>Senior Vice President, Chief Financial Officer, Chief Business Officer and Treasurer<br>(Principal Financial Officer) |