UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the quarterly period ended June 30, 2021

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
n/a
(Former name, former address and formal fiscal year, if changed since last report)

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, par value $0.00001 per share	**AKBA**	**The Nasdaq Global Market**

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

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Outstanding at July 30, 2021
174,537,458

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q 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:

- the potential therapeutic benefits, safety profile, and effectiveness of vadadustat;
- establishing vadadustat as a new oral standard of care for treatment of adult patients with anemia due to chronic kidney disease;
- the timing, investment and associated activities involved in the continued commercialization of Auryxia® (ferric citrate), its growth opportunities and Akebia's ability to execute thereon;
- the potential indications, demand and market opportunity, potential and acceptance of Auryxia and vadadustat, if approved, including the size of eligible patient populations;
- the timing of or likelihood of regulatory filings and approvals, including labeling or other restrictions, such as the anticipated timing of filing a response by the U.S. Food and Drug Administration, or FDA, to our New Drug Application for vadadustat and our planned filing of a E.U. Marketing Authorization Application for vadadustat with the European Medicines Agency, the potential approval of vadadustat and our outlook related thereto, and potential indications for vadadustat;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations with respect to (i) the ongoing anticipated financial impact and potential benefits to us related to our merger with Keryx Biopharmaceuticals, Inc., or Keryx, that was completed on December 12, 2018, (ii) integration of the businesses subsequent to the merger, and (iii) other matters related to the merger;
- 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, the period of time our cash resources and collaboration funding will fund our current operating plan, our internal control over financial reporting and disclosure controls and procedures, and remediation of the material weakness we have identified in our internal control over financial reporting relating to our inventory process or any future deficiencies or material weaknesses in our internal controls and procedures;
- the direct or indirect impacts of the coronavirus 2 (SARS-CoV-2) 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 intangible assets, goodwill, contingent consideration, debt and other assets and liabilities, including our impairment analysis and our methodology and assumptions regarding fair value measurements;
- the timing of the availability and disclosure of clinical trial data and results;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, supply, commercialization, launch, marketing and sale of Auryxia and vadadustat, if approved, and the associated timing thereof;

- the designs of our studies, and the type of information and data expected from our studies and the expected benefits 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 vadadustat, if approved;
- the targeted timing of enrollment of our clinical trials;
- the timing of initiation of our clinical trials and plans to conduct preclinical and clinical studies 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, as well as Abbreviated New Drug Applications filed by generic drug manufacturers and potential FDA approval thereof, and associated patent infringement suits that we have filed or may file, or other actions that we may take against such 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 vadadustat, if approved;
- 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 our key 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; and
- the timing, outcome and impact of current and any future legal proceedings.

Any or all of these forward-looking statements in this Quarterly Report on Form 10-Q may turn out to be inaccurate. These forward-looking statements involve risks and uncertainties, including those that are discussed below under the heading "Risk Factor Summary", and the risk factors identified further in Part II, Item 1A. "Risk Factors" included in this Quarterly Report on Form 10-Q and elsewhere in this Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q. 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 Quarterly Report on Form 10-Q 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.

In this Quarterly Report on Form 10-Q, unless otherwise stated or the context otherwise requires, references to “Akebia,” “we,” “us,” “our,” “the Company,” and similar references refer to Akebia Therapeutics, Inc. and, where appropriate, its subsidiaries, including Keryx.

AURYXIA®, AKEBIA Therapeutics®, Vafseo™ and their associated logos are trademarks of Akebia and/or its affiliates. All other trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners. All website addresses given in this Quarterly Report on Form 10-Q are for information only and are not intended to be an active link or to incorporate any website information into this document.

RISK FACTORS SUMMARY

Investing in our common stock involves numerous risks, including the risks summarized below and described in further detail in "Part II, Item 1A. Risk Factors" of this Quarterly Report on Form 10-Q, 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 significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows;
- We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts;
- Our obligations in connection with the Loan Agreement with BioPharma Credit PLC, BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership 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;
- Royalties from commercial sales of vadadustat under our Collaboration Agreement with Mitsubishi Tanabe Pharma Corporation will likely fluctuate and could impact our rights to receive future payments from our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P.;
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us;
- 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;
- We may fail to realize the anticipated benefits of our merger with Keryx, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties and liabilities, which may have a material adverse effect on our business and financial position;
- Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic;
- Our ability to successfully commercialize any approved product, including our ability to achieve their widespread market acceptance, is critical to the success of our business;
- If we are unable to maintain sales, marketing and distribution capabilities or to enter into additional agreements with third parties, we may not be successful in commercializing any approved product;
- If we are unable to obtain or maintain contracts with key distribution partners, our business could be materially harmed;
- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do;
- The commercialization of Riona and Vafseo™ in Japan 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 subject us to a variety of risks associated with international operations, which could materially adversely affect our business;
- In addition to Auryxia, we will continue to depend heavily on the success of our product candidate, vadadustat, for which we submitted an NDA to the FDA, which was accepted for filing in May 2021. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates;
- We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that delay or limit their commercial potential, or in the case of vadadustat, prevent its marketing approval;
- We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow our business;
- We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, or we may experience significant delays in doing so, any of which would materially harm our business;
- Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved;

- We are subject to a complex regulatory scheme that requires significant resources to ensure compliance. Failure to comply with applicable laws could subject us to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationships with key regulatory agencies such as the U.S Food and Drug Administration, the U.S. Securities and Exchange Commission or the European Medicines Agency;
- Our relationships with healthcare providers, physicians and third party payors are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings;
- 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 rely on third parties to conduct our clinical studies and certain of our preclinical studies for our product and product candidates. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to optimize the commercialization of Auryxia or obtain marketing approval for or commercialize vadadustat or any other product candidates, and our business could be substantially harmed;
- We rely on third parties to conduct all aspects of our product manufacturing. The loss of these manufacturers, their failure to supply us on a timely basis, or their failure to successfully carry out their contractual duties or comply with regulatory requirements or guidance could cause delays in or disruptions to our supply chain and substantially harm our business;
- We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans;
- If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property or develop similar 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;
- If we fail to attract, keep and motivate senior management and key personnel, we may be unable to successfully develop and commercialize any product candidates and approved product(s);
- Our employees, independent contractors, principal investigators, contract research organizations, contract manufacturing organizations, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws and regulations;
- We may encounter difficulties in managing our growth and expanding our operations successfully;
- Our stock price has been and may continue to be volatile, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors;
- We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting which would harm our business and the trading price of our common stock; and
- 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.

Akebia Therapeutics, Inc.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets
(Unaudited)
(in thousands, except share and per share data)

	June 30, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 246,992	$ 228,698
Available for sale securities	—	39,992
Inventory	37,898	61,017
Accounts receivable, net	35,005	26,853
Prepaid expenses and other current assets	11,181	14,877
Total current assets	331,076	371,437
Property and equipment, net	7,670	8,622
Operating lease assets	24,442	26,876
Goodwill	55,053	55,053
Other intangible assets, net	126,148	144,170
Other assets	67,474	37,981
Total assets	$ 611,863	$ 644,139
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 41,984	$ 41,308
Accrued expenses and other current liabilities	111,742	130,624
Short-term deferred revenue	11,869	15,214
Total current liabilities	165,595	187,146
Deferred revenue, net of current portion	16,598	25,345
Operating lease liabilities, net of current portion	21,735	24,621
Derivative liability	1,930	2,420
Long-term debt, net	96,917	96,378
Liability related to sale of future royalties, net	49,094	—
Other non-current liabilities	85,363	60,611
Total liabilities	437,232	396,521
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized; 0 shares issued and outstanding at June 30, 2021 and December 31, 2020	—	—
Common stock $0.00001 par value; 350,000,000 shares authorized at June 30, 2021 and December 31, 2020; 169,651,423 and 148,074,085 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively	2	1
Additional paid-in capital	1,504,752	1,425,115
Accumulated other comprehensive loss	6	13
Accumulated deficit	(1,330,129)	(1,177,511)
Total stockholders' equity	174,631	247,618
Total liabilities and stockholders' equity	$ 611,863	$ 644,139

See accompanying notes to unaudited condensed consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(in thousands, except share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenues:				
Product revenue, net	$ 32,959	$ 30,696	$ 63,367	$ 59,905
License, collaboration and other revenue	19,954	59,446	41,850	118,715
Total revenues	52,913	90,142	105,217	178,620
Cost of goods sold:				
Product	43,484	49,988	69,079	68,601
Amortization of intangibles	9,011	9,101	18,021	18,201
Impairment of intangible asset	—	115,527	—	115,527
Total cost of goods sold	52,495	174,616	87,100	202,329
Operating expenses:				
Research and development	37,214	52,819	77,825	134,050
Selling, general and administrative	41,651	35,482	82,979	73,465
License expense	894	1,044	1,590	1,720
Total operating expenses	79,759	89,345	162,394	209,235
Operating loss	(79,341)	(173,819)	(144,277)	(232,944)
Other income (expense):				
Interest expense	(4,962)	(2,308)	(9,768)	(4,280)
Other income	1,265	376	1,427	726
Net loss	$ (83,038)	$ (175,751)	$ (152,618)	$ (236,498)
Net loss per share - basic and diluted	$ (0.51)	$ (1.28)	$ (0.97)	$ (1.78)
Weighted-average number of common shares - basic and diluted	161,329,990	136,906,968	157,596,143	132,651,066
Comprehensive loss:				
Net loss	$ (83,038)	$ (175,751)	$ (152,618)	$ (236,498)
Other comprehensive loss - unrealized loss on debt securities	(3)	(9)	(7)	(9)
Total comprehensive loss	$ (83,041)	$ (175,760)	$ (152,625)	$ (236,507)

See accompanying notes to unaudited condensed consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(Unaudited)
(in thousands, except share data)

	Common Stock					
	Number of Shares	$0.00001 Par Value	Additional Paid-In Capital	Unrealized Gain/(Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2019	121,674,568	$ 1	$ 1,188,810	$ —	$ (794,054)	$ 394,757
Issuance of common stock, net of issuance costs	7,973,967	—	56,575	—	—	56,575
Proceeds from sale of stock under employee stock purchase plan	115,024	—	451	—	—	451
Share-based compensation expense	—	—	4,916	—	—	4,916
Exercise of options	64,126	—	412	—	—	412
Restricted stock unit vesting	423,755	—	—	—	—	—
Net loss	—	—	—	—	(60,747)	(60,747)
Balance at March 31, 2020	130,251,440	$ 1	$ 1,251,164	$ —	$ (854,801)	$ 396,364
Issuance of common stock, net of issuance costs	12,650,000	—	142,383	—	—	142,383
Share-based compensation expense	—	—	6,864	—	—	6,864
Exercise of options	48,103	—	409	—	—	409
Restricted stock unit vesting	179,866	—	—	—	—	—
Unrealized loss	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	(175,751)	(175,751)
Balance at June 30, 2020	143,129,409	$ 1	$ 1,400,820	$ (9)	$ (1,030,552)	$ 370,260
Balance at December 31, 2020	148,074,085	$ 1	$ 1,425,115	$ 13	$ (1,177,511)	$ 247,618
Issuance of common stock, net of issuance costs	9,228,017	1	29,497	—	—	29,498
Proceeds from sale of stock under employee stock purchase plan	154,276	—	367	—	—	367
Share-based compensation expense	—	—	5,992	—	—	5,992
Restricted stock unit vesting	1,063,711	—	—	—	—	—
Unrealized loss	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	(69,580)	(69,580)
Balance at March 31, 2021	158,520,089	$ 2	$ 1,460,971	$ 9	$ (1,247,091)	$ 213,891
Issuance of common stock, net of issuance costs	10,446,160	—	37,266	—	—	37,266
Share-based compensation expense	—	—	6,515	—	—	6,515
Exercise of options	—	—	—	—	—	—
Restricted stock unit vesting	685,174	—	—	—	—	—
Unrealized loss	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	(83,038)	(83,038)
Balance at June 30, 2021	169,651,423	$ 2	$ 1,504,752	$ 6	$ (1,330,129)	$ 174,631

See accompanying notes to unaudited condensed consolidated financial statements

AKEBIA THERAPEUTICS, INC.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(in thousands)

	Six Months Ended	
	June 30, 2021	**June 30, 2020**
Operating activities:		
Net loss	$ (152,618)	$ (236,498)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,012	1,045
Amortization of intangibles	18,021	18,201
Intangible asset impairment charge	—	115,527
Amortization of premium/discount on investments	(15)	(2)
Non-cash interest expense related to sale of future royalties	4,427	—
Non-cash royalty revenue related to sale of future royalties	(116)	—
Non-cash interest expense	539	872
Non-cash operating lease expense	(965)	(1,164)
Fair value step-up of inventory sold or written off	21,575	31,116
Write-down of inventory	5,425	10,089
Change in excess inventory purchase commitments	21,338	10,954
Stock-based compensation	12,506	11,780
Change in fair value of derivative liability	(490)	240
Changes in operating assets and liabilities:		
Accounts receivable	(8,152)	(251)
Inventory	(35,710)	(5,680)
Prepaid expenses and other current assets	3,301	(3,277)
Other long-term assets	4,149	57
Accounts payable	(1,120)	(4,979)
Accrued expense	(15,706)	13,611
Operating lease liabilities	804	869
Deferred revenue	(12,092)	(14,879)
Net cash used in operating activities	(133,887)	(52,369)
Investing activities:		
Purchase of equipment	(59)	(45)
Purchase of available for sale securities	—	(49,950)
Proceeds from the maturities of available for sale securities	40,000	245
Net cash provided by investing activities	39,941	(49,750)
Financing activities:		
Proceeds from sale of future royalties, net	44,783	—
Proceeds from the issuance of common stock, net of issuance costs	66,696	198,883
Proceeds from the sale of stock under employee stock purchase plan	367	451
Proceeds from the exercise of stock options	—	821
Net cash provided by financing activities	111,846	200,155
Increase in cash, cash equivalents, and restricted cash	17,900	98,036
Cash, cash equivalents, and restricted cash at beginning of the period	231,132	149,804
Cash, cash equivalents, and restricted cash at end of the period	$ 249,032	$ 247,840
Non-cash financing activities		
Unpaid offering costs	$ 68	$ 75

See accompanying notes to unaudited condensed consolidated financial statements

1. Nature of Organization and Operations

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007. Akebia is a biopharmaceutical company with the purpose of bettering the lives of people living with kidney disease. Akebia's lead investigational product candidate, vadadustat, is an oral therapy in development for the treatment of anemia due to chronic kidney disease, or CKD. Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which can lead to red blood cell, or RBC, production and improved oxygen delivery to tissues. Vadadustat is approved and marketed in Japan as a treatment for anemia due to CKD in both dialysis-dependent and non-dialysis dependent adult patients under the trade name Vafseo™. The Company submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in adult patients with CKD on dialysis, or DD-CKD, and adult patients with CKD not on dialysis, or NDD-CKD. The Company's NDA submission was accepted for filing by the FDA in May 2021 and at the time of filing the NDA, the FDA indicated that they were not currently planning to hold an Advisory Committee meeting to discuss the application for vadadustat. The FDA also assigned the application standard review and a Prescription Drug User Fee Act (PDUFA) target action date of March 29, 2022. In addition, the Company has a commercial product, Auryxia® (ferric citrate), which is currently approved by the FDA and marketed for two indications in the United States: the control of serum phosphorus levels in DD-CKD adult patients and the treatment of iron deficiency anemia, or IDA, in NDD-CKD adult patients. Ferric citrate is also approved and marketed in Japan as an oral treatment for IDA in adult patients and the improvement of hyperphosphatemia in adult patients with DD-CKD and NDD-CKD under the trade name Riona (ferric citrate hydrate).

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, 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 to the Company's Japanese partners Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii, on December 12, 2018 following the consummation of a merger with Keryx Biopharmaceuticals, Inc., or Keryx, or the Merger. Additionally, following regulatory approval of vadadustat in Japan, the Company began recognizing royalty revenues from Mitsubishi Tanabe Pharma Corporation, or MTPC, from the sale of Vafseo in August 2020. In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under its Collaboration Agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 5 for additional information). The Company has not generated a profit to date and may never generate profits from product sales. Vadadustat and the Company's other potential product candidates are subject to long development cycles, and the Company may be unsuccessful in its efforts to develop, obtain marketing approval for or market vadadustat and its other potential product candidates. If the Company does not successfully commercialize Auryxia, vadadustat or any other potential product candidate, it may be unable to achieve profitability.

The Company's management completed its going concern assessment in accordance with ASC 205-40, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASC 205-40. The Company believes that its cash resources will be sufficient to allow the Company to fund its current operating plan through at least the next twelve months from the filing of this Quarterly Report on Form 10-Q. There can be no assurance, however, that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company's operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all. The Company will require additional capital to pursue development and commercial activities related to Auryxia and vadadustat or any additional products and product candidates, including those that may be in-licensed or acquired. The Company expects to finance future cash needs through product revenue, public or private equity or debt transactions, payments from its collaborators, strategic transactions, or a combination of these approaches. However, adequate additional financing may not be available to the Company on acceptable terms, or at all. If the Company is unable to raise capital in sufficient amounts when needed or on attractive terms, it may not be able to pursue development and commercial activities related to Auryxia and vadadustat or any additional products and product candidates, including those that may be in-licensed or acquired.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S., or GAAP, for interim financial reporting and as required by Regulation S-X, Rule 10-01. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. 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.

In the opinion of management, all adjustments, consisting of normal recurring accruals and revisions of estimates, considered necessary for a fair presentation of the unaudited condensed consolidated financial statements have been included. Interim results for the three and six months ended June 30, 2021 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2021 or any other future period.

The accompanying unaudited condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. Management has determined that the Company operates in one segment, which is the business of developing and commercializing novel therapeutics for people with kidney disease. The information included in this Quarterly Report on Form 10-Q should be read in conjunction with the Company's consolidated financial statements and the accompanying notes included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission on February 25, 2021, or the 2020 Annual Report on Form 10-K.

The significant accounting policies used in preparation of these unaudited condensed consolidated financial statements for the three and six months ended June 30, 2021 are consistent with those discussed in Note 2 to the consolidated financial statements in the Company's 2020 Annual Report on Form 10-K and are updated below as necessary.

New Accounting Pronouncements – Recently Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes.* This standard became effective for the Company on January 1, 2021. ASU 2019-12 requires certain amendments to be applied using a modified retrospective approach, which requires a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption, while other amendments should be applied on a prospective basis. The adoption of this standard did not have a material impact on the Company's unaudited condensed consolidated financial statements and related disclosures.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: prepaid and accrued research and development expense, operating lease assets and liabilities, derivative liabilities, other non-current liabilities, including the excess purchase commitment liability, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, non-cash interest expense on the liability related to sale of future royalties, inventories, income taxes, intangible assets and goodwill. The Company has made estimates of the impact of COVID-19 within the unaudited condensed consolidated financial statements and there may be changes to those estimates in future periods including changes to sales, payor mix, reserves and allowances, intangible assets and goodwill.

Although the Company regularly assesses these estimates, actual results could differ materially from these estimates. Changes in estimates are recorded in the period they become known. The Company bases its estimates on historical experience and various other assumptions that it believes to be reasonable under the circumstances.

Liability Related to Sale of Future Royalties

The Company treats the liability related to sale of future royalties, see Note 5, 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. 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 unaudited condensed consolidated statements of operations and comprehensive loss.

3. Product Revenue and Reserves for Variable Consideration

To date, the Company's only source of product revenue has been from the U.S. sales of Auryxia. Total net product revenue was $33.0 million and $30.7 million for the three months ended June 30, 2021 and 2020, respectively, and $63.4 million and $59.9 million for the six months ended June 30, 2021 and 2020, respectively. The following table summarizes activity in each of the product revenue allowance and reserve categories for the six months ended June 30, 2021 and 2020 (in thousands):

	Chargebacks and Discounts	Rebates, Fees and other Deductions	Returns	Total
Balance at December 31, 2020	$ 802	$ 39,912	$ 649	$ 41,363
Current provisions related to sales in current year	6,084	69,163	3,616	78,863
Adjustments related to prior year sales	(6)	812	—	806
Credits/payments made	(5,588)	(63,795)	(3,715)	(73,098)
Balance at June 30, 2021	$ 1,292	$ 46,092	$ 550	$ 47,934
Balance at December 31, 2019	$ 738	$ 30,552	$ 253	$ 31,543
Current provisions related to sales in current year	5,055	66,348	2,684	74,087
Adjustments related to prior year sales	(31)	638	44	651
Credits/payments made	(4,995)	(54,945)	(2,237)	(62,177)
Balance at June 30, 2020	$ 767	$ 42,593	$ 744	$ 44,104

Chargebacks, discounts and returns are recorded as a direct reduction of revenue on the unaudited condensed consolidated statement of operations with a corresponding reduction to accounts receivable on the unaudited condensed consolidated balance sheets. Rebates, distribution-related fees, and other sales-related deductions are recorded as a reduction in revenue on the unaudited condensed consolidated statement of operations with a corresponding increase to accrued liabilities or accounts payable on the unaudited condensed consolidated balance sheets.

Accounts receivable, net related to product sales was approximately $35.0 million and $21.9 million as of June 30, 2021 and December 31, 2020, respectively.

4. License, Collaboration and Other Significant Agreements

During the three and six months ended June 30, 2021 and 2020, the Company recognized the following revenues from its license, collaboration and other significant agreements and had the following deferred revenue balances as of June 30, 2021:

License, Collaboration and Other Revenue:	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
	(in thousands)		(in thousands)	
MTPC Agreement	$ 4,594	$ 15,000	$ 4,612	$ 15,000
Otsuka U.S. Agreement	9,170	25,888	22,844	64,465
Otsuka International Agreement	4,700	12,832	11,672	32,202
Total Proportional Performance Revenue	$ 18,464	$ 53,720	$ 39,128	$ 111,667
JT and Torii	1,490	1,740	2,649	2,866
MTPC Other Revenue	—	3,986	73	4,182
Total License, Collaboration and Other Revenue	$ 19,954	$ 59,446	$ 41,850	$ 118,715

Deferred Revenue:	June 30, 2021 Short-Term	Long-Term	Total
		(in thousands)	
MTPC Agreement	$ 1,400	$ —	$ 1,400
Otsuka U.S. Agreement	$ 6,089	$ 9,485	$ 15,574
Otsuka International Agreement	4,380	2,435	6,815
Vifor Agreement	—	4,678	4,678
Total	$ 11,869	$ 16,598	$ 28,467

The following table presents changes in the Company's contract assets and liabilities during the six months ended June 30, 2021 and 2020 (in thousands):

Six Months Ended June 30, 2021	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Accounts receivable(1)	$ 3,045	$ 18,884	$ (19,112)	$ 2,817
Prepaid expenses and other current assets	$ 1,722	$ 211	$ (5)	$ 1,928
Contract liabilities:				
Deferred revenue	$ 40,559	$ 36,679	$ (48,770)	$ 28,468
Accounts payable	$ 7,227	$ —	$ (7,227)	$ —
Accrued expenses and other current liabilities	$ 10,000	$ —	$ —	$ 10,000
Six Months Ended June 30, 2020				
Contract assets:				
Accounts receivable(1)	$ 15,822	$ 118,368	$ (115,382)	$ 18,808
Prepaid expenses and other current assets	$ —	$ 756	$ —	$ 756
Contract liabilities:				
Deferred revenue	$ 72,950	$ 90,471	$ (105,350)	$ 58,071
Accounts payable	$ —	$ 5,651	$ —	$ 5,651
Accrued expenses and other current liabilities	$ —	$ 615	$ (615)	$ —

(1) Excludes accounts receivable from other services related to clinical and regulatory activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement as of June 30, 2021 and 2020 and December 31, 2020 and 2019. Also excludes accounts receivable related to amounts due to the Company from product sales which are included in the accompanying unaudited condensed consolidated balance sheet as of June 30, 2021 and December 31, 2020.

During the three and six months ended June 30, 2021 and 2020, 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:	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
Amounts included in deferred revenue at the beginning of the period	$ 5,822	$ 16,964	$ 10,895	$ 22,186
Performance obligations satisfied in previous periods	$ —	$ 3,555	$ —	$ 3,263

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC entered into a collaboration agreement, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, collectively, the MTPC Territory. In addition, the Company will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory. A more detailed description of this collaboration agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020. In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or the Royalty Agreement, 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 5 for additional information).

Revenue Recognition

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's arrangement with MTPC contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize vadadustat (the License Deliverable) in the MTPC Territory, (ii) clinical supply of vadadustat (the Clinical Supply Deliverable), (iii) knowledge transfer, (iv) Phase 2 dosing study research services (the Research Deliverable), and (v) rights to future know-how.

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.* Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the MTPC Agreement does not include a general right of return.

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. The deliverables associated with the License, Research and Clinical Supply Performance Obligation were satisfied as of June 30, 2018.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the estimated cost for the Phase 2 studies, (iii) a non-substantive milestone associated with the first patient enrolled in the NDD-CKD Phase 3 study, and (iv) the cost of all clinical supply provided to MTPC for the Phase 3 studies. No other development and no regulatory milestones were included in the transaction price at inception, as all other milestone amounts were fully constrained. Subsequent to inception, the transaction price also included certain development and regulatory milestones, as described below. As part of its evaluation of the constraint, the Company considers numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to MTPC and therefore have also been excluded from the transaction price. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the remaining consideration that may be payable to the Company subsequent to MTPC's commercial launch of Vafseo™ in the third quarter of 2020 is quarterly royalties on net sales, sales milestones, and certain regulatory milestones.

As of June 30, 2021, 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, comprised of $10.0 million relating to the JNDA filing and $15.0 million relating to regulatory approval of vadadustat in Japan, and (vi) $0.5 million in royalties from net sales of Vafseo. As of June 30, 2021, all development milestones and $25.0 million in regulatory milestones have been achieved. No other regulatory milestones have been assessed as probable of being achieved and as a result have been fully constrained. 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 recognized $0.1 million of revenue from MTPC royalties for each of the three and six months ended June 30, 2021. The Company recognized a $15.0 million regulatory milestone relating to regulatory approval of vadadustat in Japan as revenue during the three and six months ended June 30, 2020. 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 terms and conditions (see Note 5 for additional information). The revenue is classified as collaboration revenue in the accompanying unaudited condensed consolidated statements of operations and comprehensive loss. As of June 30, 2021, there was an immaterial amount in accounts receivable, no deferred revenue, and no contract assets. There were no asset or liability balances classified as long-term in the unaudited condensed consolidated balance sheet as of June 30, 2021.

Supply of Drug Product to MTPC

In March 2020, in connection with the MTPC Agreement, the Company and MTPC executed an amendment that agreed to supply MTPC with certain vadadustat process validation drug product for commercial use and MTPC agreed to reimburse the Company for certain manufacturing-related expenses. In connection with this arrangement, the Company invoiced the upfront payment of $10.4 million, which it received during the three months ended June 30, 2020. The Company does not recognize revenue under this arrangement until risk of loss passes to MTPC and delivery has occurred. No revenues were recognized for either of the three or six months ended June 30, 2021 and 2020 for drug product that was delivered under the MTPC Agreement. As of June 30, 2021, the Company recorded no accounts receivable, no deferred revenue, and $3.0 million in other current liabilities and $0.6 million in other non-current liabilities for drug product that was subject to return by MTPC.

On July 15, 2020, the Company and its collaboration partner MTPC entered into a supply agreement, or the MTPC Supply Agreement. The MTPC Supply Agreement includes the terms and conditions under which the Company will supply vadadustat drug product to MTPC for commercial use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement. A more detailed description of this supply agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

The Company recognized $4.5 million of revenue under the MTPC Supply Agreement during the three and six months ended June 30, 2021. During the six months ended June 30, 2021, the Company invoiced MTPC for $9.5 million in payments for vadadustat drug product ordered by MTPC. As of June 30, 2021, the Company recorded $0.9 million in accounts receivable, $1.4 million in deferred revenue, $15.1 million in other current liabilities and $7.6 million in other non-current liabilities.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration is focused on the development and commercialization of vadadustat in the United States.

Under the terms of the Otsuka U.S. Agreement, the Company granted to Otsuka a co-exclusive, non-sublicensable license under certain intellectual property controlled by the Company solely to perform medical affairs activities and to conduct non-promotional and commercialization activities related to vadadustat in accordance with the associated plans. The co-exclusive license relates to activities that will be jointly conducted by the Company and Otsuka pursuant to the terms of the Otsuka U.S. Agreement. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the Otsuka U.S. Agreement. A more detailed description of this collaboration agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company’s Annual Report on Form 10-K for the year ended December 31, 2020.

Revenue Recognition

The Company evaluated the elements of the Otsuka U.S. Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company’s arrangement with Otsuka contains the

following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable), and (iv) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka U.S. Agreement as follows: i) License and Development Services Combined (License Performance Obligation); (ii) Rights to Future Intellectual Property (Future IP Performance Obligation) and (iii) Joint Committee Services (Committee Performance Obligation). Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka U.S. Agreement does not include a general right of return. A more detailed description of the performance obligations under this agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

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 standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP 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. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to December 31, 2016. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that under ASC 606, the contract was modified in the second quarter of 2019 when the Otsuka Funding Option became effective and the Company became eligible to receive the Additional Funding amount. In connection with the modification, the Company adjusted the transaction price to include the Additional Funding amount as additional variable consideration. The Company constrains the variable consideration to an amount for which a significant revenue reversal is not probable. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation. The Company estimates the additional funding as a result of exercising the Otsuka Funding Option, or the Additional Funding, to total approximately $122.2 million or more, depending on the actual costs incurred toward the current global development plan. The Additional Funding is fully creditable against future payments due to the Company under the arrangement, provided that future payments due to the Company may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. As of June 30, 2021, the Additional Funding was $100.0 million.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period

and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of June 30, 2021, the transaction price totaling $479.1 million was comprised of: (i) the up-front payment of $125.0 million, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016 of $33.8 million, and (iii) the estimate of the net cost share consideration to be received of approximately $320.3 million with respect to amounts incurred by the Company subsequent to December 31, 2016. As of June 30, 2021, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the three months ended June 30, 2021 and 2020 the Company recognized revenue totaling approximately $9.2 million and $25.9 million, respectively, and approximately $22.8 million and $64.5 million, during the six months ended June 30, 2021 and 2020, respectively, with respect to the Otsuka U.S. Agreement. The revenue is classified as collaboration revenue in the accompanying unaudited condensed consolidated statements of operations. As of June 30, 2021, there was approximately $15.6 million of deferred revenue related to the Otsuka U.S. Agreement of which $6.1 million is classified as current and $9.5 million is classified as long-term in the accompanying unaudited condensed consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of June 30, 2021, there was an immaterial amount in accounts receivable and $1.3 million in prepaid expenses and other current assets in the accompanying unaudited condensed consolidated balance sheet. As of December 31, 2020, there was approximately $5.0 million in contract liabilities (included in accounts payable) and $1.2 million in prepaid expenses and other current assets in the consolidated balance sheet.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. 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, the Company is accounting for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, *Collaborative Arrangements* (ASC 808). Additionally, the Company has determined that in the context of the medical affairs, commercialization and non-promotional activities, Otsuka 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 the medical affairs, commercialization and non-promotional activities plans will be accounted for as a component of the related expense in the period incurred. During the three months ended June 30, 2021 and 2020, the Company incurred approximately $2.9 million and $0.2 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $1.4 million and $0.1 million are reimbursable by Otsuka and recorded as a reduction to research and development expense during the three months ended June 30, 2021 and 2020, respectively. During the three months ended June 30, 2021 and 2020, Otsuka incurred approximately $0.3 million and $0.4 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.1 million and $0.2 million are reimbursable by the Company and recorded as an increase to research and development expense during each of the three months ended June 30, 2021 and 2020.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On April 25, 2017, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement. The collaboration is focused on the development and commercialization of vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories, collectively, the Otsuka International Territory.
Under the terms of the Otsuka International Agreement, the Company granted to Otsuka an exclusive, sublicensable license under certain intellectual property controlled by the Company to develop and commercialize vadadustat and products containing or comprising vadadustat in the Otsuka International Territory. Additionally, under the terms of this agreement, the Company is responsible for leading the development of vadadustat, including the ongoing global Phase 3 development program. Otsuka has the sole responsibility, at its own cost, for the commercialization of vadadustat in the Otsuka International Territory, subject to the approval by the relevant regulatory authorities. A more detailed description of this collaboration agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

Revenue Recognition

The Company has accounted for the Otsuka International Agreement separately from the collaboration arrangement with Otsuka with respect to the U.S. due to the lack of interrelationship and interdependence of the elements and payment terms within each of the contracts as they relate to the respective territories. Accordingly, the Company has applied the guidance in ASC 606 solely in reference to the terms and conditions of the Otsuka International Agreement, while the Otsuka U.S.

Agreement has continued to be accounted for as a discrete agreement in its own right. The Company evaluated the Otsuka International Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, is a customer. The Company's arrangement with Otsuka related to the Otsuka International Territory contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize (including the associated packaging) vadadustat and products containing or comprising vadadustat and development services to be performed pursuant to the current global development plan (the License and Development Services Deliverable), (ii) rights to future intellectual property (the Future IP Deliverable) and (iii) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka International Agreement as follows: i) License and Development Services Combined (License Performance Obligation); (ii) Rights to Future Intellectual Property (Future IP Performance Obligation) and (iii) Joint Committee Services (Committee Performance Obligation). Factors considered in making this assessment of which material promises will be accounted for as a separate performance obligation included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the Otsuka International Agreement does not include a general right of return. A more detailed description of the performance obligations under this agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

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 standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP 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. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar. The Company has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including whether the receipt of the milestone payment is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka and therefore have also been excluded from the transaction price.

The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation.

As of June 30, 2021, the transaction price totaling $296.3 million was comprised of: (i) the up-front payment of $73.0 million, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017 of $0.2 million, and (iii) an estimate of the net cost share consideration to be received with respect to amounts incurred by the Company subsequent to March 31, 2017 of $223.1 million. As of June 30, 2021, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the three months ended June 30, 2021 and 2020, the Company recognized revenue totaling approximately $4.7 million and $12.8 million, respectively, and approximately $11.7 million and $32.2 million, respectively, during the six months ended June 30, 2021 and 2020, with respect to the Otsuka International Agreement. The revenue is classified as collaboration revenue in the accompanying unaudited condensed consolidated statements of operations. As of June 30, 2021, there was approximately

$6.8 million of deferred revenue related to the Otsuka International Agreement of which $4.4 million is classified as current and $2.4 million is classified as long-term in the accompanying unaudited condensed consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of June 30, 2021, there was an immaterial amount in accounts receivable and $0.6 million in prepaid expenses and other current assets in the accompanying unaudited condensed consolidated balance sheet. As of December 31, 2020, there was approximately $2.3 million in contract liabilities (included in accounts payable) and $0.5 million in prepaid expenses and other current assets in the consolidated balance sheet.

Janssen Pharmaceutica NV Research and License Agreement

Summary of Agreement

On February 9, 2017, the Company entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted the Company an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, Janssen granted to the Company a license for a three-year research term to conduct research on the HIF compound portfolio, which research term is now expired. During the research term, the Company could designate one or more compounds as candidates for development and commercialization. Once a compound was designated for development and commercialization, the Company was to be solely responsible for the development and commercialization of the compound worldwide at its own cost and expense.

Under the terms of the Janssen Agreement, the Company made an upfront payment of $1.0 million in cash to Janssen and issued a warrant (or "the Warrant") to purchase 509,611 shares of the Company’s common stock with an exercise price of $9.81 per share to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen. The Warrant is exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. The Warrant and the shares issuable upon exercise of the Warrant will be sold and issued without registration under the Securities Act of 1933, as amended, or the Securities Act. The Company recorded the fair value of the Warrant in the amount of $3.4 million to additional paid-in capital and research and development expense in March 2017. In addition, Janssen could be eligible to receive up to an aggregate of $16.5 million from the Company in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to $215.0 million from the Company in specified commercial milestones as well as tiered, escalating royalties ranging from a low- to mid-single digit percentage 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. A more detailed description of this collaboration agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company’s Annual Report on Form 10-K for the year ended December 31, 2020.

Cyclerion Therapeutics License Agreement

Summary of Agreement

On June 4, 2021, the Company entered into a License Agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted the Company 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, the Company made an upfront payment of $3.0 million in cash 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 (“ASU 2017-01”). The upfront payment was charged to expense at acquisition, as it relates to a development stage compound with no alternative future use.

In addition, Cyclerion could be eligible to receive up to an aggregate of $222.0 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 low-single-digit- to mid-double-digit percentage 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. The Company recorded the upfront payment in the amount of $3.0 million to research and development expense in June 2021.

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 longer of the expiration of the patents licensed under the Cyclerion Agreement, the expiration of regulatory exclusivity for such product, or 10 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.

Vifor Pharma License Agreement

Summary of Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd., or Vifor Pharma, pursuant to which the Company granted Vifor Pharma an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, or FMCNA, in the United States. On April 8, 2019, the Company and Vifor Pharma entered into an Amended and Restated License Agreement, or the Vifor Amended Agreement, which amended and restated in full the Vifor Agreement. Pursuant to the Vifor Amended Agreement, the Company granted Vifor Pharma an exclusive license to sell vadadustat to FKC and to certain third party dialysis organizations approved by the Company, or Third Party Dialysis Organizations, in the United States. A more detailed description of this collaboration agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and Vifor Pharma entered into an investment agreement, or the Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the Shares, to Vifor Pharma at a price per share of $14.00 for a total of $50.0 million. The amount representing the premium over the closing stock price of $12.69 on the date of the transaction, totaling $4.7 million, was determined by the Company to represent consideration related to the Vifor Agreement. As the parties' rights under the Vifor Agreement are conditioned upon (a) the approval of vadadustat for DD-CKD adult patients by the FDA; (b) the earlier of a determination by CMS that vadadustat will be reimbursed using Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment; and (c) payment by Vifor Pharma of a $25.0 million milestone upon the occurrence of (a) and (b), in accordance with ASC 606, the Company has determined that the full transaction price is fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including clinical and regulatory risks that must be overcome in order for the parties' rights to become effective and the probability of the $25.0 million milestone being achieved. Accordingly, the $4.7 million continues to be recorded as deferred revenue in the accompanying unaudited condensed consolidated balance sheets. Upon the satisfaction of the aforementioned conditions, revenue will be recognized as the Company supplies vadadustat to Vifor Pharma using a proportional performance method.

Vifor Pharma agreed to a lock-up restriction such that it agreed not to sell the Shares for a period of time following the effective date of the Investment Agreement as well as a customary standstill agreement. In addition, the Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The Shares 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.

Priority Review Voucher Letter Agreement

On February 14, 2020, the Company entered into a letter agreement, or the Letter Agreement, with Vifor Pharma relating to Vifor Pharma's agreement with a third party to purchase a Priority Review Voucher, or the PRV, issued by the FDA, subject to satisfaction of customary closing conditions, or the PRV Purchase. A PRV entitles the holder to priority review of a New Drug Application, or NDA, or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, Akebia paid Vifor Pharma $10.0 million in connection with the closing of the PRV Purchase. Vifor Pharma is obligated to retain all rights to, and maintain the validity of, the PRV until Akebia and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to Akebia for use with Akebia's NDA for vadadustat for the treatment of anemia due to CKD in both dialysis-dependent and non-dialysis dependent patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms. In March of 2021, the Company submitted an NDA for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. The Company's NDA submission did not include a PRV.

During the quarter ended March 31, 2020, the $10.0 million payment to Vifor Pharma was recorded to research and development expense in the unaudited condensed consolidated statement of operations and as an operating cash outflow in the unaudited condensed consolidated statement of cash flows.

License Agreement with Panion & BF Biotech, Inc.

As a result of the Merger, the Company had a license agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx, the Company's wholly owned subsidiary, was the contracting party, or the Panion License Agreement, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, the Company and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement, effective as of April 17, 2019. The Panion Amended License Agreement provides Keryx 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 the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Keryx-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. Consistent with the Panion License Agreement, 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. A more detailed description of this license agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

The Company recognized royalty payments due to Panion of approximately $2.8 million during each of the three months ended June 30, 2021 and 2020 and $5.3 million during each of the six months ended June 30, 2021 and 2020 relating to the Company's sales of Auryxia in the United States and JT and Torii's net sales of Riona in Japan, as the Company is required to pay a mid-single digit percentage of net sales of ferric citrate in the Company's licensed territories to Panion under the terms of the Panion Amended License Agreement.

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

Summary of Agreement
As a result of the Merger, the Company has an Amended and Restated Sublicense Agreement, which was amended in June 2013, with JT and Torii, or the JT and Torii Sublicense Agreement, under which Keryx, the Company's wholly owned subsidiary, remains the contracting party. Under the JT and Torii Sublicense Agreement, 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. A more detailed description of this sublicense agreement can be found in Note 4 of the Notes to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

Revenue Recognition

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's arrangement with JT and Torii contains the following material promises under the contract at inception: (i) exclusive license to develop and commercialize ferric citrate hydrate in Japan (the License Deliverable), (ii) supply of ferric citrate hydrate until JT and Torii could secure their own source (the Supply Deliverable), (iii) knowledge transfer, and (iv) rights to future know-how.

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 allocated 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 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, including 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.

The Company recognized license revenue of $1.5 million and $1.7 million during the three months ended June 30, 2021 and 2020, respectively, and $2.6 million and $2.9 million, respectively, during the six months ended June 30, 2021 and 2020, respectively, 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.

5. Liability Related to Sale of Future Royalties

On February 25, 2021, the Company entered into 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 vadadustat 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 MTPC Agreement, 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. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, the Company 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 the Company pays the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to the Company, and HCR would have no further right to any Royalty Interest Payments. The Company received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and the Company is eligible to receive an additional $5.0 million in each year from 2021 through 2023 under the Royalty Agreement if specified annual sales milestones are achieved for vadadustat in the MTPC Territory, subject to the satisfaction of certain customary conditions. The Company retains the right to receive all potential future regulatory milestones for vadadustat 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.

Although the Company sold its right to receive royalties and sales milestones for vadadustat in the MTPC Territory as described above, as a result of its ongoing involvement in the cash flows related to these royalties, the Company will continue to account for these royalties as revenue. The Company recognized the proceeds received from HCR as a liability that is being amortized using the effective interest method over the life of the arrangement. At the transaction date, the Company recorded the net proceeds of $44.8 million as a liability. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future net royalty payments to be made to HCR over the term of the Royalty Agreement. The total threshold of net royalties to be paid, less the net proceeds received, will be recorded as interest expense over the life of the liability. The Company imputes interest on the unamortized portion of the liability using the effective interest method. The annual effective interest rate as of June 30, 2021 was 19.3% which is reflected as interest expense in the unaudited condensed consolidated statements of operations and comprehensive loss. Over the course of the Royalty Agreement, the actual interest rate will be affected by the amount and timing of royalty revenue recognized and changes in forecasted royalty revenue. There are a number of factors that could materially affect the amount and timing of royalty payments from MTPC, none of which are within the Company's control. On a quarterly basis, the Company reassesses the effective interest rate and adjusts the rate prospectively as needed.

The following table shows the activity within the liability account for the six months ended June 30, 2021:

	June 30, 2021 (in thousands)
Liability related to sale of future royalties, net — beginning balance	$ —
Proceeds from sale of future royalties, net	44,783
MTPC royalties payable	(116)
Non-cash interest expense recognized	4,427
Liability related to sale of future royalties, net — ending balance	$ 49,094

The Royalty Agreement requires the Company to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, the MTPC Supply 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.

6. Available For Sale Securities

Cash, cash equivalents, and available for sale securities at June 30, 2021 and December 31, 2020 consisted of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
June 30, 2021				
Cash and cash equivalents	$ 246,992	$ —	$ —	$ 246,992
Available for sale securities:				
U.S. government debt securities	$ —	$ —	$ —	$ —
Total available for sale securities	$ —	$ —	$ —	$ —
Total cash, cash equivalents, and available for sale securities	$ 246,992	$ —	$ —	$ 246,992

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
December 31, 2020				
Cash and cash equivalents	$ 228,698	$ —	$ —	$ 228,698
Available for sale securities:				
U.S. government debt securities	$ 39,979	$ 13	$ —	$ 39,992
Total available for sale securities	$ 39,979	$ 13	$ —	$ 39,992
Total cash, cash equivalents, and available for sale securities	$ 268,677	$ 13	$ —	$ 268,690

There were no realized gains or losses on available for sale securities for the three and six months ended June 30, 2021 and 2020 and the Company did not recognize any credit losses during the three and six months ended June 30, 2021 and 2020. Additionally, the Company did not have any available for sale securities that were in an unrealized loss position as of June 30, 2021 and December 31, 2020.

7. Fair Value of Financial Instruments

The Company utilizes a portfolio management company for the valuation of the majority of its investments. This company is an independent, third-party vendor recognized to be an industry leader with access to market information that obtains or computes fair market values from quoted market prices, pricing for similar securities, recently executed transactions, cash flow models with yield curves and other pricing models. For valuations obtained from the pricing service, the Company performs due diligence to understand how the valuation was calculated or derived, focusing on the valuation technique used and the nature of the inputs.

Based on the fair value hierarchy, the Company classifies its cash equivalents and available for sale securities within Level 1 or Level 2. This is because the Company values its cash equivalents and available for sale securities using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

Assets measured or disclosed at fair value on a recurring basis as of June 30, 2021 and December 31, 2020 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
June 30, 2021				
Assets:				
Cash and cash equivalents	$ 246,992	$ —	$ —	$ 246,992
	$ 246,992	$ —	$ —	$ 246,992
Liabilities:				
Derivative liability	$ —	$ —	$ 1,930	$ 1,930
	$ —	$ —	$ 1,930	$ 1,930

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2020				
Assets:				
Cash and cash equivalents	$ 228,698	$ —	$ —	$ 228,698
U.S. government debt securities	—	39,992	—	39,992
	$ 228,698	$ 39,992	$ —	$ 268,690
Liabilities:				
Derivative liability	$ —	$ —	$ 2,420	$ 2,420
	$ —	$ —	$ 2,420	$ 2,420

The Company's Loan Agreement with Pharmakon (see Note 11) contains certain provisions that change the underlying cash flows of the debt instrument, including a potential extension to the interest-only period dependent on both no event of default having occurred and continuing and on the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The events of default include maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. The Company recorded a derivative liability related to the Company's Loan Agreement with Pharmakon of $1.9 million and $2.4 million as of June 30, 2021 and December 31, 2020, respectively. The Company classified the derivative liability as a non-current liability on the unaudited condensed consolidated balance sheet as of June 30, 2021 and December 31, 2020. The estimated fair value of the derivative liability on both June 30, 2021 and December 31, 2020 was determined using a scenario-based approach and discounted cash flow model that includes principal and interest payments under various scenarios involving clinical development success for vadadustat and various cash flow assumptions. Probabilities surrounding clinical development success were derived using industry benchmarks. Should the Company's assessment of the probabilities around these scenarios change, including for changes in market conditions, there could be a change to the fair value of the derivative liability.

The following table provides a roll-forward of the fair value of the derivative liability (in thousands):

Balance at December 31, 2020	$	2,420
Change in fair value of derivative liability, recorded as other expense		80
Balance at March 31, 2021	$	2,500
Change in fair value of derivative liability, recorded as other income		(570)
Balance at June 30, 2021	$	1,930

The Company had no other assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at June 30, 2021 and December 31, 2020.

Investment securities are exposed to various risks such as interest rate, market and credit risks. When the Company holds investment securities, due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, the Company considers if changes in risks in the near term would result in material changes in the fair value of investments.

8. Inventory

The components of inventory are summarized as follows:

	June 30, 2021	December 31, 2020
	(in thousands)	
Raw materials	$ 2,060	$ 2,542
Work in process	78,287	64,076
Finished goods	16,716	19,691
Total inventory	$ 97,063	$ 86,309

Long-term inventory, which primarily consists of raw materials and work in process, is included in other assets in the Company's unaudited condensed consolidated balance sheets.

	June 30, 2021	December 31, 2020
	(in thousands)	
Balance Sheet Classification:		
Inventory	$ 37,898	$ 61,017
Other assets	59,165	25,292
Total inventory	$ 97,063	$ 86,309

Inventory amounts written down as a result of excess, obsolescence, scrap or other reasons and charged to cost of goods sold totaled $0.4 million and $5.4 million during the three and six months ended June 30, 2021, in addition to related step-up charges of $8.7 million during the six months ended June 30, 2021. Inventory write-downs charged to cost of goods sold totaled $9.9 million and $10.1 million during the three and six months ended June 30, 2020. The decrease for the three and six months ended June 30, 2021 as compared to the three and six months ended June 30, 2020 was primarily due to lower write-downs to inventory reserves related to a previously disclosed manufacturing quality issue related to Auryxia during 2020.

If future sales of Auryxia are lower than expected, the Company may be required to write-down the value of such inventories. Inventory write-downs and losses on purchase commitments are recorded as a component of cost of sales in the unaudited condensed consolidated statement of operations.

9. Intangible Assets and Goodwill

Intangible Assets

The following table presents the Company's intangible assets at June 30, 2021 and December 31, 2020 (in thousands):

	June 30, 2021			
	Gross Carrying Value	Accumulated Amortization	Total	Estimated useful life
Acquired intangible assets:				
Developed product rights for Auryxia	$ 213,603	$ (87,455)	$ 126,148	6 years

	December 31, 2020				
	Gross Carrying Value	Accumulated Amortization	ASC 842 Adjustment	Total	Estimated useful life
Acquired intangible assets:					
Developed product rights for Auryxia	$ 213,603	$ (69,433)	—	$ 144,170	6 years
Favorable lease	545	(5)	(540)	—	N/A
Total	$ 214,148	$ (69,438)	$ (540)	$ 144,170	

On December 12, 2018, the Company completed the Merger, whereby it acquired certain definite-lived intangible assets, including the developed product rights for Auryxia and a favorable lease. The Company amortizes its definite-lived intangible assets acquired as part of the Merger using the straight-line method, which is considered the best estimate of economic benefit, over its estimated useful life. The Company recorded $9.0 million and $9.1 million in amortization expense related to the developed product rights for Auryxia during the three months ended June 30, 2021 and 2020, respectively, and $18.0 million and $18.2 million during the six months ended June 30, 2021 and 2020, respectively.

Goodwill

Goodwill was $55.1 million as of June 30, 2021 and December 31, 2020. The Company operates in one operating segment which the Company considers to be the only reporting unit. Goodwill is evaluated for impairment at the reporting unit level on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that an impairment may exist. There were no impairments of goodwill during the three and six months ended June 30, 2021 or 2020.

10. Accrued Expenses

Accrued expenses as of June 30, 2021 and December 31, 2020 are as follows:

	June 30, 2021	December 31, 2020
	(in thousands)	
Product revenue allowances	$ 38,433	$ 38,049
Accrued clinical	16,034	28,986
MTPC - Supply of commercial drug product	15,069	13,887
Otsuka PRV contribution	10,000	10,000
Accrued payroll	8,238	14,402
Lease liability	5,575	5,286
MTPC - Supply of validation drug product	2,994	4,090
Royalties	2,807	2,998
Professional fees	1,416	3,271
Accrued commercial manufacturing	1,288	514
Accrued severance	649	497
Accrued other	9,239	8,644
Total accrued expenses	$ 111,742	$ 130,624

11. Debt

Term Loans

On November 11, 2019, the Company, with Keryx as guarantor, entered into a loan agreement, or the 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, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to the Company in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term 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 first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. Each of the Tranche A Funding Date and the Tranche B Funding Date, a Funding Date.

Proceeds from the Term Loans may be used for general corporate purposes. The Company and Keryx entered into a Guaranty and Security Agreement with the Collateral Agent, or the Guaranty and Security Agreement, on the Tranche A Funding Date. Pursuant to the Guaranty and Security Agreement, the Company's obligations under the Term Loans are unconditionally guaranteed by Keryx, or the Guarantee. Additionally, the obligations of the Company and Keryx under the Term Loans and the Guarantee are secured by a first priority lien on certain assets of the Company and Keryx, including Auryxia and certain related assets, cash, and certain equity interests held by the Company and Keryx, collectively the Collateral.

The Term Loans bear interest at a floating rate per annum equal to the three-month LIBOR rate plus 7.50%, subject to a 2.00% LIBOR floor and a 3.35% LIBOR cap, payable quarterly in arrears. The Term Loans will mature on the fifth anniversary of the Tranche A Funding Date, or the Maturity Date. The Company will repay the principal under the Term Loans in equal quarterly payments starting on the 33rd-month anniversary of the applicable Funding Date or, if certain conditions are met, it will have the option to repay the principal in equal quarterly payments starting on the 48th-month anniversary of the applicable Funding Date, or collectively the Amortization Schedule. Under certain circumstances, unless certain liquidity conditions are met, the Maturity Date may decrease by up to one year, and the Amortization Schedule may correspondingly commence up to one year earlier.

On the Tranche A Funding Date, the Company paid to Pharmakon a facility fee equal to 2.00% of the aggregate principal amount of the Term Loans, or $2.0 million, in addition to other expenses incurred by Pharmakon and reimbursed by the Company, or Lender Expenses. The Tranche A draw was $77.3 million, net of facility fee, Lender Expenses and issuance costs. The Tranche B draw was $20.0 million, net of immaterial Lender Expenses and issuance costs. The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to a prepayment premium. The prepayment premium would be 2.00% of the principal amount being prepaid prior to the third anniversary of the applicable Funding Date, 1.00% on or after the third anniversary, but prior to the fourth anniversary, of the applicable Funding Date, and 0.50% on or after the fourth anniversary of the applicable Funding Date but prior to the Maturity Date, and a make-whole premium on or prior to the second anniversary of the applicable Funding Date in an amount equal to foregone interest through the second anniversary of the applicable Funding Date. A change of control triggers a mandatory prepayment of the Term Loans.

The Loan Agreement contains customary representations, warranties, events of default and covenants of the Company and its subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement. Under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. As of June 30, 2021 and December 31, 2020, the Company determined that no events of default had occurred.

The Company assessed the terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation or any beneficial conversion feature. As part of this analysis, the Company assessed the economic characteristics and risks of the Loan Agreement, including put and call features. The terms and features assessed include a potential extension to the interest-only period dependent on both no event of default having occurred and continuing and on the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The fair value of the derivative liability related to the Company's Loan Agreement with Pharmakon was $1.9 million and $2.4 million as of June 30, 2021 and December 31, 2020, respectively. The Company classified the derivative liability as a non-current liability on the unaudited condensed consolidated balance sheet as of June 30, 2021.

The Company recognized interest expense related to the Loan Agreement of $2.7 million and $2.2 million, respectively, during the three months ended June 30, 2021 and 2020, and $5.4 million and $4.4 million for the first six months ended June 30, 2021 and 2020, respectively.

12. Warrant

In connection with the Janssen Agreement, in February 2017, the Company issued a warrant to purchase 509,611 shares of the Company's common stock at an exercise price of $9.81 per share. The warrant was fully vested upon issuance and exercisable in whole or in part, at any time prior to February 9, 2022. The warrant satisfied the equity classification criteria of ASC 815, and is therefore classified as an equity instrument. The fair value at issuance of $3.4 million was calculated using the Black Scholes option pricing model and was charged to research and development expense as it represented consideration for a license for which the underlying intellectual property was deemed to have no alternative future use. As of June 30, 2021, the warrant remains outstanding and expires on February 9, 2022.

13. Stockholders' Equity

Authorized and Outstanding Capital Stock

On June 5, 2020, the Company filed a Certificate of Amendment to its Ninth Amended and Restated Certificate of Incorporation, or its Charter, to increase the number of authorized shares of common stock from 175,000,000 to 350,000,000. As of June 30, 2021, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value $0.00001 per share, of which 169,651,423 and 148,074,085 shares were issued and outstanding as of June 30, 2021 and December 31, 2020, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which no shares were issued and outstanding as of June 30, 2021 and December 31, 2020.

At-the-Market Facility

On November 12, 2019, the Company entered into an Amended and Restated Controlled Equity Offering℠ Sales Agreement with Cantor Fitzgerald & Co. for the offer and sale of common stock at the then current market prices in amounts to be determined from time to time. Also, on November 12, 2019, the Company filed a prospectus supplement pursuant to which it was able to offer and sell under the sales agreement up to $75.0 million of its common stock at the then current market prices from time to time. Through December 31, 2019, the Company sold 2,684,392 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $16.8 million. During the three months ended March 31, 2020, the Company sold 7,973,967 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $56.7 million.

On March 12, 2020, the Company filed a prospectus supplement relating to the sales agreement, pursuant to which it is able to offer and sell up to $65.0 million of its common stock at current market prices from time to time. Through December 31, 2020, the Company sold 3,509,381 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $10.6 million. During the three months ended March 31, 2021, the Company sold 5,224,278 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $15.9 million.

On February 25, 2021, the Company filed a prospectus relating to the sales agreement with its new shelf registration statement (which replaced the prior shelf registration statement and the sales agreement prospectus supplement), pursuant to which it is able to offer and sell up to $100.0 million of its common stock at current market prices from time to time. During the three and six months ended June 30, 2021 and through the date of this Quarterly Report on Form 10-Q, the Company sold 10,446,160 and 24,404,643 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $37.3 million and $67.2 million, respectively.

Equity Plans

The Company maintains one stock incentive plan, the 2014 Incentive Plan, or the 2014 Plan as well as the 2014 Employee Stock Purchase Plan, or the 2014 ESPP. The 2014 Plan replaced the Company's Amended and Restated 2008 Equity Incentive Plan, or the 2008 Plan, however, options or other awards granted under the 2008 Plan prior to the adoption of the 2014 Plan that

have not been settled or forfeited remain outstanding and effective. On June 6, 2019, the Company's shareholders approved the Amended and Restated 2014 Employee Stock Purchase Plan, or the ESPP. The Company also maintains an inducement award program 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 six months ended June 30, 2021, the Company granted 864,200 options to purchase shares of the Company's common stock to new hires as inducements material to such employees' entering into employment with the Company, of which 845,200 options to purchase Akebia Shares remained outstanding as of June 30, 2021.

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, RSUs, performance awards and other awards convertible into or otherwise based on shares of the Company's common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1 of each calendar year, by an amount equal to three percent (3%) of the number of Akebia Shares outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31, or the 2014 Plan Evergreen Provision. The Company's Board of Directors may act prior to January 1 of any year to provide that there will be no automatic increase in the number of Akebia Shares available for grant under the 2014 Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). On December 12, 2018, in connection with the consummation of the Merger, the Company assumed outstanding and unexercised options to purchase Keryx Shares, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, under the following Keryx equity plans, or the Keryx Equity Plans: the Keryx 1999 Share Option Plan, the Keryx 2004 Long-Term Incentive Plan, the Keryx 2007 Incentive Plan, the Keryx Amended and Restated 2013 Incentive Plan, and the Keryx 2018 Equity Incentive Plan, or the Keryx 2018 Plan. In addition, the number of Keryx Shares available for issuance under the Keryx 2018 Plan, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, may be used for awards granted by the Company under its 2014 Plan, or the Assumed Shares, provided that the Company uses the Assumed Shares for individuals who were not employees or directors of the Company prior to the consummation of the Merger.

The Company grants service-based stock options to employees under the 2014 Plan. During the six months ended June 30, 2021, the Company issued 1,797,200 options to employees. In addition, the Company issues stock options to directors, new hires and occasionally to other employees not in connection with the annual grant process. During the first six months ended June 30, 2021, the Company issued 200,800 options to directors under the 2014 Plan. Options granted by the Company 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 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 generally expire 10 years after the date of grant.

The Company also grants service-based restricted stock units, or RSUs to employees under the 2014 Plan. During the six months ended June 30, 2021, the Company issued 3,372,212 RSUs to employees. In addition, the Company issued 82,200 RSUs to directors under the 2014 Plan during the six months ended June 30, 2021. The Company also occasionally issues RSUs not in connection with the annual grant process to employees. Generally, RSUs granted by the Company vest in one of the following ways: (i) 100% of each RSU grant vests on either the first or the third anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, subject, in each case, to the individual's continued service through the applicable vesting date, or (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. 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 on a straight-line basis over the vesting period.

The Company also grants performance-based restricted stock units, or PSUs to employees under the 2014 Plan. The PSUs granted by the Company vest in connection with the achievement of specified commercial and regulatory milestones. The PSUs also 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 and regulatory milestones. The Company did not grant any PSUs during the six months ended June 30, 2021.

The ESPP provides for the issuance of options to purchase shares of the Company's common stock to participating employees at a discount to their fair market value. As noted above, the Company's stockholders approved the ESPP, which amended and restated the Company's 2014 ESPP, on June 6, 2019. The maximum aggregate number of shares at June 30, 2021 of the Company's common stock available for future issuance under the ESPP is 5,326,058. Under the ESPP, each offering period is six months, at the end of which employees may purchase shares of the Company's common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of each offering period is equal to the lesser of

eighty-five percent (85%) of the closing price of the Company's common stock at the beginning or end of the offering period. The Company issued 154,276 shares under the ESPP during the six months ended June 30, 2021.

14. Commitments and Contingencies

Leases

The Company leases approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in November 2020, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to the Company and did not impact rent payments. In April 2018, the Company entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by the Company was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, which commenced in September 2019. In November 2020, the Company entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000 commencing in December 2021, and is subject to annual rent escalations, which commence in December 2022.

Additionally, as a result of the Merger, the Company has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires in February 2023. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations.

The term of the Cambridge Lease with respect to the office space expires on September 11, 2026, with one five-year extension option available. The term of the Boston Lease office space expires on February 28, 2023, with an extension option for one additional five-year term available. The renewal options in these real estate leases were not included in the calculation of the operating lease assets and operating lease liabilities as the renewal is not reasonably certain. The term of the Cambridge Lease with respect to the lab space expires on January 31, 2025, with an extension option for one additional period through September 11, 2026. The renewal option in this real estate lease was included in the calculation of the operating lease assets and operating lease liabilities as the renewal is reasonably certain. The lease agreements do not contain residual value guarantees. Operating lease costs were $1.7 million for each of the three months ended June 30, 2021 and 2020 and $3.3 million for each of the six months ended June 30, 2021 and 2020. Cash paid for amounts included in the measurement of operating lease liabilities was $1.8 million for each of the three months ended June 30, 2021 and 2020 and $3.5 million for each of the six months ended June 30, 2021 and 2020, respectively.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease is subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement, and expires on February 27, 2023. Foundation is obligated to pay Keryx rent that approximates the rent due from Keryx to its landlord with respect to the Boston Lease. Sublease rental income is recorded to other income. Keryx continues to be obligated for all payment terms pursuant to the Boston Lease, and the Company will guaranty Keryx's obligations under the sublease. Keryx recorded $0.4 million in sublease rental income from Foundation during each of the three months ended June 30, 2021 and 2020 and $0.9 million during each of the six months ended June 30, 2021 and 2020.

The Company has not entered into any material short-term leases or financing leases as of June 30, 2021.

The total security deposit in connection with the Cambridge Lease is $1.6 million as of June 30, 2021. Additionally, the Company recorded $0.4 million for the security deposit under the Boston Lease. Both the Cambridge Lease and the Boston Lease have their security deposits in the form of a letter of credit, all of which are included as restricted cash in other assets in the Company's unaudited condensed consolidated balance sheets as of June 30, 2021.

As of June 30, 2021, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter are as follows:

	Operating Leases	Lease Payments to be Received from Sublease	Net Operating Lease Payments
		(in thousands)	
Remaining 2021	$ 3,582	$ 902	$ 2,680
2022	7,328	1,824	5,504
2023	5,954	307	5,647
2024	5,746	—	5,746
2025	5,823	—	5,823
Thereafter	4,052	—	4,052
Total	$ 32,485	$ 3,033	$ 29,452

In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.22% to 6.94%, which were based on the remaining lease term at either the date of adoption of ASC 842 or the effective date of any subsequent lease term extensions. As of June 30, 2021, the remaining lease terms ranged from 1.67 years to 5.20 years. As of June 30, 2021, the following represents the difference between the remaining undiscounted minimum rental commitments under non-cancelable leases and the operating lease liabilities:

	Operating Leases
	(in thousands) Total
Undiscounted minimum rental commitments	$ 32,485
Present value adjustment using incremental borrowing rate	(4,836)
Operating lease liabilities	$ 27,649

Manufacturing Agreements

As a result of the Merger, the Company's contractual obligations include Keryx’s commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or Siegfried, to supply commercial drug substance for Auryxia.

Pursuant to the Manufacture and Supply Agreement with BioVectra and the Product Manufacture and Supply and Facility Construction Agreement with BioVectra, collectively the BioVectra Agreement, the Company agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices. On September 4, 2020, the Company and BioVectra entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement, which provided for reduced minimum quantity commitments and revised the predetermined prices. The price per kilogram decreases with an increase in quantity above the predetermined purchase quantity tiers. In addition, the Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra, collectively the Amended BioVectra Agreement, requires the Company to reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of Auryxia drug substance. These construction costs are recorded in other assets and amortized into drug substance as inventory is released to the Company from BioVectra. The term of the Manufacture and Supply Agreement with BioVectra expires on December 31, 2022. The term of the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement expires on December 31, 2026, after which it automatically renews for successive one-year terms unless either party gives notice of its intention to terminate within a specified time prior to the end of the then-current term. In addition, the Company and BioVectra each have the ability to terminate these agreements upon the occurrence of certain conditions. As of June 30, 2021, the Company is required to reimburse BioVectra for certain costs in connection with the construction of the new facility and to purchase minimum quantities of Auryxia drug substance annually for a total cost of approximately $84.3 million through the end of the contract term.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, as amended (the most recent amendment having been executed on February 11, 2021), or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The term of the Siegfried Agreement expires on December 31, 2022, subject to our option to extend the term through December 31, 2023 by providing 12 months’ prior written notice to Siegfried. The Siegfried Agreement provides the Company and Siegfried with certain early termination rights. As of June 30, 2021, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $32.4 million through the year ending December 31, 2022.

As part of purchase accounting, the Company identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast. The Company regularly reviews its estimate of the excess purchase commitment liability including a review of assumptions of expected future demand, estimates of anticipated expiry of inventory under firm purchase commitments that are estimated to expire before they could be sold as well as any modifications to supply agreements during each reporting period. During the second quarter ended June 30, 2021, the Company completed a routine update of its long-range plan and related estimates of expiry. This routine update included the impact of recent activity with regards to our long-term payor contract strategy which continues to focus on contract economics and net revenue growth and resulted in a $30.3 million increase in the estimated excess purchase commitments liability with an associated charge to cost of goods sold during the quarter ended June 30, 2021. The liability related to the amount of purchase commitments that exceed the current forecast or were estimated to expire prior to sale was $77.1 million and $55.8 million as of June 30, 2021 and December 31, 2020, respectively. As of June 30, 2021, the Company also considered whether this increase was a potential indicator of impairment of the Auryxia asset group as of June 30, 2021. As part of its assessment, the Company reviewed the Auryxia net sales and estimated future cash flows included in its long-range plan and concluded that the increase in excess purchase commitment liability was not an indicator of impairment of the Auryxia asset group as of June 30, 2021. In addition, during the first quarter ended March 31, 2021, the Company recorded a non-cash gain to cost of goods sold of $9.0 million driven largely by a reduction in purchase commitments due to the amendment to the Siegfried Agreement during the first quarter of 2021.

On April 9, 2019, the Company entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement includes the terms and conditions under which Esteve will manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, the Company provides rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflects the Company's needs for vadadustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadadustat drug substance per calendar quarter. The parties have agreed to a volume-based pricing structure under the Esteve Agreement. The Esteve Agreement has an initial term of four years, beginning April 9, 2019 and ending April 9, 2023. Pursuant to the Esteve Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from Esteve. As of June 30, 2021, the Company has committed to purchase $36.7 million of vadadustat drug substance from Esteve through the fourth quarter of 2022.

On March 11, 2020, the Company entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for commercial use. Pursuant to the Patheon Agreement, the Company provides Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects the Company's needs for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement has an initial term beginning March 11, 2020 and ending June 30, 2023. Pursuant to the Patheon Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of June 30, 2021, the Company had a minimum commitment with Patheon for $2.6 million through the third quarter of 2021.

On April 2, 2020, the Company entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, the Company provides rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects the Company's needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of June 30, 2021, the Company has committed to purchase $45.5 million of vadadustat drug substance from WuXi STA through the first quarter of 2022.

On February 10, 2021, the Company entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, the Company will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that the Company expects to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, the Company has agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by the Company and WuXi STA. The Company will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by

mutual agreement of the Company and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows the Company to terminate the agreement 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.

Other Third Party Contracts

Under the Company's agreement with IQVIA to provide contract research organization services for the PRO_2TECT and $INNO_2VATE$ programs, the total remaining contract costs as of June 30, 2021 were approximately $8.3 million, of which Otsuka reimburses a significant portion back to the Company. Substantive performance for the committed work with IQVIA was completed in 2020 and close out activities will be performed throughout 2021. The Company also contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately $187.6 million at June 30, 2021. The scope of the services under these research and development 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

From time to time, the Company may become subject to legal proceedings and claims which arise in the ordinary course of its business. Consistent with ASC 450, *Contingencies*, the Company's policy is to record a liability if a loss in a significant legal dispute is considered probable and an amount can be reasonably estimated. 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. The Company's estimates change as litigation progresses and new information comes to light. Changes in Company estimates could have a material impact on the Company's results and financial position. As of June 30, 2021, the Company does not have any significant legal disputes that require a loss liability to be recorded. The Company continually monitors the need for a loss liability for litigation and related matters.

15. Net Loss per Share

For purposes of the diluted net loss per share calculation, preferred stock, stock options, warrants, restricted stock and RSUs are considered to be common stock equivalents and have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented in the unaudited Condensed Consolidated Statement of Operations and Comprehensive Loss. 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:

	As of June 30,	
	2021	2020
Warrant	509,611	509,611
Outstanding stock options	11,532,673	9,632,240
Unvested restricted stock units	5,574,476	6,399,834
Total	17,616,760	16,541,685

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following information should be read in conjunction with our unaudited condensed consolidated financial statements and related notes included in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission on February 25, 2021, or the 2020 Annual Report on Form 10-K, including the audited consolidated financial statements and related notes therein. This discussion and analysis contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" in Part II, Item 1A. of this Quarterly Report on Form 10-Q, our actual results may differ materially from those anticipated in these forward-looking statements.

Business Overview

We are a biopharmaceutical company with the purpose of bettering the life of each person impacted by kidney disease. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative renal therapeutics that we believe serves as a foundation for future growth. As a leader in the kidney community, we remain

committed to helping patients and others where we believe our current and future products have the ability to deliver value. Our portfolio includes a late-stage product candidate and a commercial product:

- ***Vadadustat*** is an investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and leads to red blood cell, or RBC, production and improved oxygen delivery to tissues. The significance of the HIF pathway was recognized by the 2019 Nobel Prize and the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. We believe that, based on the HIF-PHI mechanism of action and clinical data to date, vadadustat has the potential to set a new oral standard of care for the treatment of anemia due to chronic kidney disease, or CKD.

  We completed the global Phase 3 clinical development program for vadadustat in 2020, which included two separate programs, $INNO_2VATE$ and PRO_2TECT. $INNO_2VATE$ evaluated vadadustat for the treatment of anemia due to CKD in adult patients on dialysis, or DD-CKD, and PRO_2TECT evaluated vadadustat for the treatment of anemia due to CKD in adult patients not on dialysis, or NDD-CKD.

  In May of 2020, we announced positive top-line results from our Phase 3 $INNO_2VATE$ program that showed vadadustat was non-inferior to darbepoetin alfa, an injectable erythropoiesis-stimulating agent, or ESA, with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (assessed in a time to the first occurrence of a major adverse cardiovascular event (MACE) analysis, which is the composite of all-cause mortality, nonfatal myocardial infarction, or a nonfatal stroke) in treating anemia due to CKD in DD-CKD adult patients. In addition to meeting the primary endpoints of the $INNO_2VATE$ program, vadadustat met the key secondary hematological efficacy endpoint in each of the two studies in the program and also met the program's key secondary safety endpoints. The results of the $INNO_2VATE$ program were presented at American Society of Nephrology, or ASN, in October of 2020 and published in the *New England Journal of Medicine* in April of 2021.

  In September of 2020, we announced top-line results from our Phase 3 PRO_2TECT program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients. While the PRO_2TECT data showed that vadadustat achieved both the primary and key secondary hematological efficacy endpoints, it did not meet the program's primary cardiovascular safety (MACE) endpoint. These cardiovascular outcomes contrast with those reported within the $INNO_2VATE$ program, which evaluated vadadustat for the treatment of anemia due to CKD in DD-CKD adult patients. The results of the PRO_2TECT program were presented at ASN in October of 2020 and published in the *New England Journal of Medicine* in April of 2021. Simultaneous with the PRO_2TECT ASN presentation, we presented additional analyses, conducted by Akebia, of data from the PRO_2TECT program that 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 United States where significant differences in treatment patterns for NDD-CKD patients were observed.

  We submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for vadadustat in March of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. Our NDA submission was accepted for filing by the FDA in May 2021 and at the time of filing the NDA, the FDA indicated that they were not currently planning to hold an Advisory Committee meeting to discuss the for vadadustat. The FDA also assigned the application standard review and a Prescription Drug User Fee Act (PDUFA) target action date of March 29, 2022. We expect to have frequent communications with the FDA with respect to the NDA, including attending meetings, responding to information requests, and engaging in labeling negotiations, among other things. We plan to provide updates, if and as appropriate, on these communications through our Quarterly Reports on Form 10-Q and Annual Reports on Form 10-K filed with the SEC.

  We are also working in close collaboration with our collaboration partner, Otsuka Pharmaceutical Co. Ltd., to prepare a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients for submission to the European Medicines Agency, or EMA, expected in 2021. However, as vadadustat did not meet the PRO_2TECT program's primary safety

endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

In June of 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients in Japan. Our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo™, in August 2020.

In addition to anemia due to CKD, we believe that vadadustat has the potential to treat other serious or life-threatening conditions, including preventing and lessening the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. More specifically, in July of 2020, we announced an investigator-sponsored clinical study by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and lessen the severity of ARDS in up to 400 adult patients who have been hospitalized due to COVID-19. Within this randomized, double-blind, placebo-controlled study, patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under an FDA Investigational New Drug application, or IND, with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded $5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

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- ***Auryxia® (ferric citrate)*** is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for IDA in adult patients and the improvement of hyperphosphatemia in adult patients with CKD, including DD-CKD and NDD-CKD, under the trade name Riona (ferric citrate hydrate). Auryxia is our only product approved for sale in the United States and it generated approximately $33.0 million and $30.7 million in revenue from U.S. product sales during the three months ended June 30, 2021 and 2020, respectively.

We plan to commercialize vadadustat, subject to FDA approval, in the United States with our well-established, nephrology-focused commercial organization, while leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. We granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. We granted MTPC exclusive rights to commercialize vadadustat in Japan, where MTPC commenced commercial sales of vadadustat under the trade name, Vafseo™, in August 2020, and in certain other countries in Asia, subject to marketing approvals. In addition, we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, or FMCNA, and to certain third party dialysis organizations approved by us, or Third Party Dialysis Organizations, which combined manage up to approximately 60% of the dialysis patients in the United States, which would be effective upon FDA approval of vadadustat, the earlier of vadadustat's reimbursement under a bundled reimbursement model or using the Transitional Drug Add-On Payment Adjustment, or the TDAPA, and a milestone payment by Vifor Pharma. During the term of the license agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the United States to FKC or its affiliates or to any Third Party Dialysis Organization, and we may not directly supply vadadustat to FKC or any other affiliate of FMCNA or any Third Party Dialysis Organization.

Operating Overview

We have never been profitable and have incurred net losses in each year since inception. Our net losses were $83.0 million and $175.8 million for the three months ended June 30, 2021 and 2020, respectively, and $152.6 million and $236.5 million for the six months ended June 30, 2021 and 2020, respectively. Substantially all of our net losses resulted from costs incurred in connection with the continued commercialization of Auryxia and development efforts relating to vadadustat, including preparing for and conducting clinical studies of vadadustat, providing general and administrative support for these operations and protecting our intellectual property.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct any post-marketing approval studies, Phase 4 studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- adapt to any regulatory changes, including changes relating to reimbursement;
- adapt to any changes in reimbursement practices by third party payors;
- continue our integration activities as a result of our merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx;
- enroll patients in our clinical trials;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintain marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;
- seek to discover and develop 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;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any delays or encounter issues with any of the above.

We have not generated, and may not generate, enough product revenue to realize net profits from product sales. We have no manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize contract research organizations, or CROs, to carry out our clinical development activities. If we obtain marketing approval for vadadustat, and as we continue to commercialize Auryxia, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. 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 vadadustat, if approved, 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.

From inception through June 30, 2021, we raised approximately $771.4 million of net proceeds from the sale of equity, including $519.8 million from various underwritten public offerings, $201.6 million from at-the-market offerings, or ATM offerings, pursuant to sales agreements with Cantor Fitzgerald & Co., and $50.0 million from the sale of 3,571,429 shares of common stock to Vifor Pharma. During the quarter ended June 30, 2021 and through the date of this Quarterly Report on Form 10-Q, we raised $53.4 million of net proceeds from ATM offerings. At inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately $573.0 million or more in cost-share funding, which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately $272.0 million at the onset of the collaboration agreements. On November 11, 2019, we entered into a loan agreement, or the Loan Agreement, with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. As of March 31, 2021, we had drawn down the full amount $100.0 million made available to us under the Loan Agreement. In addition, on February 25, 2021, we received an upfront payment of $44.8 million (net of certain transaction expenses) in connection with our sale to HealthCare Royalty Partners IV, L.P., or HCR, of the right to receive all royalties and sales milestones payable to us under our collaboration agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions described elsewhere in this Quarterly Report.

Impacts of COVID-19 Pandemic

The ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, CROs, contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning the COVID-19 pandemic, any resurgences or mutations of COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

We believe our revenue growth was negatively impacted in the first half of 2021 primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact our patient population; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees have been working from home since March 2020. In addition, several healthcare facilities have restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers could negatively impact our access to healthcare providers and, ultimately, our sales. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, restrictions may be put in place again due to a resurgence in COVD-19 cases, including those involving new variants of COVID-19 which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia, including the potential for further declines or changes in prescription trends and customer orders.

At this time, our third party contract manufacturing partners continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturing partners' ability to manufacture and deliver Auryxia and vadadustat (which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in delays in, increased costs or disruptions to manufacturing and supply of our products.

COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials. We are using remote monitoring and central monitoring, where possible.

This uncertain COVID-19 pandemic environment has presented new risks to our business. While we are working aggressively to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control.

For additional information on the various risks posed by the COVID-19 pandemic, please refer to Part II, Item 1A. Risk Factors.

Financial Overview

Revenue

To date, our revenues have been derived from collaboration revenues, which include license and milestone payments, royalty and cost-sharing revenue generated through collaboration and license agreements with partners for the development and commercialization of vadadustat and, following the Merger, commercial sales of Auryxia and royalty revenue from sales of Riona in Japan. Cost-sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements.

We expect our revenue to continue to be generated primarily from our collaborations with Otsuka and MTPC and any other collaborations into which we may enter, as well as commercial sales of Auryxia in the United States, and royalty revenue from Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, based on net sales of Riona in Japan.

Cost of Goods Sold

Cost of goods sold includes direct costs to manufacture commercial drug substance and drug product for Auryxia, as well as indirect costs including costs for packaging, shipping, insurance and quality assurance, idle capacity charges, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, excess purchase commitment charges, and royalties due to the licensor of Auryxia related to the U.S. product sales recognized during the period.

As a result of the Merger and the application of purchase accounting, costs of goods sold also includes both amortization expense and, if applicable, impairment charges associated with the fair value of the developed product rights for Auryxia as well as expense associated with the fair value inventory step-up. The fair value of the developed product rights for Auryxia is being amortized over its estimated useful life, which as of June 30, 2021 is estimated to be six years. The fair value inventory step-up as a result of the Merger was fully amortized as of the first quarter of 2021.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of vadadustat, which include:

- personnel-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense of our research and development personnel;
- expenses incurred under agreements with CROs and investigative sites that conduct our clinical studies;
- the cost of acquiring, developing and manufacturing clinical study materials through CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and
- costs associated with preclinical, clinical and regulatory activities.

Research and development costs are expensed as incurred. 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 current or future clinical studies of Auryxia and vadadustat or if, when, or to what extent we will generate revenue from the commercialization and sale of vadadustat, if approved. We may never succeed in achieving marketing approval for vadadustat.

The duration, costs and timing of clinical studies and development of Auryxia and vadadustat will depend on a variety of factors including, but not limited to, those described in Part II, Item 1A. Risk Factors. A change in the outcome of any of these variables with respect to the development of Auryxia and vadadustat could mean a significant change in the costs and timing associated with that development. For example, if the FDA, the EMA, or other regulatory authorities were to require us to conduct clinical studies in addition to or different from those that we currently anticipate, or if we experience delays in any of our clinical studies, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through June 30, 2021, we have incurred $1.4 billion in research and development expenses. We expect to have significant research and development expenditures for the foreseeable future as we continue the development of Auryxia and vadadustat.

Our direct research and development expenses consist principally of external costs, such as fees paid to clinical trial sites, consultants, central laboratories and CROs in connection with our clinical studies, and drug substance and drug product manufacturing for clinical studies.

In 2020, we completed our global Phase 3 clinical program for vadadustat to which the majority of our research and development costs have been attributable. A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis. 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. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the three and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
	(in thousands)		(in thousands)	
Vadadustat external costs	$ 12,917	$ 31,072	$ 29,720	$ 89,420
External costs for other programs	5,122	2,972	11,564	6,205
Total external research and development expenses	18,039	34,044	41,284	95,625
Headcount, consulting, facilities and other	19,175	18,775	36,541	38,425
Total research and development expenses	$ 37,214	$ 52,819	$ 77,825	$ 134,050

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our commercial personnel, including our field sales force and other commercial support personnel, as well as personnel in executive and other administrative or non-research and development functions. Other selling, general and administrative expenses include facility-related costs, fees for directors, accounting and legal services fees, recruiting fees and expenses associated with obtaining and maintaining patents.

Results of Operations

Comparison of the Three Months Ended June 30, 2021 and 2020

	Three Months Ended		Increase
	June 30, 2021	June 30, 2020	(Decrease)
	(In Thousands)		
Revenues:			
Product revenue, net	$ 32,959	$ 30,696	$ 2,263
License, collaboration and other revenue	19,954	59,446	(39,492)
Total revenues	52,913	90,142	(37,229)
Cost of goods sold:			
Product	43,484	49,988	(6,504)
Amortization of intangibles	9,011	9,101	(90)
Impairment of intangible asset	—	115,527	(115,527)
Total cost of goods sold	52,495	174,616	(122,121)
Operating expenses:			
Research and development	37,214	52,819	(15,605)
Selling, general and administrative	41,651	35,482	6,169
License expense	894	1,044	(150)
Total operating expenses	79,759	89,345	(9,586)
Operating loss	(79,341)	(173,819)	94,478
Other expense, net	(3,697)	(1,932)	(1,765)
Net loss	$ (83,038)	$ (175,751)	$ 92,713

Product Revenue, Net. Net product revenue is derived from sales of our only commercial product in the United States, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. Net product revenue was $33.0 million for the three months ended June 30, 2021, compared to net product revenue of $30.7 million for the three months ended June 30, 2020. The increase was primarily due to an increase in units sold, partially offset by the negative impact from COVID-19. We believe our revenue growth continues to be negatively impacted primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19.

In September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use in the Hyperphosphatemia Indication. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. See Part II, Item 1. Legal Proceedings for further information. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication.

License, Collaboration and Other Revenue. License, collaboration and other revenue was $20.0 million for the three months ended June 30, 2021 compared to $59.4 million for the three months ended June 30, 2020. We recognized $18.5 million in collaboration revenue for the three months ended June 30, 2021 from our cost sharing arrangement under the Otsuka collaboration agreement for the United States, or the Otsuka U.S. Agreement, and the Otsuka collaboration agreement for certain territories outside the United States, or the Otsuka International Agreement, and royalty revenue under our collaboration agreement with MTPC, or the MTPC Agreement. We recognized $53.7 million in collaboration revenue for the three months ended June 30, 2020 from our cost sharing arrangement under the Otsuka U.S. Agreement and the Otsuka International Agreement. The $35.2 million decline in collaboration revenue was driven by lower payments recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement as we completed our global Phase 3 clinical development program for vadadustat in 2020 and are currently engaged in close-out activities with respect to the program. We expect our Otsuka collaboration revenue to continue to decrease in the near term for that reason.

Cost of Goods Sold - Product. Cost of goods sold of $43.5 million for the three months ended June 30, 2021 consisted of costs associated with the manufacturing of Auryxia and a $30.3 million million non-cash charge related to an increase to the liability for excess purchase commitments. Refer to Note 14 to our condensed consolidated financial statements for further details on the excess purchase commitments liability.

Cost of goods sold of $50.0 million for the three months ended June 30, 2020 consisted of costs associated with the manufacturing of Auryxia, $19.9 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, $11.0 million in non-cash charges related to an increase to the liability for excess purchase commitments, and $9.9 million primarily related to the write-down of inventory associated with specific lots of Auryxia as it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia. During the three months ended June 30, 2021, this intangible asset was being amortized using a straight-line method over its estimated useful life of approximately six years. Amortization of intangibles during the three months ended June 30, 2021 and 2020 was $9.0 million and $9.1 million, respectively.

Cost of Goods Sold - Impairment of Intangible Asset. In the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the compounding impact of the CMS Decisions that rescinded Medicare Part D coverage of Auryxia for the IDA Indication, and imposed a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset during the three months ended June 30, 2020.

Research and Development Expenses. Research and development expenses were $37.2 million for the three months ended June 30, 2021, compared to $52.8 million for the three months ended June 30, 2020, a decrease of $15.6 million. The decrease was primarily due to the following:

	(in millions)
Vadadustat development expenses	$ (18.2)
Headcount, consulting and facilities	0.4
Other research and development	2.2
Total net decrease	$ (15.6)

The decrease in the costs related to the development of vadadustat is primarily attributable to a decrease in external costs related to our global Phase 3 program (INNO$_2$VATE and PRO$_2$TECT), for which we reported top-line data in the second and third quarters of 2020, respectively. Although we expect our research and development expenses to continue to decrease in the near

term compared to the full year 2020 as we completed our global Phase 3 clinical development program for vadadustat in 2020, we will continue to incur significant research and development expenses in future periods in support of our overall development program for vadadustat and ongoing or planned studies with respect to Auryxia, vadadustat and development of other potential product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $41.7 million for the three months ended June 30, 2021, compared to $35.5 million for the three months ended June 30, 2020. The increase of $6.2 million was primarily due to higher marketing expenses. For the remainder of 2021, we expect our selling, general and administrative expenses for our ongoing commercialization of Auryxia and for support of our ongoing research and development and potential commercialization of vadadustat and other product candidates to continue to increase modestly from 2020.

License Expenses. License expense related to royalties due to Panion relating to sales of Riona in Japan were $0.9 million and $1.0 million the three months ended June 30, 2021 and 2020, respectively.

Other Expense, Net. Other expense, net, was $3.7 million for the three months ended June 30, 2021 compared to $1.9 million for the three months ended June 30, 2020. Other expense, net, for the three months ended June 30, 2021 was primarily due to interest expense associated with our Term Loans and non-cash interest expense on the liability related to the sale of our right to receive royalties and sales milestones from MTPC as further described in Note 5 to our condensed consolidated financial statements in Part I, Item 1. Financial Statements (unaudited). Other expense, net, for the three months ended June 30, 2020 was primarily due to interest expense associated with our Term Loans.

Comparison of the Six Months Ended June 30, 2021 and 2020

	Six Months Ended		Increase
	June 30, 2021	June 30, 2020	(Decrease)
	(In Thousands)		
Revenues:			
Product revenue, net	$ 63,367	$ 59,905	$ 3,462
License, collaboration and other revenue	41,850	118,715	(76,865)
Total revenues	105,217	178,620	(73,403)
Cost of goods sold:			
Product	69,079	68,601	478
Amortization of intangibles	18,021	18,201	(180)
Impairment of intangible asset	—	115,527	(115,527)
Total cost of goods sold	87,100	202,329	(115,229)
Operating expenses:			
Research and development	77,825	134,050	(56,225)
Selling, general and administrative	82,979	73,465	9,514
License expense	1,590	1,720	(130)
Total operating expenses	162,394	209,235	(46,841)
Operating loss	(144,277)	(232,944)	88,667
Other expense, net	(8,341)	(3,554)	(4,787)
Net loss	$ (152,618)	$ (236,498)	$ 83,880

Product Revenue, Net. Net product revenue is derived from sales of our only commercial product in the United States, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. Net product revenue was $63.4 million for the six months ended June 30, 2021, compared to net product revenue of $59.9 million for the six months ended June 30, 2020. The increase was primarily due to an increase in units sold, partially offset by the negative impact from COVID-19. We believe our revenue growth continues to be negatively impacted primarily

as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19.

License, Collaboration and Other Revenue. License, collaboration and other revenue was $41.9 million for the six months ended June 30, 2021 compared to $118.7 million for the six months ended June 30, 2020. We recognized $39.1 million in collaboration revenue for the six months ended June 30, 2021 from our cost sharing arrangement under the Otsuka collaboration agreement for the United States, or the Otsuka U.S. Agreement, and the Otsuka collaboration agreement for certain territories outside the United States, or the Otsuka International Agreement, and royalty revenue under our collaboration agreement with MTPC, or the MTPC Agreement. We recognized $111.7 million in collaboration revenue for the six months ended June 30, 2020 from our cost sharing arrangement under the Otsuka U.S. Agreement and the Otsuka International Agreement and recognition of a milestone earned under the MTPC Agreement. The $76.9 million decline in collaboration revenue was driven by lower payments recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement as we completed our global Phase 3 clinical development program for vadadustat in 2020 and are currently engaged in close-out activities with respect to the program. We expect our Otsuka collaboration revenue to continue to decrease in the near term for that reason.

Cost of Goods Sold - Product. Cost of goods sold of $69.1 million for the six months ended June 30, 2021 consisted of costs associated with the manufacturing of Auryxia, $21.3 million in non-cash charges related to an increase to the liability for excess purchase commitments, $21.6 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, and $5.4 million related to inventory reserves associated with a previously disclosed manufacturing quality issue related to Auryxia. Refer to Note 14 to our condensed consolidated financial statements for further details of the increase to the liability for excess purchase commitments.

Cost of goods sold of $68.6 million for the six months ended June 30, 2020 consisted primarily of costs associated with the manufacturing of Auryxia and $31.1 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, $11.0 million in non-cash charges related to an increase to the liability for excess purchase commitments and $10.1 million primarily related to the write-down of inventory associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia. During the six months ended June 30, 2021, this intangible asset was being amortized using a straight-line method over its estimated useful life of approximately six years. Amortization of intangibles during the six months ended June 30, 2021 and 2020 was $18.0 million and $18.2 million, respectively.

Cost of Goods Sold - Impairment of Intangible Asset. In the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the compounding impact of the CMS Decisions that rescinded Medicare Part D coverage of Auryxia for the IDA Indication, and imposed a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset during the six months ended June 30, 2020. There were no such impairment charges during the six months ended June 30, 2021.

Research and Development Expenses. Research and development expenses were $77.8 million for the six months ended June 30, 2021, compared to $134.1 million for the six months ended June 30, 2020, a decrease of $56.2 million. The decrease was primarily due to the following:

	(in millions)
Vadadustat development expenses	$ (59.7)
Headcount, consulting and facilities	(1.9)
Other research and development	5.4
Total net decrease	$ (56.2)

The decrease in the costs related to the development of vadadustat is primarily attributable to a decrease in external costs related to our global Phase 3 program (INNO$_2$VATE and PRO$_2$TECT), for which we reported top-line data in the second and third quarters of 2020, respectively. Although we expect our research and development expenses to continue to decrease in the near term compared to the full year 2020 as we completed our global Phase 3 clinical development program for vadadustat in 2020, we will continue to incur significant research and development expenses in future periods in support of our overall development

program for vadadustat and ongoing or planned studies with respect to Auryxia, vadadustat and development of other potential product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $83.0 million for the six months ended June 30, 2021, compared to $73.5 million for the six months ended June 30, 2020. The increase of $9.5 million was primarily due to higher marketing expenses and increased people costs. For the remainder 2021, we expect our selling, general and administrative expenses for our ongoing commercialization of Auryxia and for support of our ongoing research and development and potential commercialization of vadadustat and other product candidates to continue to increase modestly from 2020.

License Expenses. License expense related to royalties due to Panion relating to sales of Riona in Japan were $1.6 million and $1.7 million for the six months ended June 30, 2021 and 2020, respectively.

Other Expense, Net. Other expense, net, was $8.3 million for the six months ended June 30, 2021 compared to $3.6 million for the six months ended June 30, 2020. Other expense, net, for the six months ended June 30, 2021 was primarily due to interest expense associated with our Term Loans and non-cash interest expense on the liability related to the sale of our right to receive royalties and sales milestones from MTPC as further described in Note 5 to our condensed consolidated financial statements in Part I, Item 1. Financial Statements (unaudited). Other expense, net, for the six months ended June 30, 2020 was primarily due to interest expense associated with our Term Loans.

Liquidity and Capital Resources

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners, and following the Merger, product sales, debt and a royalty transaction. As of June 30, 2021, we had cash and cash equivalents and available for sale securities of approximately $247.0 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Accordingly, available for sale securities, consisting principally of corporate and government debt securities stated at fair value, are also available as a source of liquidity. At the inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately $573.0 million or more in cost-share funding, of which we received approximately $272.0 million at the onset of the collaborations, and the remainder of which we generally continue to receive on a quarterly prepaid basis, and through license payments.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Six Months Ended	
	June 30, 2021	June 30, 2020
	(In Thousands)	
Net cash provided by (used in):		
Operating activities	$ (133,887)	$ (52,369)
Investing activities	39,941	(49,750)
Financing activities	111,846	200,155
Net increase in cash, cash equivalents, and restricted cash	$ 17,900	$ 98,036

Operating Activities. Net cash used in operating activities of $133.9 million for the six months ended June 30, 2021 was largely driven by payroll-related expenses, rebate payments and payments for inventory. These payments were partially offset by adjustments for non-cash items, including fair value step-up of inventory sold or written off of $21.6 million, an increase to the liability for excess purchase commitments of $21.3 million, amortization of intangibles of $18.0 million, stock-based compensation expense of $12.5 million, write-downs of inventory of $5.4 million, and non-cash interest expense related to sale of future royalties of $4.4 million.

Net cash used in operating activities of $52.4 million for the six months ended June 30, 2020 was largely driven by timing of payments on our Phase 3 development program for vadadustat and payments for inventory. These payments were partially offset by adjustments for non-cash items, including the intangible asset impairment charge of $115.5 million, fair value step-up of inventory sold or written off of $31.1 million, amortization of intangibles of $18.2 million, stock-based compensation expense of $11.8 million, an increase to the liability for excess purchase commitments of $11.0 million and write-downs of

inventory of $10.1 million primarily associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Investing Activities. Net cash provided by investing activities for the six months ended June 30, 2021 was $39.9 million and was comprised of proceeds from the maturities of available for sale securities of $40.0 million, partially offset by immaterial purchases of equipment.

Financing Activities. Net cash provided by financing activities for the six months ended June 30, 2021 was $111.8 million and consisted of net proceeds from the sale of future royalties of $44.8 million, net proceeds from the public issuance of common stock in connection with our ATM sales agreement of $66.7 million, and proceeds from the sale of stock under our employee stock purchase plan.

Operating Capital Requirements

We have one product, Auryxia, approved for commercial sale in the United States, but have not generated, and may not generate, enough product revenue from the sale of Auryxia to realize net profits from product sales. We have incurred losses and cumulative negative cash flows from operations since our inception in February 2007, and as of June 30, 2021, we had an accumulated deficit of $1.3 billion. We anticipate that we will continue to incur losses for the foreseeable future, and we expect to continue to incur additional research and development and selling, general and administrative expenses for our ongoing research and development and potential commercialization of vadadustat and our ongoing development and commercialization of Auryxia. We expect our cash resources to fund our current operating plan for at least twelve months from the date of this filing. Additionally, we expect our cash runway would extend beyond the next twelve months assuming timely regulatory approval of vadadustat and the receipt of associated regulatory milestones. We expect to continue to incur significant costs and we anticipate that we will need to obtain substantial additional funding in connection with our operating plan beyond that period. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Furthermore, our regulatory milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. The period over which our cash runway extends is also dependent on the execution of our commercial plan, which is dependent on the overall market, the competitive environment, and the execution of reimbursement strategies.

We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaboration partners, royalty transactions, strategic transactions, or a combination of these approaches. Additionally, we will require additional capital to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. Additional funds may not be available to us on acceptable terms or 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 vadadustat, if approved, or any additional products or product candidates, including those that may be in-licensed or acquired. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders or increased fixed payment obligations, and any such securities may have rights senior to those of our common stock. Any of these events could significantly harm our business, financial condition and prospects.

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 risks and uncertainties, and actual results could vary as a result of a number of factors. 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 II, Item 1A. Risk Factors.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Obligations

As of June 30, 2021, other than as disclosed in Note 14 to our condensed consolidated financial statements, there have been no material changes to our contractual obligations and commitments from those described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in our 2020 Annual Report on Form 10-K.

Term Loans

On November 11, 2019, Akebia, with Keryx as guarantor, entered into a loan agreement, or the 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, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in

two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term 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 first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. A more detailed description of the term loans can be found in Note 11 to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q.

Liability Related to Sale of Future Royalties

On February 25, 2021, we entered into 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 vadadustat in the MTPC Territory, such payments collectively the Royalty Interest Payments, in each case, payable to us under the MTPC Agreement, 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. 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, and we are eligible to receive an additional $5.0 million in each year from 2021 through 2023 under the Royalty Agreement if specified annual sales milestones are achieved for vadadustat in the MTPC Territory, subject to the satisfaction of certain customary conditions. We retain the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. A more detailed description of the liability related to the sale of future royalties can be found in Note 5 to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q.

Off-Balance Sheet Arrangements

As of June 30, 2021, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our unaudited condensed consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these unaudited condensed consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our unaudited condensed consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, prepaid and accrued research and development expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies.

During the six months ended June 30, 2021, we had the following material change to our critical accounting policies as reported in our Annual Report on Form 10-K:

Liability Related to Sale of Future Royalties

We treat the liability related to sale of future royalties (see Note 5 to our condensed consolidated financial statements in Part I, Item 1. Financial Statements (unaudited)) 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 our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments. To the extent our 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, we will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. 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 unaudited condensed consolidated statements of operations and comprehensive loss in Part I, Item 1. Financial Statements (unaudited).

There were no other material changes to our critical accounting policies as reported in our 2020 Annual Report on Form 10-K.

Recent Accounting Pronouncements

For additional discussion of recent accounting pronouncements, please refer to *New Accounting Pronouncements – Recently Adopted* included within Note 2 to our condensed consolidated financial statements in Part I, Item 1. Financial Statements (unaudited).

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

We are exposed to market risk related to changes in interest rates. As of June 30, 2021 and December 31, 2020, we had cash and cash equivalents and available for sale securities of $247.0 million and $268.7 million, respectively, consisting primarily of money market mutual funds consisting of U.S. government debt securities, certificates of deposit and corporate debt securities. Interest rate sensitivity is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

In addition, we are exposed to market risk related to exchange rates. A substantial portion of our revenues for the six months ended June 30, 2021 was received in U.S. dollars, including revenues we receive from royalty payments converted to U.S. dollars based on the net sales of Riona and Vafseo™ in Japanese yen. Our exchange rate risk arises from such foreign currency net sales. As a result, we are exposed to movements in the exchange rates of the Japanese yen against the U.S. dollar.

For the royalty payments we received based on net sales of Riona and Vafseo in Japan for the six months ended June 30, 2021 a 5.0% appreciation or depreciation of the Japanese yen against the U.S. dollar would have increased or decreased, respectively, our revenues in the six months ended June 30, 2021 by approximately $0.1 million.

We have generally accepted the exposure to exchange rate movements without using derivative financial instruments to manage this foreign currency risk.

Item 4. Controls and Procedures.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, is (1) recorded, processed, summarized, and reported within the time periods specified in the U.S. Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of June 30, 2021, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended). Our 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. Based on our evaluation, our management concluded that, as of June 30, 2021, our disclosure controls and procedures were not effective because our internal controls over financial reporting were not adequate due to the material weakness described below.

As reported in our Annual Report on Form 10-K for the year ended December 31, 2020, or the 2020 Annual Report on Form 10-K, our internal control activities over financial reporting as of December 31, 2020 was not effective due to the following material weakness: the Company did not design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. 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. Specifically, we did not maintain effective controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the periodic assessment of excess and obsolete inventory related reserves. Management has taken actions to remediate the deficiencies in its internal control over financial reporting and implemented additional processes and controls designed to address the underlying causes associated with the material weakness. Management is committed to finalizing the remediation of the material weakness during 2021.

As management continues to evaluate and work to improve its 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. As such, management has concluded that the material weakness cannot be considered remediated as of June 30, 2021.

Changes in Internal Control over Financial Reporting

During the six months ended June 30, 2021, we implemented certain internal controls in connection with our remediation efforts described above. There have been no other changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Securities Exchange Act of 1934, as amended, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

Legal Proceedings Relating to Vadadustat

Opposition Proceedings Against Akebia

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the ’005 EP Patent, in the European Patent Office, or the EPO. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the EPO maintained the ’005 EP Patent. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division of the EPO. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. In September 2018, Dr. Reddy’s Laboratories Limited filed an opposition to our issued Indian Patent No. 287720 in the Indian Patent Office.

Proceedings Filed by Akebia Against FibroGen, Inc.

Europe

We filed an opposition in the EPO against FibroGen, Inc.’s, or FibroGen’s, European Patent No. 1463823, or the ’823 EP Patent on December 5, 2013, and an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the Opposition Division of EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen has appealed that decision. Likewise, we also filed an invalidity proceeding before the Japan Patent Office, or JPO, on June 2, 2014 against certain claims of FibroGen’s Japanese Patent No. 4804131, or the ’131 JP Patent, which is the Japanese counterpart to the ’823 EP Patent, and the JPO issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting ’131 JP Patent does not cover vadadustat or any pyridine carboxamide compounds.

On May 13, 2015, May 20, 2015 and July 6, 2015, we filed oppositions to FibroGen’s European Patent Nos. 2322155, or the ’155 EP Patent, 1633333, or the ’333 EP Patent, and 2322153, or the ’153 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. These related patents claim, among other things, various compounds that either stabilize HIFα or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase, or HIF-PH, for treating or preventing various conditions, including, among other things, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin and microcytosis in microcytic anemia. Such method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting HIF-PH for the treatment of anemia due to chronic kidney disease, or CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia due to CKD, we filed these oppositions to provide us and our collaborators with maximum flexibility for developing vadadustat and our pipeline of investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, compounds.

Oppositions to the ’155 EP Patent and the ’153 EP Patent were also filed in the EPO by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or, collectively, Bayer. Glaxo withdrew its oppositions on March 2, 2020 and Bayer withdrew its oppositions on June 30, 2021.

With regard to the opposition that we filed in Europe against the ’333 EP Patent, an oral proceeding took place on December 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the ’333 EP Patent. An oral proceeding for the appeal is scheduled for February 2022.

In oral proceedings held on May 29, 2017, regarding the ’155 EP Patent, the European Opposition Division ruled that the ’155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017. An oral proceeding for the appeal is scheduled for February 2022.

Subsequently, in related oral proceedings held on May 31, 2017 and June 1, 2017 for the ’153 EP Patent, the Opposition Division of the EPO maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017. An oral proceeding for the appeal is scheduled for February 2022.

On April 3, 2019, we filed oppositions to FibroGen’s European Patent Nos. 2289531, or the ’531 EP Patent, and 2298301, or the ’301 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. Oral proceedings for oppositions to the two patents are scheduled for September 2021.

On February 10, 2020, we filed an opposition to FibroGen’s European Patent No. 2324834, or the ’834 EP Patent, in the EPO requesting the patent to be revoked in its entirety. Oral proceedings for opposition to the ‘834 EP Patent are currently scheduled for October 2021.

Canada

On May 21, 2018, we filed a Statement of Claim in Canadian Federal Court to challenge the validity of three of FibroGen’s HIF-related patents in Canada: CA 2467689, CA 2468083, and CA 2526496. On June 25, 2020, the parties agreed to dismiss the CA 2467689 patent from the lawsuit. On February 16, 2021, the parties agreed to dismiss the lawsuit in its entirety.

Japan

On June 22, 2018, we and our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, jointly filed a Request for Trial before the JPO to challenge the validity of one of FibroGen’s HIF-related patents in Japan, JP4845728. On July 20, 2018 and August 13, 2018, we and MTPC jointly filed a Request for Trial before the JPO to challenge the validity of two additional FibroGen HIF-related patents in Japan, JP5474872 and JP5474741, respectively. On September 26, 2019, the JPO conducted an invalidation trial for JP5474872 and JP4845728. On November 11, 2019, the JPO conducted an invalidation trial for JP5474741. On February 10, 2020, the JPO issued a pre-notice of a trial decision for JP4845728, which invalidated all claims except two claims in amended form. On March 11, 2020, the JPO issued a pre-notice of a trial decision for JP5474872, which invalidated all claims except one claim in amended form. On April 2, 2020, the JPO issued a pre-notice of a trial decision for JP5474741, which invalidated all claims except two claims in amended form. We expect the JPO to issue a final decision this year. We do not believe these decisions will prevent our collaboration partner MTPC from commercializing vadadustat for the treatment of anemia due to CKD in Japan.

United Kingdom

On December 13, 2018, we and our collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, filed Particulars of Claim in the Patents Court of the United Kingdom, to challenge the validity of FibroGen’s six HIF-related patents in the UK: the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK), European Patent (UK) No. 2,289,531, or the ’531 EP Patent (UK), and European Patent (UK) No. 2,298,301, or the ’301 EP Patent (UK). In May 2019, Astellas Pharma Inc., or Astellas, the exclusive licensee of FibroGen’s HIF-related patents, sued Akebia and Otsuka for patent infringement in the Patents Court of the UK. In September 2019, we and Otsuka filed an Amended Particulars of Claim to include FibroGen’s European Patent No. 1487472, or the ’472 EP Patent (UK). On February 28, 2020, the parties agreed to dismiss the ’472 EP Patent (UK) from the trial.

A trial was conducted in March 2020. On April 20, 2020, the Patents Court of the UK issued a judgment in favor of Akebia, which invalidated all the claims at issue in each of the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK) and the ’301 EP Patent (UK). The ’531 EP Patent (UK) was amended to a single claim to recite one specific compound; this claim was held to be valid but not infringed by vadadustat. On June 11, 2020, FibroGen and Astellas appealed the Patents Court’s judgment on the invalidity of the ’823 EP Patent (UK), the ’301 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), and the ’155 EP Patent (UK) in the Court of Appeal (Civil Division). On June 8, 2021 - June 10, 2021, the United Kingdom Court of Appeal held a three-day hearing for the appeal. We expect the Court of Appeal to issue its judgment in the third quarter of 2021.

United States

On March 29, 2021, we and our collaboration partner Otsuka America Pharmaceutical, Inc. filed a lawsuit against FibroGen and AstraZeneca AB in the United States District Court for the District of Delaware to seek a declaratory judgment of non-infringement and invalidity of FibroGen’s twelve HIF-related patents in the United States: U.S. Patent Nos. 8,318,703, 8,466,172, 8,614,204, 9,920,011, 8,629,131, 8,604,012, 8,609,646, 8,604,013, 10,626,090, 10,894,774, 10,882,827, and 10,927,081. The defendants filed a motion to dismiss the lawsuit on June 4, 2021. We and Otsuka filed an opposition to the defendants’ motion on July 2, 2021, and the defendants filed a reply brief on July 16, 2021. We and Otsuka requested oral

argument on the motion on July 23, 2021. The Court has discretion whether to hear oral argument on the motion. The decision on the motion to dismiss may take up to six months.

Legal Proceedings Relating to Auryxia

ANDA Litigation

On October 31, 2018, November 6, 2018, December 24, 2018 and February 4, 2019, Keryx Biopharmaceuticals, Inc., or Keryx, received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the U.S. Food and Drug Administration, or FDA, by Lupin Atlantis Holdings SA, or Lupin, Teva Pharmaceuticals USA, Inc., or Teva, Chemo Research S.L., or Chemo, and Mylan Pharmaceuticals Inc., or Mylan, respectively, requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). On December 13, 2018, Keryx and its licensors, Panion & BF Biotech, Inc., or Panion, and Chen Hsing Hsu, M.D., filed a complaint for patent infringement against Lupin and Lupin Ltd., or the Lupin Defendants, in the United States District Court for the District of Delaware, or the Delaware District Court, arising from Lupin's ANDA filing with the FDA. On December 19, 2018, Keryx and Panion filed a complaint for patent infringement against Teva and Teva Pharmaceutical Industries Limited, or the Teva Defendants, in the Delaware District Court arising from Teva's ANDA filing with the FDA. On February 1, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Chemo and Insud Pharma S.A., or the Chemo Defendants, in the Delaware District Court arising from Chemo's ANDA filing with the FDA. On March 15, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Mylan in the United States District Court for the Northern District of West Virginia arising from Mylan's ANDA filing with the FDA. On April 18, 2019, Keryx, Panion and Dr. Hsu filed a motion with the Judicial Panel on Multidistrict Litigation seeking to consolidate these four cases in the Delaware District Court for pretrial proceedings.

On March 29, 2019, April 2, 2019, and April 12, 2019, Keryx received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA by Lupin Ltd., Watson Laboratories, Inc., or Watson, a wholly-owned, indirect subsidiary of Teva, and Par Pharmaceutical, Inc., or Par, an Endo International company, or Endo, respectively, requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). On May 10, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Lupin Ltd. in the Delaware District Court arising from Lupin Ltd.'s ANDA filing with the FDA. On May 10, 2019, Keryx and Panion filed a complaint for patent infringement against Watson and the Teva Defendants, or the Watson Defendants, in the Delaware District Court arising from Watson's ANDA filing with the FDA. On May 15, 2019, Keryx and Panion filed a complaint for patent infringement against the Watson Defendants in the United States District Court for the District of Nevada, or the Nevada District Court, from Watson's ANDA filing with the FDA. On May 23, 2019, Keryx and Panion filed a complaint for patent infringement against Par in the Delaware District Court arising from Par's ANDA filing with the FDA. On May 24, 2019, Keryx and Panion filed a complaint for patent infringement against Par, in the United States District Court for the Southern District of New York, or the Southern New York District Court, arising from Par's ANDA filing with the FDA. On June 4, 2019, Keryx and Panion filed a notice of voluntary dismissal to dismiss the suit in the Nevada District Court in view of the Watson Defendants' consent to venue of the Delaware District Court. On June 26, 2019, Keryx, Panion and Dr. Hsu notified the Judicial Panel on Multidistrict Litigation of additional actions in the Delaware District Court against the Lupin Defendants and the Watson Defendants. On July 31, 2019, the Judicial Panel on Multidistrict Litigation issued an order to consolidate all of our ANDA cases in Delaware District Court for pretrial proceedings. On August 26, 2019, Keryx filed an amended complaint against the Lupin Defendants in the Delaware District Court arising from the Lupin Defendants' ANDA filings with the FDA. On September 19, 2019, the Delaware District Court set a trial date for February 8, 2021. The trial was rescheduled for June 28, 2021. On January 13, 2021, the Delaware District Court vacated the deadlines for the case involving Mylan pending resolution of a discovery dispute.

On July 22, 2019, Keryx received from Teva a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 22, 2019, Keryx received from Watson a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin Ltd. a supplemental Paragraph IV certification notice letter regarding its ANDA. On September 17, 2019, Keryx received from Par a supplemental Paragraph IV certification notice letter regarding its ANDA. On October 16, 2019, Keryx received from Mylan a supplemental Paragraph IV certification notice letter regarding its ANDA. On May 14, 2020, Keryx received from Chemo a supplemental Paragraph IV certification notice letter regarding its ANDA.

On April 27, 2020, the Delaware District Court conducted a Markman hearing concerning certain claim construction issues with respect to four Orange Book-listed patents, and issued an order in favor of Keryx.

On August 2, 2019, Keryx and Panion entered into a settlement and license agreement with Par. This settlement resolved patent litigation brought by Keryx and Panion in response to Par's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Par a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation between Keryx and Panion and Par regarding Auryxia patents pending

in the Delaware District Court and the Southern New York District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On August 5, 2019, the parties filed a request to stay the litigation pending a review of the settlement and license agreement by these regulatory authorities. On September 6, 2019 and September 9, 2019, the Southern New York District Court and the Delaware District Court, respectively, entered a stipulation and order of dismissal filed by the parties to terminate the actions against Par.

On April 30, 2020, Keryx and Panion entered into a settlement and license agreement with Teva and Watson. This settlement resolved patent litigation brought by Keryx and Panion in response to Teva and Watson's ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Teva and Watson a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation between Keryx and Panion and Watson and Teva regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On May 4, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against Teva and Watson.

On September 24, 2020, Keryx, Panion and Dr. Hsu entered into a settlement and license agreement with the Lupin Defendants. This settlement resolved patent litigation brought by Keryx and Panion in response to Lupin and Lupin Ltd.'s ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Lupin and Lupin Ltd. a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, the Lupin Defendants and Dr. Hsu regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On October 5, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against the Lupin Defendants.

On March 25, 2021, Keryx and Panion entered into a settlement and license agreement with the Chemo Defendants. This settlement resolved patent litigation brought by Keryx and Panion in response to Chemo's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Chemo a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, and the Chemo Defendants regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On March 26, 2021, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against the Chemo Defendants.

As a result of the timely filing of the lawsuit against Mylan in accordance with the relevant statute, a 30-month stay of approval expiring August 4, 2021 was imposed by the FDA on Mylan's ANDA, absent an earlier judgment by the Court in the lawsuit finding the patents at issue invalid, unenforceable or not infringed. We are seeking, among other relief, an order that the effective date of FDA approval of the ANDA be a date no earlier than the expiration of each of the patents at issue and equitable relief enjoining Mylan from infringing these patents. On January 13, 2021, the Delaware District Court vacated the deadlines for the case involving Mylan pending resolution of a discovery dispute.

CMS Litigation

On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts, or the Massachusetts District Court, against Centers for Medicare & Medicaid Services, or CMS, the U.S. Department of Health and Human Services, Alex M. Azar II in his official capacity as Secretary of Health and Human Services, and Seema Verma in her official capacity as administrator for CMS challenging CMS's decision that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or the IDA Indication, and imposing a prior authorization requirement for Auryxia in the treatment of adult patients with CKD on dialysis, or the Hyperphosphatemia Indication. On October 29, 2019, we filed a motion for a preliminary injunction asking the court to provide relief while the lawsuit is pending, specifically, to restore coverage of Auryxia for the IDA Indication, and to remove the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. In the alternative, we filed a motion for summary judgment with the court asking it to decide the case on the merits. On February 4, 2020, the court denied our request for a preliminary injunction. We filed an expedited appeal with the Court of Appeals for the First Circuit challenging the District Court's denial of our motion for a preliminary injunction. The First Circuit Court of Appeals held oral argument on August 14,

2020, and affirmed the District Court's denial of our request for a preliminary injunction on September 30, 2020. As a result, Auryxia remains not covered by Medicare for the IDA Indication and the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication also remains in place. The case remains before the District Court, following the District Court's denial of defendants' motion to dismiss on July 9, 2021.

Shareholder Litigation Relating to Auryxia Supply

Four putative class action lawsuits were filed against Keryx, and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur, and James Oliviero) and consolidated in the Massachusetts District Court, captioned Karth v. Keryx Biopharmaceuticals, Inc., et al. (filed October 26, 2016, with an amended complaint filed on February 27, 2017). Plaintiff sought to represent all stockholders who purchased shares of Keryx common stock between May 8, 2013 and August 1, 2016. The complaint alleges that Keryx and the named individual defendants violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning Keryx, its supplier relationships, and future prospects, and that the allegedly misleading statements were not made known to the market until Keryx's August 1, 2016 announcement of an interruption in its supply of Auryxia.

On September 23, 2019, the Massachusetts District Court issued a Memorandum and Order denying plaintiff's motion for class certification, granting defendants' motion for judgment on the pleadings, and denying plaintiff's motion for leave to further amend his Complaint. That same day, the Massachusetts District Court entered a final judgment in favor of defendants on all claims. On September 24, 2019, plaintiff filed a notice of appeal. On June 21, 2021, the First Circuit affirmed the District Court's judgment in its entirety. The time for plaintiff to seek a rehearing before the First Circuit has now lapsed. Plaintiff has until September 17, 2021 to file a petition for certiorari to the United States Supreme Court to the extent Plaintiff wishes to seek any further appellate review.

Two stockholder derivative complaints also were filed on December 16, 2016 against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur and James Oliviero) certain of its former directors (Kevin J. Cameron, Daniel P. Regan, Steven C. Gilman, Michael Rogers Michael P. Tarnok, Joseph Feczko, Jack Kaye Wyche Fowler, Jr. and John P. Butler), some of whom are current directors and officers of ours, in the Superior Court of Massachusetts, one captioned Venkat Vara Prasad Malledi v. Keryx Biopharmaceuticals, Inc., et al., and one captioned James Anderson v. Keryx Biopharmaceuticals, Inc., et al. Each of these two complaints generally alleged breach of fiduciary duty, unjust enrichment, abuse of control, mismanagement and corporate waste. On June 27, 2017, the Superior Court of Massachusetts granted the parties' motion to consolidate and stay the derivative litigations pending the outcome of the federal securities litigation. On July 15, 2021, the plaintiffs in these actions filed a Notice of Dismissal, without prejudice, of all claims.

Shareholder Litigation Relating to the Merger

On June 28, 2018, we entered into an Agreement and Plan of Merger with Keryx and Alpha Therapeutics Merger Sub, Inc., or the Merger Sub, pursuant to which the Merger Sub would merge with and into Keryx, with Keryx becoming a wholly owned subsidiary of ours, or the Merger. On December 12, 2018, we completed the Merger. In October and November 2018, four purported shareholders of Keryx filed four separate putative class actions, or the Merger Securities Actions, against Keryx, a former officer and director of Keryx (Jodie P. Morrison), former directors of Keryx (Kevin J. Cameron, Mark J. Enyedy, Steven C. Gilman, Michael T. Heffernan, Daniel P. Regan and Michael Rogers, some of whom are current members of our Board of Directors), and, with respect to the Rosenblatt action discussed below, the Merger Sub and Akebia, challenging the disclosures made in connection with the Merger.

Three of the Merger Securities Actions were filed in the Delaware District Court: Corwin v. Keryx Biopharmaceuticals, Inc., et al. (filed October 16, 2018); Van Hulst v. Keryx Biopharmaceuticals, Inc., et al. (filed October 24, 2018); and Andreula v. Keryx Biopharmaceuticals, Inc., et al. (filed November 1, 2018). The fourth Merger Securities Action was filed in the Massachusetts District Court: Rosenblatt v. Keryx Biopharmaceuticals, Inc., et al. (filed October 23, 2018). On February 19, 2019, the plaintiff in the Rosenblatt action filed a notice of voluntary dismissal of the action without prejudice. On March 27, 2019, the plaintiff in the Van Hulst action filed a notice of voluntary dismissal of the action without prejudice.

On April 2, 2019, the Delaware District Court granted Abraham Kiswani, a member of the putative class in both the Andreula and Corwin actions, and plaintiff John Andreula's motion to consolidate the remaining two Merger Securities Actions pending in the Delaware District Court and consolidated the Corwin and Andreula cases under the caption In re Keryx Biopharmaceuticals, Inc., or the Consolidated Action. The Delaware District Court also appointed Kiswani and plaintiff Andreula as lead plaintiffs for the Consolidated Action. On June 3, 2019, the lead plaintiffs filed a consolidated amended complaint in the Consolidated Action, or the Consolidated Complaint. The Consolidated Complaint generally alleged that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 14(a) and 20(a) of the Exchange Act, and Rule 14a-9

promulgated thereunder. The alleged misstatements or omissions related to (i) certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors and (ii) any alleged negotiations that may have taken place regarding the conversion of certain convertible notes of Keryx in connection with the Merger. The Consolidated Complaint sought compensatory and/or rescissory damages, a declaration that the defendants violated Sections 14(a) and 20(a) of the Exchange Act and Rule 14a-9 thereunder, and an award of lead plaintiffs' costs, including reasonable allowance for attorneys' fees and experts' fees. The defendants in the Consolidated Action moved to dismiss the Consolidated Complaint in its entirety and with prejudice on August 2, 2019. On April 15, 2020, the Delaware District Court granted the defendants' motion and dismissed the Consolidated Complaint in its entirety. On July 2, 2020, lead plaintiffs filed a second consolidated amended complaint, or the Second Consolidated Complaint. The Second Consolidated Complaint (i) asserts the same claims under the Exchange Act as the Consolidated Complaint, (ii) names the same defendants as the Consolidated Complaint, (iii) seeks the same relief as the Consolidated Complaint and (iv) as with the Consolidated Complaint, challenges as false or misleading alleged misstatements or omissions related to certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors. The defendants in the Consolidated Action moved to dismiss the Second Consolidated Amended Complaint in its entirety with prejudice on August 10, 2020. On April 1, 2021, the Delaware District Court granted the defendants' motion and dismissed the Second Consolidated Complaint in its entirety. On April 29, 2021, lead plaintiffs filed a notice of appeal in the United States Court of Appeals for the Third Circuit. Briefing on the appeal is ongoing and is currently scheduled to be complete on September 9, 2021.

On July 15, 2021, a purported former Keryx stockholder filed a putative class action, or the State Merger Securities Action, in the Supreme Court of the State of New York against Akebia, a current officer of Akebia (John P. Butler), a former officer of Akebia (Jason A. Amello), former directors of Akebia (Muneer A. Satter, Scott A. Canute, Michael D. Clayman, Maxine Gowen, Duane Nash, Ronald C. Renaud, Jr., and Michael S. Wyzga), a current director of Akebia (Cynthia Smith), a former director and officer of Keryx (Jodie P. Morrison), a former officer of Keryx (Scott A. Holmes) and former directors of Keryx (Michael Rogers, Kevin J. Cameron, Steven C. Gilman, Daniel P. Regan, Mark J. Enyedy, and Michael T. Heffernan, some of whom are current members of our Board of Directors). The State Merger Securities Action is captioned Loper v. Akebia Therapeutics Inc., et al. The complaint in the State Merger Securities Action alleges that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 11, 12(a)(2), and 15 of the Securities Act of 1933, as amended. The alleged misstatements or omissions relate to the safety, approvability, and commercial viability of vadadustat. The complaint in the State Merger Securities Action seeks damages including interest thereon, an award of plaintiffs' and the class's costs and expenses, including counsel fees and expert fees, and rescission, disgorgement, or such other equitable or injunctive relief that the Court deems appropriate.

We deny any allegations of wrongdoing and intend to continue vigorously defending against the shareholder lawsuits described in this Legal Proceedings section. There is no assurance, however, that we will be successful in the defense of these lawsuits, or any associated appeals, or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of these lawsuits in a manner adverse to us, however, could have a material effect on our financial position and results of operations in the period in which a particular lawsuit is resolved.

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. If any of the following risks occurs, our business, financial statements and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, and anticipate that we will continue to incur significant 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 entails upfront capital expenditures and 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 research and development, including our preclinical and clinical development activities and, following the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of ours, commercialization. We have financed our operations primarily through sales of equity securities, our strategic collaborations and, following the Merger, product revenues, a royalty monetization transaction and debt. Prior to the Merger, we had no products approved for commercial sale and had not generated any revenue from the sale of products. We are not currently profitable and have incurred net losses each year since our inception, including net losses of $152.6 million for the six months ended June 30, 2021. As of June 30, 2021,

we had an accumulated deficit of $1.3 billion. We cannot guarantee when, if ever, we will become profitable. Our ability to generate product revenue and achieve profitability depends significantly on our success in many areas, including the following:

- developing, commercializing and marketing Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and the timing of such approvals, and maintaining marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- developing sustainable and scalable manufacturing processes for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate products that are compliant with good manufacturing practices, or GMPs, and services to support the clinical development and the market demand for Auryxia, vadadustat, if approved, and any other product and product candidate, including those that may be in-licensed or acquired;
- obtaining sufficient pricing and reimbursement for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, from private and governmental payors;
- obtaining and maintaining market acceptance of Auryxia, vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- the size of any market in which Auryxia, vadadustat 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;
- competing effectively with any competitive products and any disruptive technologies;
- identifying, assessing, acquiring, in-licensing and/or developing new product candidates;
- negotiating favorable terms in any transaction into which we may enter, including collaboration, merger, acquisition and licensing arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- integrating following the Merger; and
- attracting, hiring and retaining qualified personnel.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct any post-marketing approval studies, Phase 4 studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- adapt to any regulatory changes, including changes relating to reimbursement;
- adapt to any changes in reimbursement practices by third party payors;
- enroll patients in our clinical trials;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintain marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;
- seek to discover and develop 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;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;

- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any delays or encounter issues with any of the above.

We also could be forced to expend significant resources in our legal proceedings, as described under Part II, Item 1. Legal Proceedings, or any other such legal proceedings brought by or against us in the future.

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. 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, 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.

Even if we succeed in receiving marketing approval for and are able to commercialize vadadustat in the United States and other regions, we will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia, vadadustat and any other products, including those that may be in-licensed or acquired, as well as costs relating to the research and development of any other product candidate, including those that may be in-licensed or acquired. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or 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 repeat any of our clinical trials, to perform studies in addition to, different from or larger than those currently expected, if there are any delays in completing our clinical trials or if there are delays to or issues with obtaining marketing approval for vadadustat in the United States, the EU or other jurisdictions. Even if vadadustat and any other product candidate, including those that may be in-licensed or acquired, are approved for commercial sale, we anticipate incurring significant costs associated with commercialization. In addition, our ability to generate revenue would be negatively affected if the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, 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 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 to become and remain profitable, and we will need to obtain additional funding to continue operations.

We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of June 30, 2021, our cash and cash equivalents and available for sale securities were $247.0 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia and develop and commercialize vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired. These expenditures will include costs associated with research and development, manufacturing, potentially obtaining marketing approvals and marketing products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete the clinical development, including post-marketing studies, and commercialization of Auryxia and vadadustat. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical studies or any post-marketing approval requirements, Phase 4 studies or any other clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- the cost and timing of commercialization activities for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired, including product manufacturing, marketing, sales and distribution costs;
- 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, study design, study size and resulting operating costs;

- difficulties or delays in enrolling patients in our clinical trials;
- the timing of, and the costs involved in obtaining, and, if approved, maintaining, marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, including to fund the preparation and filing of regulatory submissions, and the costs of maintaining marketing approvals for Auryxia or any other product, including those that may be in-licensed or acquired;
- the outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions and any other product candidates, including those that may be in-licensed or acquired;
- the cost of securing and validating commercial manufacturing of vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Auryxia 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 ability to attract, hire and retain qualified personnel;
- costs related to the creation of additional infrastructure and expansion of additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would develop and market commercial products, or develop other product candidates and technologies.

Furthermore, we expect to continue to incur costs associated with operating as a fully integrated, publicly traded biopharmaceutical company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We expect our cash resources to fund our current operating plan beyond the expected U.S. launch of our product candidate, vadadustat, assuming timely regulatory approval and the receipt of associated regulatory milestones. We have based these estimates on assumptions that may prove to be wrong due to a variety of factors, including due to the effects of the ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, pandemic, and we could use our available capital resources sooner than we currently expect. Furthermore, our regulatory milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

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, vadadustat 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. 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, vadadustat, if approved, 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.

Our obligations in connection with the Loan Agreement with Pharmakon could adversely affect our financial condition and restrict our operations.

In November 2019, we entered into a loan agreement, or the Loan Agreement, with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which senior secured term loans in an aggregate principal amount of $100.0 million, or the Term Loans, were made available to us in two tranches. The first tranche of $80.0 million closed on November 25, 2019, and the second tranche of $20.0 million closed on December 10, 2020. See Note 11 to our unaudited condensed consolidated financial statements in Part I, Item 1. Financial Statements (unaudited) for additional information regarding our obligations under the Loan Agreement. Our Loan Agreement with Pharmakon contains affirmative and negative covenants applicable to us and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold starting in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia, which started in the fourth quarter of 2020. Failure to maintain compliance with these covenants could result in an event of default under the Loan Agreement.

In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the Loan Agreement as a result of an event of default, 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 Pharmakon could seek to enforce security interests in the collateral securing the Loan Agreement and Keryx's guarantee of the Term Loans, which could have a material adverse effect on our business, financial condition and results of operations.

The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to prepayment premiums and make-whole premiums prior to certain dates. Upon a change of control, mandatory prepayment provisions require us to prepay the principal amount outstanding, the applicable prepayment premium and make-whole premium and accrued and unpaid interest. In addition, our obligations in connection with the Loan 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, incurring certain additional indebtedness, creating certain liens, paying dividends or making certain other distributions and making certain investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a 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, research and development 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.

On February 25, 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 the to receive royalties and sales milestones for vadadustat, 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 vadadustat 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. In the event we violate certain covenants and other provisions, we may not receive sales milestones from HCR even if the applicable sales thresholds are met. 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.

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

On February 25, 2021, we entered into the Royalty Agreement with HCR, pursuant to which we sold to HCR our right to receive the Royalty Interest Payments payable to us under our the MTPC Agreement, subject to the Annual Cap of $13.0 million and the Aggregate Cap of $150.0 million. 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, and we are eligible to receive an additional $15.0 million under the Royalty Agreement if specified sales milestones are achieved for vadadustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions.

The royalty revenues under the MTPC Agreement may fluctuate considerably because they depend upon, among other things, the rate of growth of sales of vadadustat in the territory covered under the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate our right to receive up to the additional $15.0 million under the Royalty Agreement upon achievement of the specified sales milestones, 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.

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

We expect to finance our cash needs through product revenues, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. 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. 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 royalty 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 candidate, 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 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 acquisition of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, 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.

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, such as the Auryxia intangible asset impairment in the second quarter of 2020 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 direct prior 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 the Merger

We may fail to realize the anticipated benefits of our merger with Keryx, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties and liabilities, which may have a material adverse effect on our business and financial position.

On December 12, 2018, we completed the Merger. There can be no assurance that we will realize the full benefit of the anticipated synergies and cost savings relating to the Merger or that these benefits will be realized within the expected time frames or at all. Our ability to realize the anticipated benefits of the Merger will depend, to a large extent, on our ability to continue to integrate our business and Keryx's business and realize anticipated growth opportunities and synergies. If we are unable to successfully integrate the businesses, or integrate them in a timely fashion, we have faced, and may continue to face, adverse effects, some of which may be material, including, but not limited to (i) diversion of the attention of management and key personnel and potential disruption of our ongoing business, (ii) the loss of employees, (iii) challenges of managing a larger company, including challenges of conforming standards, controls, procedures and accounting and other policies and compensation structures, (iv) difficulties in achieving anticipated cost savings, (v) declines in our results of operations, financial condition or cash flows, (vi) a decline in the market price of our common stock, and (vii) potential liabilities, adverse consequences, increased expenses or other problems associated with our company following completion of the Merger. Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially impact our business, financial statements and prospects.

In addition, following the Merger, we have become responsible for Keryx's liabilities and obligations, including with respect to legal, financial, regulatory and compliance matters, including certain post-approval regulatory requirements with respect to Auryxia and obligations under collaboration, license, supply and manufacturing agreements. These obligations have, and will continue to, result in additional cost and investment by us and, if we have underestimated the amount of these costs and investments or if we fail to satisfy any such obligations, we may not realize the anticipated benefits of the transaction. Also, due to the Merger and ongoing integration, we may forego or delay pursuit of other opportunities that may have proven to have greater commercial potential.

Further, it is possible that there may be unknown, contingent or other liabilities or problems that may arise in the future, the existence and/or magnitude of which we were previously unaware. Any such liabilities or problems could have an adverse effect on our business, financial condition or results of operations.

Lawsuits have been filed challenging the Merger and additional lawsuits may be filed in the future. Any monetary damages, or other adverse judgment could have a material adverse effect on us.

There is an ongoing appeal of a putative class action lawsuit filed in federal court, and an ongoing putative class action lawsuit in state court, each filed by purported Keryx shareholders challenging the disclosures made in connection with the Merger. See Part II, Item 1. Legal Proceedings for further information relating to the lawsuits. Additional lawsuits arising out of the Merger may be filed in the future. We could be forced to expend significant resources in the defense of these lawsuits, including but not limited to, costs associated with the indemnification of Keryx and Akebia directors and officers, and the lawsuits, regardless of outcome, could have a negative effect on our reputation, stock price and results of operations. In addition, monetary damages or other adverse judgment would have a material adverse effect on our business and financial position.

Our financial statements include goodwill and an intangible asset as a result of the Merger. The intangible asset has become impaired and could become further impaired in the future under certain conditions. In addition, goodwill could become impaired in the future under certain conditions. Any potential future impairment of goodwill or intangible assets may significantly impact our results of operations and financial condition.

As of June 30, 2021, we had approximately $181.2 million of goodwill and a definite lived intangible asset from the Merger. In accordance with generally accepted accounting principles, or GAAP, we are required annually, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill and our definite lived intangible assets when indicators of impairment are present. Events giving rise to impairment of goodwill or intangible 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 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, and 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 that goodwill and/or definite lived intangible 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. For example, in the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the impact of the September 2018 Centers for Medicare & Medicaid Services, or CMS, decision that Auryxia would no longer by covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use of Auryxia for the control of serum phosphorus levels in adult patients with CKD on dialysis, or the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million during the three months ended June 30, 2020, which was entirely allocated to our only intangible asset, the developed product rights for Auryxia, and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia, which we again adjusted during the three months ended December 31, 2020. The estimates, judgments and assumptions used in our impairment testing, and the results of our testing, are discussed in Note 9 to the consolidated financial statements in the Company’s 2020 Annual Report on Form 10-K. If these estimates, judgments and assumptions change in the future, including if the Auryxia asset group does not meet its current forecasted projections, additional impairment charges 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.

Risks Related to the COVID-19 Pandemic

Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.

The ongoing COVID-19 pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, contract research organizations, or CROs, our contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, any resurgences or mutations of COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

We believe our revenue growth was negatively impacted in the first half of 2021 primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact our patient population; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees have been working from home since March 13, 2020. In addition, several healthcare facilities have restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers could negatively impact our access to healthcare providers and, ultimately, our sales. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, 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. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia, 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.

While most of our office-based operations can be performed remotely, there is no guarantee that we will continue to be as effective while working remotely because our team is dispersed, many employees may have additional personal needs to attend to (such as looking after children as a result of school closures or family members who may become sick), and employees may become sick themselves and be unable to work. Further, our increased reliance on remote access to our information systems increases our exposure to potential cybersecurity breaches.

Moreover, our future success and profitability substantially depends on the management skills of our executives and certain other key employees. The unanticipated loss or unavailability of key employees due to the pandemic could harm our ability to operate our business or execute our business strategy. We may not be successful in finding and integrating suitable successors in the event of key employee loss or unavailability.

In addition, the pandemic or the response efforts to the pandemic may cause disruptions to, closures of or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our products and product candidates. These impacts could lead to delays, increased costs or disruptions in supply of our products and product candidates and have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

The pandemic has resulted in closures of and may continue to impact clinical trial sites on which we rely and will rely for the completion of certain clinical trials and COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials. We are using remote monitoring and central monitoring, where possible. Further, the pandemic could also potentially affect the business of the FDA, the EMA or other governmental authorities, which could result in delays in meetings, reviews, inspections and approvals relating to our product and product candidate. Any decision by the FDA, EMA or other governmental authorities to delay meeting with us or our collaboration partners or scheduling inspections in light of COVID-19 could have a material adverse effect on clinical trials of our product candidates or on our efforts to obtain marketing approvals for our product candidate, which could increase our operating expenses and have a material adverse effect on our financial results, including the timing and amount of future regulatory milestones we could receive from our partners.

If we or any of the third parties with whom we engage, including our collaboration partners, were to experience shutdowns, delays or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results. At this time, our third party contract manufacturing partners continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturing partners' ability to manufacture and deliver Auryxia and vadadustat (which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in delays in or disruptions to manufacturing and supply of our products. In addition, COVID-19 precautions may cause a delay in enrolling new clinical trials. We are using remote monitoring and central monitoring, where possible.

The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, that could impact our ability to raise additional funds and has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. Even after the COVID-19 pandemic has been contained or mitigated, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

The global impact of COVID-19 continues to rapidly evolve, and we will continue to monitor the situation closely. In particular, areas we are monitoring include possible COVID-related changes in our commercial revenue payor mix, overall product sales, and reserves and allowances, as well as negative trends that could potentially have a further significant impact on product demand and, ultimately, product revenue, or could indicate goodwill, intangible assets, and other assets to be impaired. This uncertain COVID-19 pandemic environment has presented new risks to our business. While we are working to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control. The extent to which COVID-19 impacts our business will depend on future developments, which are highly uncertain and the magnitude of which cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others.

Risks Related to Commercialization

Our ability to successfully commercialize any approved product, including our ability to achieve widespread market acceptance, is critical to the success of our business.

Our ability to generate significant product revenue will depend almost entirely on our ability to execute on our commercialization plans, the level of market adoption for, and the availability of and continued use of any approved product by physicians, hospitals, dialysis clinics, wholesalers, patients, and/or healthcare payors, including government payors, consumers, managed care organizations, pharmacy benefit managers, or PBMs, and pharmacies. If we are not successful in commercializing any approved product, including achieving and maintaining an adequate level of market adoption, our

profitability and our future business prospects will be adversely impacted. Market acceptance of any approved product depends on a number of other factors, including:

- the availability of adequate coverage and reimbursement by third party payors, PBMs, and governmental authorities;
- 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 collaborators 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;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- adverse publicity about our products or favorable or adverse publicity about competing products;
- the availability of discounts, rebates, and price concessions;
- the effectiveness of our and our collaborators' sales, marketing and distribution efforts; and
- the restrictions on the use of the product together with other medications, if any.

Market acceptance is critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If any of our approved products is not accepted by the market to the extent that we expect, we may not be able to generate significant product revenue and our business would suffer.

Generic competitors are seeking approval of generic versions of Auryxia and the market entry of one or more generic competitors would limit Auryxia sales and have an adverse impact on our business and results of operation.

Although composition and use of Auryxia are currently claimed by 15 issued patents that are listed in the FDA's Orange Book, we cannot assure that we will be successful in defending against third parties attempting to invalidate or design around our patents or assert that our patents are invalid or otherwise unenforceable or not infringed, or in competing against third parties introducing generic equivalents of Auryxia or any of our future products.

The Hatch-Waxman Act allows applicants seeking to market a generic equivalent of a drug that relies, in whole or in part, on the FDA's prior approval of a patented brand name drug, to provide notice to the holder of the New Drug Application, or NDA, for the brand name drug of its application, called a Paragraph IV certification notice, if the applicant is seeking to market its product prior to the expiration of the patents with claims directed to the brand name drug. After the introduction of a generic competitor, a significant percentage of the prescriptions written for a product may be filled with the generic version, resulting in a loss in sales of the branded product. We have received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet), have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with certain such ANDA filers. See Part II, Item 1. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements. Although the United States District Court for the District of Delaware conducted a Markman hearing concerning certain claim construction issues with respect to four Orange Book-listed patents, and issued an order in favor of Keryx, we may not ultimately be successful in the ANDA litigation. Generic competition for Auryxia or any of our future products could have a material adverse effect on our sales, results of operations and financial condition.

In addition, litigation to enforce or defend intellectual property rights is complex, costly and involves significant management time. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched, revenue from Auryxia could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

If we are unable to maintain sales, marketing and distribution capabilities or to enter into additional agreements with third parties, we may not be successful in commercializing any approved product.

In order to market any approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We will need to devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is significant.

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

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential inability of sales personnel to obtain access to physicians;
- 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, marketing and distribution capabilities and our arrangements with third parties with respect to sales, marketing and distribution, or we are unsuccessful in entering into additional arrangements with third parties to sell, market and distribute or are unable to do so on terms that are favorable to us, we will not be successful in commercializing any approved product.

Coverage and reimbursement may be limited or unavailable in certain market segments for any approved product, which could make it difficult for us or our collaboration partners to sell any approved products profitably.

Market acceptance and sales of any approved products 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, 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. Coverage and reimbursement by a governmental authority, third-party payor or PBM 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, 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 United States, 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 is 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 Part D plans and/or PBMs operating on behalf of Medicare Part D 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 is covered by Medicare only under Part D. In September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use in the Hyperphosphatemia Indication. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication. For example, in the second quarter of 2020, we reduced our short-term and long-term Auryxia revenue forecast, primarily driven by

the compounding impact of the CMS Decision. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset associated with the developed product rights for Auryxia during the three months ended June 30, 2020.

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 may be required to enter into contracts with third party payors and/or PBMs offering rebates or discounts on our products in order to obtain favorable formulary status. We may not be able to agree upon commercially reasonable terms with such 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, third party payors, PBMs and other entities that purchase our products may impose restrictions on our ability to raise prices for our products over time without incurring additional costs. We cannot be sure that coverage or adequate reimbursement will be available for our product or any of our potential future products. Even if we obtain coverage for any 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 commercialize certain of our products.

Furthermore, vadadustat 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.

If we are unable to obtain or maintain contracts with key distribution partners, our business could be materially harmed.

We have four distributors, Fresenius Medical Care Rx, McKesson Corporation, Cardinal Health, Inc. and Amerisource Bergen Drug Corporation, that, in the aggregate, accounted for a significant percentage of our gross accounts receivable as of June 30, 2021. If we are not able to maintain our contracts with these key distributors on favorable terms, on a timely basis or at all, or if there is any adverse change in one or more of these distributors' business practices or financial condition, or such distributors' end users' prescribing practices or clinical protocols, it would adversely impact the market opportunity for Auryxia, our product revenues and operating results.

Further, if vadadustat is approved in the United States and included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, we would be required to enter into contracts to supply vadadustat to specific dialysis providers, instead of through distributors, which we believe could be challenging. The dialysis market is unique and is dominated by two providers: DaVita and Fresenius, which account for a vast majority of the dialysis population in the United States. In May 2017, we entered into a license agreement, which was amended and restated in April 2019, pursuant to which we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat to Fresenius Kidney Care Group LLC, or FKC, and certain third party dialysis organizations, or the Third Party Dialysis Organizations, approved by us, in the United States. The license would be effective upon the following: FDA approval of vadadustat for anemia due to CKD in adult patients with dialysis-dependent CKD, the earlier of CMS's determination that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment, or the TDAPA, and inclusion in the bundle, and a milestone payment by Vifor Pharma. Under this amended license agreement with Vifor Pharma, or the Vifor Agreement, FKC and the Third Party Dialysis Organizations are not obligated to utilize vadadustat in their U.S. clinics. In addition, even if FKC and the Third Party Dialysis Organizations choose to utilize vadadustat in their clinics in the United States, they are not restricted from utilizing other therapies for anemia due to CKD. The Vifor Agreement restricts us from directly supplying vadadustat to FKC or any other affiliate of Fresenius Medical Care North America and the Third Party Dialysis Organizations. The Vifor Agreement does not restrict us from entering into supply agreements with other dialysis clinics, such as DaVita; however, these dialysis clinics may choose not to contract with us for vadadustat or they may choose to contract with us for a limited supply of vadadustat. If vadadustat is approved and we are not able to maintain the Vifor Agreement or enter into a supply agreement with DaVita, our business may be materially harmed.

Although we currently believe it is likely that vadadustat, if approved, will be reimbursed using the TDAPA followed by reimbursement via the bundled reimbursement model, if vadadustat is neither reimbursed under the TDAPA nor the bundled reimbursement model, then the Vifor Agreement will not become effective, and patients would access vadadustat through contracts we negotiate with third party payors for reimbursement of vadadustat, which would be subject to the risks and uncertainties described above. Additionally, applying for and obtaining reimbursement under the TDAPA may take several months following approval, which would affect adoption, uptake and product revenue for vadadustat, and if there are updates to

the TDAPA rule that decrease the basis for reimbursement or eligibility criteria during the transition period or if the TDAPA is eliminated, then our profitability may be adversely affected**.** For example, the Medicare Payment Advisory Commission, or MedPAC, an independent legislative branch advisory body to Congress on issues related to the Medicare program, has recommended that TDAPA not be provided to newly approved drug products considered to fall within "functional categories" for which costs are already accounted for in the bundled reimbursement model, such as for anemia management drugs.

In addition, we may be unable to sell vadadustat, if approved, 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 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 are central to patient and provider acceptance of any products for which we receive marketing approval.

The successful commercialization of any approved product, will depend in part on the extent to which third party payors, PBMs and governmental authorities establish adequate reimbursement levels and pricing policies.

Third party payors are increasingly attempting to contain healthcare costs by limiting both coverage and reimbursement levels for new drugs. As a result, significant uncertainty exists as to whether and how much reimbursement third party payors will provide for newly approved drugs which, in turn, will put downward pressure on the pricing of drugs. Cost control initiatives may decrease coverage and payment levels for any drug and, in turn, the price that we will be able to charge and/or the volume of our sales. Certain third party payors require prior authorization for, or even refuse to provide, reimbursement for Auryxia, and others may do so in the future with respect to Auryxia, vadadustat and any of our other products or product candidates. In addition, certain third party payors require some form of prior authorization for the administration of ESAs for the treatment of anemia due to CKD within the non-dialysis patient population, and a similar prior authorization may be applicable to the HIF-PHI class for the treatment of anemia due to CKD within the non-dialysis patient population. Our business would be materially adversely affected if we are not able to receive approval for reimbursement from third party payors on a broad, timely or satisfactory basis; if reimbursement is subject to overly broad or restrictive prior authorization requirements; or if reimbursement is not maintained at satisfactory levels or becomes subject to prior authorization. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payors.

In addition, in some countries, including member states of the European Union, or EU, 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 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.

Recently, there has been considerable public and government scrutiny in the United States of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates, if approved, and could diminish our ability to establish what we believe is a fair price for our products, ultimately diminishing our revenue for our products if they are approved.

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, vadadustat and any other product or product candidate, including those that

may be in-licensed or acquired. Our objective is to continue to commercialize Auryxia and develop and commercialize new products with superior efficacy, convenience, tolerability and/or safety. In many cases, any approved products that we commercialize will compete with existing, market-leading products.

Auryxia is competing in the hyperphosphatemia market in the United States 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), that may impact the market for Auryxia.

Auryxia is competing in the IDA market in the United States 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 United States for the treatment of IDA on July 1, 2021.

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 pre-clinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia.

Drugs that may compete with vadadustat 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 United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by Vifor Pharma in the United States and Roche Holding Ltd. outside the United States.
We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PHI product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by companies such as FibroGen Inc., together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, Japan Tobacco International, or JT, GlaxoSmithKline plc, or GSK, and Bayer HealthCare AG, or Bayer.

In the United States, FibroGen Inc., or FibroGen, has filed an NDA for its product candidate, roxadustat, with the FDA. In Europe, the EMA Committee for Medical Products for Human Use recently recommended that roxadustat be approved for the treatment of anemia in patients with CKD.

In Japan, roxadustat is approved for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD, and patients not on dialysis, or NDD-CKD. 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. In addition. Bayer HealthCare AG has submitted an NDA for its product candidate for the treatment of renal anemia in Japan. In China, roxadustat has launched for the treatment of anemia of DD-CKD and for the treatment of anemia due to CKD in NDD-CKD patients.

Recently, GSK announced that its Phase 3 ASCEND program, evaluating the efficacy and safety profile of daprodustat for patients with anemia due to CKD, met its primary endpoints and across the ASCEND program, daprodustat was generally well tolerated in both non-dialysis and dialysis patients. Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat 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.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved 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 United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch our product. Several biosimilar versions of injectable ESAs are available

for sale in the EU. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018.

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 and Roche, 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 Riona and Vafseo™ in Japan 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 subject us to a variety of risks associated with international operations, which could materially adversely affect our business.

Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or 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 iron deficiency anemia, or IDA, in Japan. We also granted Otsuka Pharmaceutical Co. Ltd., or Otsuka, exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo™. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing Auryxia and vadadustat outside the United States, including:

- political, regulatory, compliance and economic developments 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;
- our ability to develop relationships with qualified local distributors and trading companies;
- political and economic instability in particular foreign economies and markets;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation;
- compliance with the EU General Data Protection Regulation, or GDPR;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- potentially negative consequences from changes in or interpretations of tax laws;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- 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 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 exchange rates between the Japanese yen 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 the Japanese yen depreciates 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 Clinical Development

In addition to Auryxia, we will continue to depend heavily on the success of our product candidate, vadadustat, for which we submitted an NDA to the FDA, which was accepted for filing in May 2021. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. We depend heavily on the successful commercialization of Auryxia and the successful clinical development, marketing approval and commercialization of vadadustat in the United States and other jurisdictions, which may never occur. 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. 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 clinical trial process. 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, while we announced positive top-line results from $INNO_2VATE$ and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO_2TECT studies, the PRO_2TECT program did not meet the primary MACE safety endpoint. 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. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. For example, the PRO_2TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients. Our 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 for a variety of other reasons, such as:

- the costs are 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 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, or IDMCs, institutional review boards, or IRBs, 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, 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;
- failure to initiate, delay of or failure 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;
- we may determine to change or expand 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;
- delay or failure in having patients complete a clinical trial or return for post-treatment follow-up;
- delay or failure in recruiting and enrolling suitable patients to participate in a clinical trial;
- 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;
- 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;
- 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;
- 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;
- the design of our clinical trials;
- failure 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
- changes in governmental regulations or administrative actions.

The COVID-19 pandemic has resulted in closures of and may continue to impact clinical trial sites on which we rely and will rely for the completion of certain clinical trials and may delay enrollment of certain planned and ongoing clinical trials.

We may be unable to successfully complete clinical trials of Auryxia and vadadustat, if the results of those trials and studies are not positive or are only modestly positive, or if there are concerns with the profile due to efficacy or safety. For example, the PRO_2TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients. If any of the foregoing occurs, the following may occur:

- 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 vadadustat;
- we may not obtain marketing approval for vadadustat 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 Risk Evaluation and Mitigation Strategies, or REMS, or FDA-imposed risk management plans 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 vadadustat or any other product candidate, 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 studies, which could delay or prevent clinical studies of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

Identifying and qualifying patients to participate in clinical studies is critical to our success. The timing of our clinical studies 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 studies because of concerns about adverse events observed with 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 studies 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. 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 studies 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 studies 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;
- 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 study sites for prospective patients;
- availability of competing therapies and clinical studies 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 studies;
- clinical trial sites and investigators failing to perform effectively;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have a material adverse effect on our business.

We may not be able to conduct clinical trials in some jurisdictions outside of the United States.

Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States is subject to numerous additional risks unique to conducting business in jurisdictions outside the United States, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- different local standards for the conduct of clinical studies;
- difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries; and
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Data obtained from studies conducted in the United States may not be accepted by the EMA, the PMDA and other regulatory authorities outside of the United States. Also, certain jurisdictions require data from studies conducted in their country in order to obtain approval in that country.

If we or our collaboration partners have difficulty conducting our clinical studies in jurisdictions outside the United States as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have an adverse effect on our business.

Positive results from preclinical and clinical studies are not necessarily predictive of the results of any future clinical studies.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, successful results from early or small clinical trials may not be replicated in later and larger clinical trials, and successful interim results from ongoing clinical studies may not be indicative of results obtained when those studies are completed. For example, while we announced positive top-line results from INNO$_2$VATE and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO$_2$TECT studies, the PRO$_2$TECT program did not meet the primary 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. If the results of our ongoing or future clinical trials for a product candidate are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are safety concerns or adverse events, we may be prevented from or delayed in obtaining marketing approval a product candidate. For example, the PRO$_2$TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients.

We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and the development and potential commercialization of vadadustat, a key element of our long-term growth strategy is to acquire, 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 research and development 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 otherwise does not meet applicable regulatory criteria;
- 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 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 research and development efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, which would have a material adverse effect on our business.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of proposing, 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, including, for example, with respect to the Merger. 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 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 products that we develop or approved products that we acquire will be manufactured profitably, 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 additional therapeutic opportunities for Auryxia or vadadustat or to acquire 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.

Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that delay or limit their commercial potential, or in the case of vadadustat, prevent its marketing approval.

Undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat 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. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of undesirable effects or unexpected characteristics.

If we or others identify undesirable effects caused by or other undesirable properties of Auryxia, vadadustat, or any other product or product candidate, including those that may be in-licensed or acquired, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- we may be unable to obtain marketing approval or regulatory authorities may withdraw marketing approval;
- regulatory authorities may require warnings on the label, such as the warning on Auryxia’s label regarding iron overload;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies, may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining marketing approval and, ultimately, market acceptance or penetration of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, vadadustat 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 potential patient populations for vadadustat, if approved, 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$_2$VATE Phase 3 program, the incidence of treatment emergent adverse events during the incident dialysis patient study (*Correction and Conversion*) in vadadustat treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the prevalent dialysis patient study (*Conversion*) in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/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 treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients.

With respect to the global PRO$_2$TECT Phase 3 program, the incidence of treatment emergent adverse events during the erythropoiesis stimulating agent, or ESA,-untreated patients study (*Correction*) in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events 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 treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the ESA-treated patients study (*Conversion*) in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events 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 treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

Serious adverse events considered related to vadadustat and any other product candidates could have material adverse consequences on the development of such product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of our product candidates may change as we gather more information, and additional unexpected adverse events may be observed in future clinical trials or in the market. For example, we previously reported that in our Phase 2b study of vadadustat in non-dialysis patients with anemia due to CKD, one subject had a serious adverse event of an abnormal liver function test, considered a case of drug induced liver injury, or DILI, meeting the biochemical criteria of Hy's Law. Following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program. The review of hepatic safety included a blinded assessment of all hepatic events in the studies by a panel of hepatic experts and analysis by an independent hepatic expert and our team. Based on this review, we concluded that the data across the clinical program showed that the overall hepatic safety profiles of vadadustat and darbepoetin alfa appear to be similar. In addition, we concluded that there were no events across the clinical program that met the biochemical criteria for Hy's Law. More specifically, we concluded that the DILI from our Phase 2b study of vadadustat in non-dialysis patients with anemia due to CKD that we previously reported as Hy's Law did not, in fact, meet the biochemical criteria of Hy's Law. Our conclusion on this case was reflected in our NDA for vadadustat.

The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia for the Hyperphosphatemia Indication in the United States included diarrhea (21%), discolored feces (19%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing Auryxia (14%) in clinical trials for the Hyperphosphatemia Indication. The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia in the United States for the IDA Indication included discolored feces (22%), diarrhea (21%), constipation (18%), nausea (10%), abdominal pain (5%) and hyperkalemia (5%). Diarrhea was the most common reason for discontinuing Auryxia (2.6%) in clinical trials for the IDA Indication.

Any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia, vadadustat 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, as Auryxia 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 studies. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia or any other products are associated with serious undesirable effects, undermining our commercialization efforts.

Further, if we or others identify previously unknown undesirable effects, if known undesirable effects are more frequent or severe than in the past, if we or others detect and confirm unexpected safety signals for Auryxia, vadadustat, or any other product or product candidate perceived to be similar to Auryxia, vadadustat, 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:

- sales may be impaired;
- regulatory approvals may be restricted or withdrawn;
- 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 nonclinical or clinical studies, 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
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia or, if approved, vadadustat 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, vadadustat or any other products or product candidate.

Risks Related to Regulatory Approval

We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, 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 United States and other jurisdictions. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing 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 United States and in other jurisdictions, only a small percentage successfully complete the FDA's and other jurisdictions' marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and commercialization efforts, we may be unable to continue commercialization of Auryxia or successfully develop or commercialize vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

We and Otsuka, our collaboration partner, are not permitted to market vadadustat in the United States until we receive approval from the FDA, in the EU until we receive approval from the EMA, or in any other jurisdiction until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for vadadustat, we must complete Phase 3 studies and any additional preclinical or clinical studies required by the FDA, the EMA or other regulatory authorities. Vadadustat may not receive marketing approval. We submitted an NDA to the FDA for vadadustat for the treatment of anemia due to CKD in adult dialysis-dependent and non-dialysis dependent patients in March 2021. Our NDA submission was accepted for filing by the FDA in May 2021. The FDA assigned the application standard review and a Prescription Drug User Fee Act (PDUFA) target action date of March 29, 2022. At the time of filing, the FDA also indicated that they were not currently planning to hold an Advisory Committee meeting to discuss the application for vadadustat. While we remain cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients as vadadustat did not meet the primary safety endpoint of the PRO_2TECT program, we look forward to working with the FDA in their review of all of the data.

Further, vadadustat may not receive marketing approval even if it is approved in other countries. For example, although vadadustat is approved in Japan for the treatment of adult patients with anemia due to CKD, such approval does not guarantee approval in the United States by the FDA.

Obtaining marketing approval in the United States and other jurisdictions 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, following completion of the review process, may not grant marketing approval. Furthermore, approval of a drug does not ensure successful commercialization. For example, on September 23, 2015, the

European Commission, or EC, approved Fexeric 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 addition, the safety concerns associated with the current standard of care for the indications for which we are seeking marketing approval for vadadustat and any other product candidate, including those that may be in-licensed or acquired, may affect the FDA's, the EMA's or other regulatory authorities' review of the safety results of our compounds in development. 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 vadadustat and any other product candidate, including those that may be in-licensed or acquired, will never obtain marketing approval in certain jurisdictions or at all. The FDA may delay, limit or deny approval of vadadustat or any other product candidate, including those that may be in-licensed or acquired, for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating adult patients with anemia due to CKD or that any other product candidate is safe and effective for its proposed indications to the satisfaction of the FDA;
- 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 FDA for review and/or for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications we request for vadadustat or any other product candidate;
- the FDA may approve vadadustat or any other product candidate for use only in a small patient population or for fewer or more limited indications than we request;
- the FDA may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA may grant approval contingent on the performance of costly post-marketing clinical trials;
- the FDA's onsite inspections may be delayed due to the COVID-19 pandemic;
- we, or our CROs or other vendors, may fail to comply with GXP or fail to pass any regulatory inspections or audits;
- the CROs that we retain to conduct our clinical trials may not perform effectively or take actions that adversely impact our clinical trials, or we may fail to communicate effectively or provide the appropriate level of oversight of our CROs;
- we or our third party manufacturers may fail to perform in accordance with the FDA's cGMP requirements and guidance;
- the FDA may disagree with inclusion of data obtained from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA 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;
- although at the time of filing the NDA, the FDA indicated that they were not currently planning to hold an Advisory Committee meeting to discuss the NDA, 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 FDA may require development of a REMS as a condition of approval or post-approval;
- the FDA's review process and decision-making regarding vadadustat and any other 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 vadadustat and any other product candidate are being developed;

- the FDA may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requires us to amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or other regulatory authorities to delay, limit or deny approval of vadadustat or any other product candidate outside the United States.

If we experience delays in obtaining approval, or if we fail to obtain approval of vadadustat or any other product candidate, including those that may be in-licensed or acquired, the commercial prospects for vadadustat or any other such product candidate may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business.

We may be delayed in obtaining, or be unable to obtain, marketing approval or reimbursement for vadadustat or any other product candidate in certain countries outside of the United States.

Regulatory authorities outside of the United States will require compliance with numerous and varying requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, 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 FDA does not ensure approval by regulatory or reimbursement authorities outside the United States, and approval by one regulatory or reimbursement authority outside the United States does not ensure approval by the FDA or any other regulatory or reimbursement authorities. However, the failure to obtain approval or reimbursement in one jurisdiction may negatively impact our ability to obtain approval or reimbursement in another jurisdiction. The marketing approval process in countries outside of the United States may include all of the risks associated with obtaining FDA approval and, in some cases, additional risks. We may not be able to file for or obtain such regulatory or reimbursement approvals on a timely basis, if at all. Also, favorable pricing in certain countries depends on a number of factors, some of which are outside of our control.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom, or UK, as a result of the recent withdrawal of the UK from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the United Kingdom withdrew from the EU, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing vadadustat or any other product candidate, including those that may be in-licensed or acquired, in the UK and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK and/or the EU for vadadustat or any other product candidate, which could significantly and materially harm our business.

Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.

Marketing approvals may be subject to limitations on the approved indicated uses for which the product may be marketed or 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, we initially committed to the FDA to conduct certain post-approval pediatric studies of Auryxia under the Pediatric Research Equity Act of 2003, or PREA. With regard to the Hyperphosphatemia Indication, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. With regard to our IDA Indication, we initially committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023. We cannot guarantee that we will be able to complete these studies and submit the final reports in a timely manner. For example, with regard to the Hyperphosphatemia Indication, we did not complete and submit the post-marketing requirement pediatric clinical study report by December 31, 2019, and we received a notification of noncompliance with PREA. Our request to extend this deadline was denied, and the study is considered delayed. With regard to the IDA Indication, we did not meet a milestone relating to the 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 study

timelines for the IDA Indication. If we are unable to complete these studies successfully, we will need to inform the FDA, have further discussions, and if the FDA finds that we failed to comply with pediatric study requirements, it could initiate proceedings to seize or enjoin the sale of Auryxia, 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, 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 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.

Moreover, the FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on companies' communications regarding use of their products, and if we promote any approved product beyond its approved indications or inconsistent with the approved label, we may be subject to enforcement actions or prosecution arising from such activities. Violations of the U.S. Federal Food, Drug, and Cosmetic Act, or the FD&C Act, relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws, insurance fraud laws, third party payor actions, shareholder actions and other lawsuits.

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 recently had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future 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, Vafseo™, in Japan or vadadustat for commercial and clinical use.

Non-compliance with 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 United States 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 a complex regulatory scheme that requires significant resources to ensure compliance. Failure to comply with applicable laws could subject us to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationships with key regulatory agencies such as the FDA, the U.S. Securities and Exchange Commission, or the SEC, or the EMA.

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

- laws and regulations governing the conduct of preclinical and clinical studies in the United States and other countries in which we are conducting such studies;
- laws and regulations in the United States and in countries in which we are interacting with healthcare providers, patients, patient organizations and other constituencies that prohibit promoting a drug prior to approval and/or reimbursement;
- laws and regulations of countries outside the United States that prohibit pharmaceutical companies from promoting prescription drugs to the general public;
- laws, regulations and industry codes that vary from country to country and govern our relationships with healthcare providers, patients, patient organizations, and other constituencies, prohibit certain types of gifts and entertainment, establish codes of conduct and, in some instances, require disclosure to, or approval by, regulatory authorities for us to engage in arrangements with such constituencies;
- anti-corruption and anti-bribery laws, including the FCPA, the UK Bribery Act and various other anti-corruption laws in countries outside of the United States;
- data privacy laws existing in the United States, the EU 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, the GDPR, and state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, as well as state consumer protection laws;
- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws; 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.

Compliance with these and other applicable laws and regulations requires us to expend significant resources. Failure to comply with these laws and regulations may subject us to government investigations, enforcement actions by regulatory authorities, penalties, damages, fines, the restructuring of our operations, or the imposition of a clinical hold, 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 vadadustat, any of which could have a material adverse effect on our business.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, acquire or in-license 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 United States for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia.

Promoting a drug off-label is a violation of the FD&C Act 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 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. In addition, under some relatively recent guidance from the FDA, companies may also promote information that is consistent with the prescribing information 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, Auryxia is our first commercial product in the United States, so our implementation of our compliance program in connection with commercialization activities is still relatively new.

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.

Disruptions in the FDA and other government agencies caused by funding shortages or global health concerns could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the United States government has shut down. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. This risk-based assessment system identifies the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. In May 2021, the FDA issued a new report "Resiliency Roadmap for FDA Inspectional Oversight" which include its detailed plan to move towards a more consistent state of operations; best-case, base-case and worst-case scenarios are identified, as well as the drivers that determine these scenarios and the impact these will have on inspection activities. Regulatory authorities outside the United States may also impose similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to 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.

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 European Economic Area, or EEA, in May 2018. 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 with respect to sponsors with clinical trial sites 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. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA 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 United States. 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 global revenues 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.

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 United States. 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 and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR. 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). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of potential consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Our relationships with healthcare providers, physicians and third party payors are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third party payors play a primary role in the recommendation and prescription of Auryxia and any other product candidates for which we obtain marketing approval. Our arrangements with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and vadadustat, if approved, and any other products for which we may obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by federal and state governments and by governments in foreign

jurisdictions in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the FD&C Act 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 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 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, currently set at $11,181 to $22,363, per false claim for penalties assessed between January 29, 2018 and June 19, 2020, and $11,665 to $23,331, per false claim for penalties assessed after June 19, 2020, and violations of the FD&C Act, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA 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 Physician Payments Sunshine Act (renamed the Open Payments Act) requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, 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, known as the PhRMA Code. Additionally, some state and local laws require the registration 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, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. 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. 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.

Recently enacted and future legislation 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 United States or foreign jurisdictions.

In the United States 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 vadadustat, or any other product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and vadadustat, if approved. 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 in additional downward pressure on the price that we receive for any FDA approved product, such as Auryxia.

In the United States, 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. Among the provisions of the ACA of potential importance to our business including, without limitation, our ability to commercialize and the prices we obtain for Auryxia and may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal anti-kickback statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes and regulatory 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 2% per fiscal year. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester, through 2030. 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 vadadustat, if approved, or the frequency with which Auryxia and vadadustat, if approved, is prescribed or used.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With the enactment of the Tax Cuts and Jobs Act of 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. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. The prior administration also took executive actions to undermine or delay implementation of the ACA. In addition, CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

Further, on December 14, 2018, a United States District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and, therefore, because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On November 10, 2020, the United States Supreme Court heard this case. On June 17, 2021, the Supreme Court dismissed this case after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Accordingly, all of the provisions in the ACA but the individual mandate to buy health insurance remain in effect. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business.

The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent United States 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.

Specifically, there have been several recent United States congressional inquiries and proposed federal and proposed and enacted state 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.

For example, the former administration issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction. The current administration has frozen certain of the previous administration’s measures to reform drug prices, pending further review It remains to be seen how the current administration will address this issue but, under Medicare Part D, the new administration may seek to establish a ceiling for the launch prices of all branded, biologic, and certain generic drugs by referencing the average price of these drugs in other developed countries. At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue Plan Act of 2021, comprehensive COVID-19 relief legislation recently enacted under the current administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

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. 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 United States 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 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 and any products 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 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.

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

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 the rights to our product, Auryxia. We have licensed and sublicensed the 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 Keryx in writing that Panion would terminate the Panion License Agreement on November 21, 2018 if Keryx did not cure the breach alleged by Panion, specifically, that Keryx failed to use commercially reasonable best efforts to commercialize Auryxia

outside the United States. Keryx 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, Keryx 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 United States 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 4 to the Condensed Consolidated Financial Statements (unaudited) contained in this Quarterly Report on Form 10-Q 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.

We rely on third parties to conduct our clinical studies 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 optimize the commercialization of Auryxia or obtain marketing approval for or commercialize vadadustat, and our business could be substantially harmed.

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

- if the quantity or accuracy of the data obtained by the third parties is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if the third parties otherwise fail to comply with clinical trial protocols, perform effectively or meet expected deadlines;
- if third parties experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if third parties undergo changes in priorities or corporate structure or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

Any of these events could cause our preclinical 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 obtain and maintain marketing approval of vadadustat or any other product candidates on a timely basis, or at all, or fail to maintain marketing approval of Auryxia, or any other products, any of which would adversely affect our business operations. In addition, if the third parties on 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 continued optimization of the commercialization of Auryxia and the development and commercialization of vadadustat or any other product candidates.

Even though we do not directly control the third parties on whom we rely to conduct our preclinical 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 and preclinical trials 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 on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

We rely on third parties to conduct all aspects of our product manufacturing. The loss of these manufacturers, their failure to supply us on a timely basis, or their failure to successfully carry out their contractual duties or comply with regulatory 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 product 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, including the vadadustat drug product that we supply to our collaboration partner, MTPC, for the Japanese market. Our reliance on third party manufacturers increases the risk that we will not have sufficient quantities of Auryxia and vadadustat 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 have two suppliers of Auryxia drug substance, Siegfried Evionnaz SA (two approved sites) and BioVectra Inc. (one approved site), and one supplier of Auryxia drug product, Patheon Inc., or Patheon (three approved sites). We have entered into supply agreements with Esteve Química, S.A. and STA Pharmaceutical Hong Kong Limited, a subsidiary of Wuxi AppTec, or STA, for the commercial manufacture of vadadustat drug substance and Patheon Inc. and STA for the commercial manufacture of vadadustat drug product. If any of the following occurs, we may not have sufficient quantities of Auryxia and/or vadadustat to support our clinical trials, commercialization, or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in implementing additional redundant supply arrangements for commercial quantities of vadadustat or in maintaining our redundant supply arrangements for commercial quantities of Auryxia and vadadustat;
- our commercial supply arrangements for Auryxia or vadadustat are terminated;
- any of our third party manufacturers is unable to fulfill the terms of their agreements with us or is unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings; or
- any of our third party manufacturers breaches our supply agreements, does not comply with quality or regulatory requirements and guidance, is subject to regulatory review or ceases its operations for any reason.

If any of our third party manufacturers cannot or do not perform as agreed or expected, including as a result of COVID-19, a misappropriation of 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 the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers, which we may not be able to do in a timely manner or on favorable or reasonable terms, if at all. 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 file to obtain licenses in order to have another third party manufacture Auryxia or vadadustat. 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 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 vadadustat, where approved, in a timely manner within budget or at all.

There are a limited number of manufacturers that are capable of manufacturing Auryxia and vadadustat for us and complying with cGMP regulations and guidance and other stringent regulatory requirements and guidance enforced by the FDA, EMA, PDMA 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 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 vadadustat 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 secure and maintain marketing approval for vadadustat.

If the FDA, the EMA or other regulatory authorities do not approve the facilities being used to manufacture vadadustat, or if they withdraw any approval of the facilities being used to manufacture Auryxia or Vafseo™, in Japan, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or develop, obtain marketing approval for or market our product candidates, if approved. Moreover, our failure or the failure of our third party manufacturers 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, 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 vadadustat, 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 vadadustat. For example, we recently had 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, Vafseo in Japan or vadadustat for commercial and clinical use. Also, if our starting materials, drug substance or drug product are damaged or lost while in our or our third party manufacturers' control, it may adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

In addition, Auryxia and vadadustat may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols, including, in each case, relating to the COVID-19 pandemic. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia or vadadustat due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' ability to meet our demand, which could adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

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

Third party manufacturers may be unable to manufacture Auryxia and vadadustat in sufficient quality and quantity, which would delay or prevent us from commercializing and developing.

As a result of the large quantity of materials required for the production of Auryxia and vadadustat and the large quantities of tablets that are required for our commercial success, the commercial viability of Auryxia and vadadustat, if and where approved, depends on adequate supply of starting materials that meet quality, quantity and cost standards and the ability of our contract manufacturers to continually produce drug substance and finished drug product that meets all manufacturing requirements on a commercial scale. Failure to achieve and maintain these levels of supply can jeopardize and prevent the successful continued commercialization of Auryxia and commercialization of vadadustat, if and where approved. 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 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 Keryx's revenues in 2016. Although this supply interruption was resolved and actions designed to prevent future interruptions in the supply of Auryxia are ongoing, any future supply

interruptions, whether quality or quantity based, for Auryxia and vadadustat, if and where approved, would negatively and materially impact our reputation and financial condition.

In addition, in order to complete our development of and commercialize vadadustat, if approved in regions beyond Japan, we will need to work with third party manufacturers to manufacture vadadustat in large quantities, including to prepare for launch demand. Our current and future third party manufacturers may be unable to successfully achieve commercial scale production of vadadustat in a timely or cost-effective manner, if at all. COVID-19 may also impact our third party manufacturers and their ability to supply vadadustat in sufficient quantities, or at all. In addition, quality issues may arise during scale-up activities. Any changes in our manufacturing processes as a result of scaling up may result in the need to obtain additional marketing approvals. If our third party manufacturers are unable to achieve commercial scale production or there is a need for additional marketing approvals of vadadustat, the development, marketing approval and commercialization of vadadustat may be delayed or infeasible, or ongoing commercialization of Auryxia or Vafseo™, in Japan may be unsuccessful, any of which could significantly harm our business.

We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona and vadadustat. If our 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 vadadustat, and our business could be materially harmed.

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We entered into collaboration agreements with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other territories. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. In addition, we have a license agreement with Vifor Pharma pursuant to which we granted an exclusive license to sell vadadustat to FKC and the Third Party Dialysis Organizations, approved by us, in the United States, which license would become effective only upon the satisfaction of certain conditions. 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 our and our partners' development and commercialization efforts with respect to vadadustat and any other product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may not be able to maintain our collaborations and our 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 collaborations 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 collaborations, 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 collaborations, 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, 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 or commercialization of Auryxia or vadadustat 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;

- 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 requirements.

If any of these events occurs, the market potential of Auryxia and vadadustat, if and where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. We also cannot be certain that, following a collaboration, 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, we may have to alter our development and commercialization plans.

We will require substantial additional cash to fund the continued commercialization of Auryxia and the development and potential commercialization of vadadustat and any other product candidates. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia. 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, or disrupt our management and 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;
- inability to negotiate collaborations on acceptable terms;
- inability to negotiate collaborations on a timely basis;
- a potential collaborator’s evaluation of Auryxia, vadadustat and any other product or product candidate;
- a potential collaborator’s resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations, we may have to delay or curtail the commercialization of Auryxia or vadadustat, if and where approved, reduce or delay its development program or other of our other development programs, or increase our expenditures and undertake 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 or vadadustat, in the case of commercialization, where approved.

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.

We may incur losses as a result of unforeseen or catastrophic events, including the emergence of a pandemic, terrorist attacks, extreme weather events or other natural disasters.

The occurrence of unforeseen or catastrophic events, including the emergence of a pandemic, such as COVID-19 discussed above, or other widespread health emergency (or concerns over the possibility of such an emergency), terrorist attacks, extreme terrestrial or solar weather events or other natural disasters, could create economic and financial disruptions, and could lead to operational difficulties that could impair our ability to manage our businesses or result in reduced sales or delays in our clinical studies, which could have a material adverse effect on our financial results. If we or any of the third parties with whom we engage were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results.

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 United States 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 product 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 product.

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 United States 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 product and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the United States 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, thus reducing any advantage of the patent. 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.

Additionally, the laws of foreign countries may not protect our intellectual property rights to the same extent as do the laws of the United States. For example, claims in a patent application directed to methods of treatment of the human body are not patentable or are restricted in many non-U.S. countries. Further, we may not pursue or obtain patent protection in all major markets. In addition, in jurisdictions outside the United States where we own or license patent rights, we may be unable to prevent unlicensed parties from selling or importing products or technologies derived elsewhere using our proprietary technology.

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 United States, 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 United States 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, or the Act, which reformed certain patent laws in the United States, 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 United States. 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.

In July 2011, a third party filed an opposition to our issued European patents, European Patent No. 2044005, or the ’005 EP Patent, which covers vadadustat. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the ’005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in

the divisional application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

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 United States 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 United States 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.

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, we share ownership and publication rights to data relating to our drug product and technologies with our research collaborators and scientific advisors. 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.

The intellectual property and related non-patent exclusivity that we own or have licensed relating to our product, Auryxia, is limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.

The patent rights and related non-patent exclusivity that we own or have licensed relating to Auryxia are 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 not market a product for methods of use 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 from marketing and selling Auryxia, increase the risk that a generic or other similar version of Auryxia could enter the market to compete with Auryxia, limit our development and commercialization of Auryxia, or otherwise harm our competitive position and result in additional significant costs. In addition, any successful claim of infringement asserted against us could subject us to monetary damages or injunction, which could prevent us from making or selling Auryxia. We also may be required to obtain licenses to use the relevant technology. Such licenses may not be available on commercially reasonable terms, if at all.

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 the United States, 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 to patent protection, we may utilize, if granted by the FDA, pediatric exclusivity or other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, to provide non-patent exclusivity for a drug product. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first applicant to gain approval of a new drug application, or 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). 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 applicant does not own or have a legal right of reference to all the data required for approval. However, an ANDA or 505(b)(2) NDA 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, 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 applicant 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, an applicant 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 applicant.

On August 23, 2018, Keryx submitted a Citizen Petition requesting, *inter alia*, that the FDA recognize that Auryxia is eligible for five years of new chemical entity, or NCE, exclusivity based on its novel active ingredient and for three years exclusivity for the IDA Indication. On January 19, 2019, the FDA responded that Auryxia is eligible for a three-year exclusivity period for the IDA Indication, which expired on November 6, 2020. FDA, however, denied the NCE exclusivity based on its determination that Auryxia contains a previously-approved active moiety (ferric cation). FDA's decision on the Citizen Petition is subject to further review both within the FDA and in the courts. On February 21, 2019, we filed a Petition for Reconsideration of the FDA's decision on the NCE determination for Auryxia.

The FDA's determination as to whether to grant NCE exclusivity to Auryxia may also affect the timing of the 30-month stay barring the FDA from granting final approval to generic versions of Auryxia. When an ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant 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 after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier 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 applicant. We have received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA, from generic drug manufacturers requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet), have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with certain such ANDA filers. See Part II, Item 1. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements.

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 applicant.

We cannot assure that Auryxia or any drug candidates we may acquire or in-license will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the United States, 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 that Auryxia or any drug candidates we may acquire or in-license will obtain patent term extension.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to assist with research, development and manufacture of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, services agreements, material transfer agreements, consulting agreements, research agreements or other similar agreements with our advisors, employees, third party contractors, collaborators and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such information becomes known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third party contractors, and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution with which we may collaborate will usually expect to be granted rights to publish data arising out of such collaboration. We often grant such rights, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration and remove confidential or trade secret information from any such publication. In the future, we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties or independent development or disclosure or publication of information by any of our employees, advisors, consultants, third party contractors or collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Litigation or third party claims of intellectual property infringement 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. In addition, third parties may have or may obtain patents in the future and claim that our product or any 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, vadadustat or any other 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 use such products or other technologies. 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. 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 candidate. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidate is in preclinical studies and clinical trials, we believe that the use of our product candidate in these preclinical studies and clinical trials in the United States 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 United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. As a result of the Merger, our portfolio includes a commercial product, Auryxia. Consequently, there is an increased possibility of a patent infringement claim against us. We attempt to ensure that our product and product candidate 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.

Third parties may hold or obtain patents or other intellectual property rights and allege in the future that the use of our product or product candidate infringes these patents or intellectual property rights, or that we are employing their proprietary technology without authorization. We do not believe that there are any currently issued United States patents that will prevent us from commercializing Auryxia or vadadustat; nor do we make any admission that any of such patents are valid, enforceable or infringed. Under United States law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid United States patents issued to FibroGen, or any other person, that claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia due to CKD. For example, we are aware of certain patents that have been acquired by FibroGen directed to certain heterocyclic carboxamide compounds that are described as inhibitors of prolyl-4-hydroxylase. Those patents, however, are believed to have expired as of December 2014.

FibroGen has also filed other patent applications in the United States and other countries directed to purportedly new methods of using such previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. To the extent any such patents issue or have been issued, we may initiate opposition or other legal proceedings with respect to such patents. We discuss the status of the opposition and/or invalidation proceedings against certain FibroGen patents in Part II, Item 1. Legal Proceedings of this Quarterly Report on Form 10-Q.

There may be other patents of FibroGen or patents of other 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 candidate. 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.

Third parties, including FibroGen, may in the future claim that our product and product candidate and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and vadadustat, if approved. 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 further develop and commercialize vadadustat or any other 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, including patient selection methods, 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.

We are currently involved in a patent infringement lawsuit, a declaratory judgment of non-infringement and invalidity lawsuit, opposition and invalidation proceedings, and may in the future be involved in additional lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or misappropriate our trade secrets or confidential information. To counter infringement or unauthorized use, we may be required to file infringement or misappropriation claims, which can be expensive and time-

consuming. 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 United States. 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. An adverse result in any litigation or 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, 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. 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.

For example, we are currently involved in a patent infringement lawsuit against a generic company in the federal district courts. We are also involved in an action against our competitors in the federal district court to obtain a declaratory judgment of non-infringement and invalidity of certain patents of the competitors. In addition, we are currently involved in opposition and invalidation proceedings in the European Patent Office, the Japan Patent Office, and the Patents Court of the UK. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from 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” and Part II, Item 1. Legal Proceedings of this Quarterly Report on Form 10-Q.

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.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

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, which would have a material adverse effect on our business.

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.

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

Filing, prosecuting and defending patents on our 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 United States may be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States 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 enforcement is not as strong as in the United States. These products may compete with our product and product candidate 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 marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in countries outside of the United States 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 from the intellectual property that we develop or license.

Risks Related to our Business and Industry

If we fail to attract, keep and motivate senior management and key personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize Auryxia and vadadustat.

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 members of our commercial organization. The loss of the services of our executives, senior managers or other key employees, including employees in our commercial, development, regulatory, manufacturing and quality organizations, could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Losing such 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, obtain and/or maintain marketing approval of and commercialize Auryxia and vadadustat. Our future financial performance and our ability to develop, obtain and/or maintain market approval of and commercialize Auryxia and vadadustat 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 personnel with sufficient experience. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic region.

We also experience competition for the hiring of personnel from universities and research institutions. In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our research and development 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 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 expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on products, research programs and product candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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 studies, 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 cyber security 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, 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 some 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. 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. 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, cyber-attack 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 United States protecting confidential or personal information, that could be expensive to defend and could result in significant fines or other penalties. Cyber-attacks can include malware, computer viruses, hacking 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 cyber-attacks. 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.

Likewise, 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 vulnerable to attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers in 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. In

the recent past, cyber-attacks have become more prevalent and much harder to detect and defend against and, because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, 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, inadvertent diversion of cash, divert the attention of our management and key information technology resources, disrupt key business operations, harm our reputation and deter business partners from working with us. A compromise with respect to our information security could lead to public exposure of personal information of our clinical trial patients, Auryxia patients and others, and negative publicity. Publicity about vulnerabilities and attempted or successful incursions could damage the integrity of our studies or delay their completion. If a compromise to our information security were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, any loss of clinical trial data could result in delays in our regulatory approval efforts for our product candidates and significantly increase our costs to recover or reproduce the data. In addition, such attacks could compromise our ability to protect our trade secrets and proprietary information from unauthorized access or misappropriation and a loss of, or damage to, our data or marketing applications. Inappropriate public disclosure of confidential or proprietary information could subject us to liability and cause delays in our product research, development and commercialization efforts. We currently do not maintain cybersecurity insurance to protect against losses due to security breaches.

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 Auryxia 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.

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:

- the 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
- United States state and federal securities laws and regulations and their non-U.S. equivalents.

We are currently closing out global clinical 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 United States companies and their intermediaries, such as CROs or CMOs, from making improper payments to foreign government officials for the purposes of obtaining or keeping business or to obtain 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 U.S. Securities and Exchange Commission, or 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 are conducting clinical trials 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 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 are conducting 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 sanctions 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 people and products among 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 United States federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. 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 our 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 Global 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. 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 unknown or unmanaged risks or 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.

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 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. An independent contractor is generally distinguished from an employee by his or her degree of autonomy and independence in providing services. A high degree of autonomy and independence is generally indicative of an independent contractor relationship, while a high degree of control is generally indicative of an employment relationship. Tax or other regulatory authorities may challenge our characterization of services providers as independent contractors both under existing laws and regulations and under laws and regulations adopted in the future. If such regulatory authorities or state, federal or foreign courts were to determine that our service providers are employees and not independent contractors, we would, among other things, may be required to withhold income taxes, to withhold and pay Social Security, Medicare and similar taxes, to pay unemployment and other related payroll taxes, and to provide certain employee benefits. We could also be liable for unpaid past taxes, interest and other costs and subject to penalties. Likewise, our service providers themselves may later successfully challenge their classification as independent contractors, which may result in additional damages, including back wages,

penalties, interest and attorneys' fees. As a result, any legally binding determination that the service providers we characterize as independent contractors are actually our employees could have a material adverse effect on our business, financial condition and results of operations.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we commercialize Auryxia and advance vadadustat through development and, if approved, commercialization, we have expanded and may need to further expand our capabilities or contract with third parties to provide these capabilities for us. In addition, we may encounter difficulties in managing the expanded operations of a larger and more complex company following the Merger as well as challenges associated with managing an increasingly diversified business.

We have strategic collaborations for the commercialization of Riona and the development and commercialization of vadadustat, which is now being marketed under the trade name Vafseo™ by our collaboration partner, MTPC, in Japan. As our operations expand, including as they relate to vadadustat in the United States, we expect that we will need to manage additional relationships with various strategic collaborators, consultants, vendors, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management.

In addition, in connection with the Merger and our increasingly diversified business, we have experienced and may to continue to experience significant growth in our employee base. This growth has imposed and will continue to impose significant added responsibilities on members of management, including the need to recruit, hire, retain, motivate and integrate additional employees, including employees who joined us in connection with the Merger. Also, our management may have 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 activities, including the integration of Keryx's business with our business.

Our future financial performance and our ability to commercialize Auryxia and vadadustat, if and where approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To manage our recent and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes, expand our facilities and continue to recruit, train, and retain additional qualified personnel. 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. Moreover, the systems, procedures and processes currently in place or to be implemented may not be adequate for such growth. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, along with the competitive landscape for talent acquisition and retention in the biopharmaceutical industry, we may not be able to effectively manage the expansion of our operations or recruit, train, and retain additional qualified personnel. 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 diversion of management attention, disruptions to our business, and related expenses. The physical 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 growing our company or realizing the anticipated benefits of the Merger.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia and vadadustat, if approved.

We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and vadadustat. For example, we may be sued if Auryxia or vadadustat allegedly causes injury or is found to be otherwise unsuitable during product testing, 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 vadadustat, if approved. 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 vadadustat, if approved;
- 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 or vadadustat;
- 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 vadadustat;
- loss of revenue;
- the inability to commercialize any Auryxia or vadadustat, if approved; 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 product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

Risks Related to our Common Stock

Our stock price has been and may continue to be volatile, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors.

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 have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Since our initial public offering in March 2014, the price of our common stock as reported on The Nasdaq Global Market has ranged from a low of $2.09 on October 30, 2020 to a high of $31.00 on June 20, 2014. The daily closing market price for our common stock has varied between a high price of $13.08 on July 2, 2020 and a low price of $2.22 on October 30, 2020 in the twelve-month period ending on June 30, 2021. During this time, the price of our common stock has ranged from an intra-day low of $2.09 per share to an intra-day high of $13.71 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, developments related to and results of our clinical studies, developments related to our regulatory submissions, developments related to our ability to commercialize Auryxia and vadadustat, if approved, and any other product candidates, announcements by us or our competitors of significant mergers, acquisitions, licenses, strategic collaborations, joint ventures, collaborations or capital commitments, negative publicity around Auryxia or vadadustat, the results of competitive clinical trials, products or technologies, regulatory or legal developments in the United States and other countries, developments or disputes concerning patent applications, issued patents or other proprietary rights, the recruitment or departure of key personnel, the level of expenses related to Auryxia and vadadustat or any other product or product candidate, actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, variations in our financial results or those of companies that are perceived to be similar to us, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector, general economic, industry and market conditions and others beyond our control. As a result of this volatility, our shareholders may not be able to sell their common stock at or above the price at which they purchased it.

In addition, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. See Part II, Item 1. Legal Proceedings for information concerning securities class action and shareholder derivative lawsuits initiated against Keryx and certain current and former directors and officers of ours and Keryx's. In addition, we could be the target of other such litigation in the future. Class action and shareholder derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

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 shareholders will dilute our shareholders' 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 June 30, 2021 and based on the amounts reported in the most recent filings made under Section 13(d) and 13(g) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, State Street Corporation, or State Street, beneficially owned approximately 8.8% of our outstanding shares of common stock, Wellington Management Group LLP, or Wellington, beneficially owned approximately 7.9% of our outstanding common stock, and BlackRock, Inc., or BlackRock, beneficially owned approximately 7.2% of our outstanding shares of common stock. In addition, as of June 30, 2021, our former director, Muneer Satter, beneficially owned approximately 1.9% of our outstanding common stock. In addition, pursuant to our Fourth Amended and Restated Investors' Rights Agreement, as amended, with Mr. Satter, he has the right, subject to certain conditions and with certain exceptions, to require us to file registration statements covering the shares common stock he owns or to include his shares in registration statements that we may file or in public offerings of our shares of common stock. Following their registration and sale under the applicable registration statement, those shares would become freely tradable. By selling a large number of shares of common stock, BlackRock, State Street, Wellington, or Mr. Satter could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options, restricted stock units and a warrant, and in the future we may issue additional options, restricted stock units, warrants or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, warrants or other derivative 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. Also, the Merger was financed by the issuance of shares of our common stock to shareholders of Keryx, comprising approximately 50.6% of our issued and outstanding shares of common stock, calculated based on our fully diluted market capitalization as of the date of signing the Agreement and Plan of Merger relating to the Merger. Keryx shareholders may decide not to hold the shares of our common stock they received in the Merger. Other Keryx shareholders, such as funds with limitations on the amount of stock they are permitted to hold in individual issuers, may be required to sell the shares of our common stock they received in the Merger. 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, which allows us to offer and sell certain 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.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other shareholders 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.

Insiders and significant stockholders could cause us to take actions that may not be, or refrain from taking actions that may be, in our best interest or in the best interest of all of our stockholders.

As of June 30, 2021, we believe that our directors and executive officers, together with their affiliates, owned, in the aggregate, approximately 1.8% of our outstanding common stock. In addition, we have certain significant stockholders, including Wellington, which beneficially owned approximately 7.9% of our outstanding common stock, State Street, which beneficially owned approximately 8.8% of our outstanding shares of common stock, and BlackRock, which beneficially owned approximately 7.2% of our outstanding shares of common stock based on the amounts reported in the most recent filings made by such significant stockholders under Section 13(d) and 13(g) of the Exchange Act. If they were to choose to act together, they would have significant influence on all matters submitted to our stockholders for approval, as well as our management and affairs, such as:

- the composition of our Board of Directors;
- the adoption of amendments to our Ninth Amended and Restated Certificate of Incorporation, as amended, or Charter, and our Amended and Restated By-Laws, or Bylaws;
- the approval of mergers or sales of substantially all of our assets;
- our capital structure and financing; and
- the approval of contracts between us and these shareholders or their affiliates, which could involve conflicts of interest.

This concentration of ownership could harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of our company and making some transactions more difficult or impossible without the support of these stockholders, even if such transactions are beneficial to other stockholders;
- impeding a merger, consolidation, takeover or other business combination involving our company; or
- entrenching our management or our Board of Directors.

Moreover, the interests of these stockholders may conflict with the interests of other stockholders, and we may be required to engage in transactions that may not be agreeable to or in the best interest of us or other stockholders.

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, and particularly since December 31, 2019 when we ceased to be an “emerging growth company” and December 31, 2020 when we became a "large accelerated filer", we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the SOX Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global 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. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to increase our legal and financial compliance costs and make some activities more time-consuming and costly.

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.

We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting which would harm our business and the trading price of our common stock.

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 SOX Act, or Section 404, or any testing by our independent registered public accounting firm, which became required for us as of December 31, 2019, 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 financial statements or identify other areas for further attention or improvement. For example, as of December 31, 2019, management and our independent registered public accounting firm concluded that our internal control over financial reporting relating to our inventory process was not effective because of a material weakness due to our failure to design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. Despite remediation efforts we undertook during fiscal 2020 and continue to make, our management and independent registered public accounting firm concluded that, as of December 31, 2020, our internal control over financial reporting relating to our inventory process was not effective because of a material weakness due to our failure to design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. For more information about this material weakness, see Part I, Item 4. Controls and Procedures of this Quarterly Report on Form 10-Q and Part II, Item 9A. Controls and Procedures of our Annual Report on Form 10-K for the year ended December 31, 2020. Additionally, as revised and enhanced controls need to be in operation for a sufficient period of time and be tested to ensure that the controls are operating as designed, management has concluded that the material weakness cannot be considered remediated as of June 30, 2021. Although we have initiated remediation measures to address the material weakness, 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 controls will be effective in the future. Even if this material weakness is remediated in the future, our internal control over financial reporting could in the future have additional material weaknesses, deficiencies or conditions that could require correction or remediation.

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 inventory process 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 SEC, the Nasdaq Stock Market or other regulatory authorities as well as shareholder litigation which would require additional financial and management resources and could adversely affect the market price of our common stock. 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.

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 Charter and our Bylaws 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.

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.

Any provision of our Charter, our Bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

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 United States 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 United States taxable income. As described above under "—Risks Related to our Financial Position and Need for Additional Capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the United States taxable income necessary to utilize our NOLs. A valuation allowance has been provided for the entire amount of 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 (1) any derivative action or proceeding brought on our behalf, (2) 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, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL our Charter or our Bylaws, or (4) 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.

We are currently subject to legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.

We are currently subject to legal proceedings as described in Part II, Item 1. Legal Proceedings and additional claims may arise in the future. In addition, securities class action and derivative lawsuits and other legal proceedings are often brought against companies for any of the risks described in this Quarterly Report on Form 10-Q following a decline in the market price of their securities. In connection with any litigation or other legal proceedings, we could incur substantial costs, and such costs and any related settlements or judgments may not be covered by insurance. 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.

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. 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. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of the Loan Agreement preclude us from paying cash dividends 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 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Sales of Unregistered Securities

During the quarter ended June 30, 2021, we did not have any sales of unregistered securities.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

Exhibits

3.1	Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 28, 2014).
3.2	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Akebia Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on June 9, 2020).
3.3	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, filed on March 28, 2014).
10.1*#	Amendment #1 to the Supply Agreement, dated as of April 15, 2021, by and between Akebia Therapeutics, Inc, and STA Pharmaceutical Hong Kong Limited.
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.
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 portions of the exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

SIGNATURES

Pursuant to the requirements 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: August 5, 2021

By: /s/ John P. Butler

John P. Butler

President and Chief Executive Officer (Principal Executive Officer)

Date: August 5, 2021

By: /s/ David A. Spellman

David A. Spellman

Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer)

Date: August 5, 2021

By: /s/ Violetta Cotreau

Violetta Cotreau

Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)

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.

Exhibit 10.1

AMENDMENT #1 TO SUPPLY AGREEMENT

This Amendment #1 (the "Amendment") to the Supply Agreement (the "Agreement") by and between **Akebia Therapeutics, Inc.** ("Akebia") and **STA Pharmaceutical Hong Kong Limited** ("STA") is effective as of April 15, 2021 (the "Amendment Effective Date"). Akebia and STA are each referenced individually herein as a "Party" and together as the "Parties".

WHEREAS, STA and Akebia entered into a Supply Agreement dated April 2, 2020, as amended ("Agreement") under which STA manufactures Product for purchase by Akebia; and

WHEREAS, the Parties desire to amend the Agreement as set forth in this Amendment;

NOW, THEREFORE the Parties agree as follows:

1. Section 1.3 (Definition of Akebia Improvements) of the Agreement is hereby deleted in its entirety and replaced with the following:

   "Akebia Improvements" means any Intellectual Property and discoveries, inventions, developments, modifications, innovations, updates, enhancements, improvements, writings or rights (whether or not protectable under patent, trademark, copyright or similar laws) that are conceived, discovered, invented, developed, created, made or reduced to practice during the provision of the Services by Akebia, STA, or both Parties jointly, but solely to the extent specific to any (i) Akebia Materials, (ii) the Intermediate Compounds, (iii) the Manufacturing Process, or (iv) the Product, which in each case of (i)-(iv) is solely owned by and/or proprietary to Akebia.

2. Section 1.19 (Definition of Intermediate Compounds) of the Agreement is hereby deleted in its entirety and replaced with the following:

   "Intermediate Compounds" means [**] used in the Manufacturing Process of the Product [**].

3. Section 1.31 (Definition of Raw Materials) of the Agreement is hereby deleted in its entirety and replaced with the following:

4. **"Raw Materials"** means the chemical entities required to synthesize the Intermediate Compounds and produce the Product through performance of the Manufacturing Process [**].

5. A new Section 4.6 will be added immediately following Section 4.5 of the Agreement as following:

   Section 4.6 Price Adjustments. The Product Price shall be fixed in the first [**] after the Effective Date. Thereafter, the Parties will review the Product Price on [**] basis. During the [**] price review, STA and Akebia shall discuss in good faith an adjusted Product Price, if necessary to reflect any changes caused by unforeseen reasons such as a material change in the Producer Price Index, extraordinary changes in material costs, or currency exchange rate fluctuations. Any such decision shall be reached and agreed to in writing by the Parties by [**], and shall be effective on [**]. Notwithstanding the foregoing, if there is any proposed change to the Specifications or Manufacturing Process, prior to the implementation of any such change, the Parties shall promptly negotiate in good faith any amendments to the Product Price necessary to reflect such change.

Also notwithstanding the foregoing,

(a) STA shall be entitled to request an immediate adjustment (and immediate implementation thereof) to the Product Price to reflect the impact of extraordinary increases in a single Material cost at any time if both of the following criteria are met:

i. the unit price of such Material increases by [**] of the unit price upon which then-current Product Price quote is based; and

ii. the impact on Product Price from such Material unit price increase is greater than [**] of then-current Product Price.

(b) Akebia shall be entitled to request an immediate adjustment (and immediate implementation thereof) to the Product Price to reflect the impact of extraordinary decreases in a single Material cost at any time if both of the following criteria are met:

i. the unit price of such Material decreases by [**] of the unit price upon which then-current Product Price quote is based; and

ii. the impact on Product Price from such Material unit price decrease is greater than [**] of then-current Product Price.

STA and Akebia shall discuss in good faith any adjusted Product Price requested under Section 4.6(a) or 4.6(b) above, and any such decision shall be reached and agreed to in writing by the Parties.

6. All capitalized terms not defined herein shall have meaning set forth in the Agreement.

7. Except as otherwise provided herein, all provisions of the Agreement, as amended shall remain in full force and effect.

(*Signature Page to Follow*)

IN WITNESS WHEREOF, the Parties have executed this Amendment to the Supply Agreement effective as of the Amendment Effective Date written above.

AKEBIA THERAPEUTICS, INC.		**STA PHARMACEUTICAL HONG KONG LIMITED**	
By:	/s/ Michel Dahan	By:	/s/ Xiaoyong Fu
Print Name:	Michel Dahan	Print Name:	Xiaoyong Fu
Title:	SVP & Chief Business Officer	Title:	SVP, API Development & Commercialization
Date:	April 15, 2021	Date:	April 15, 2021

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 Quarterly Report on Form 10-Q 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: August 5, 2021

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, David A. Spellman, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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: August 5, 2021

By: /s/ David A. Spellman

David A. Spellman
Senior Vice President, Chief Financial 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 Quarterly Report of Akebia Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2021 (the "Report"), I, John P. Butler, as Chief Executive Officer and President of the Company, and I, David A. Spellman, as Senior Vice President, Chief Financial 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, to my knowledge:

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: August 5, 2021

By: /s/ John P. Butler
John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: August 5, 2021

By: /s/ David A. Spellman
David A. Spellman
Senior Vice President, Chief Financial Officer and Treasurer
(Principal Financial Officer)