Akebia® THERAPEUTICS

Unlocking the Power of the Hypoxia-Inducible Factor (HIF) Pathway

Delivering Innovation for Patients with Chronic Kidney Disease (CKD)

January 2024 **Nasdaq: AKBA**

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

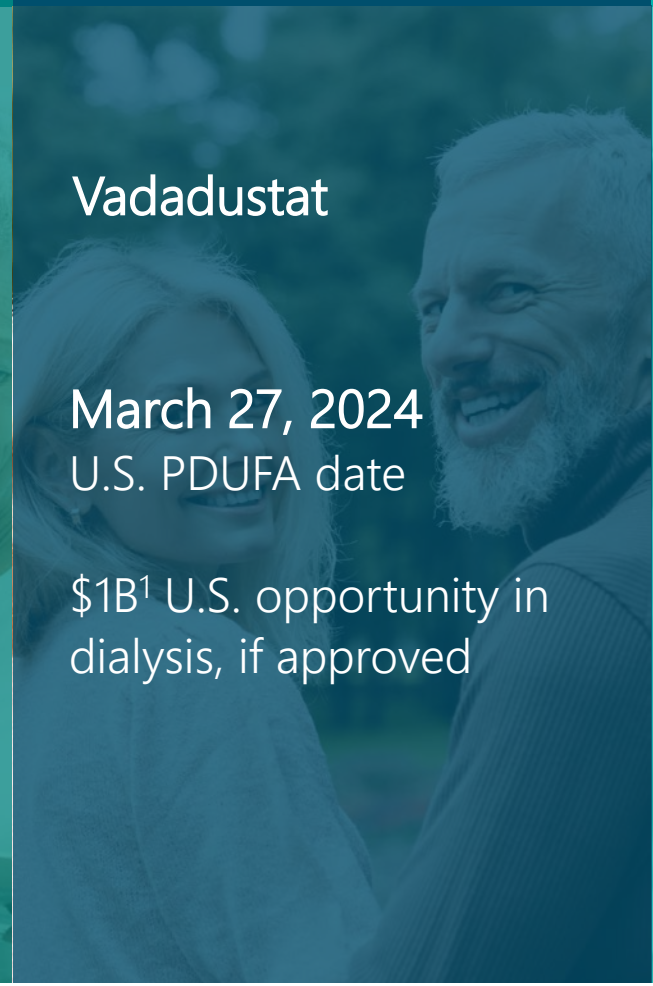
Statements in this presentation regarding Akebia Therapeutics, Inc.'s ("Akebia's") strategy, plans, prospects, expectations, beliefs, intentions and goals are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, and include, but are not limited to, statements regarding: Akebia's plans, strategies and prospects for its business; statements regarding Akebia's 2023 and cumulative preliminary unaudited net product revenue for Auryxia®; the anticipated FDA decision on the new drug application ("NDA") for vadadustat; Akebia's ability to enable a successful commercial launch of, and maximize the value of, vadadustat if approved, including statements regarding vadadustat's ability to offer providers and patients a new choice in anemia management, to deliver a potential new oral standard of care and differentiate to drive to adoption if approved; Akebia's expectations regarding the spend needed to support such commercial launch, including the availability of sufficient supply; Akebia's plans with respect to vadadustat label expansion opportunities and the potential market potential thereof; Akebia's expectations and beliefs regarding the impact that the amendment with Pharmakon will have on Akebia; Akebia's plans and expectations with respect to commercializing Vafseo in Europe, including the timing thereof and the market potential; Akebia's plans with respect to exploring review processes in Canada, China and Latam; statements regarding the beliefs about the benefits that vadadustat could provide to patients and shortcomings of the current standard of care; statements regarding expectations related to Auryxia revenue in 2024, 2025 and 2026 and Auryxia patent expiration and generic entry, including expectations that **Auryxia will continue to contribute meaningful near-term cash to business**; Akebia's plans with respect to vadadustat as a treatment of anemia due to chronic kidney disease in patients on dialysis in the U.S., including statements regarding potential revenue from vadadustat in the U.S. if approved and the potential market opportunity, timing of TDAPA designation if approved and the anticipated favorable economics from TDAPA designation; Akebia's ability to achieve anticipated catalysts in the timeframe expected, or at all; Akebia's expectations with respect to Akebia's pipeline, including Akebia's ability to execute on its development plans, expectations of the timing of the studies in Acute Respiratory Distress Syndrome (ARDS), Acute Kidney Injury (AKI), Retinopathy of Prematurity (ROP) and Bronchopulmonary dysplasia (BPD); Akebia's early Hypoxia-Inducible Fact (HIF) research and the potential therapeutic applications of the hypoxia inducible factor pathway and market potential; Akebia's goals, objectives and expectations with respect to its operating plan, expenses, cash resources and sources of funding for its cash runway, including its expectations that it has a path to profitability and that ongoing financial discipline and revenue from Auryxia expected to provide a foundation to maximize value for vadadustat.

The terms "intend," "believe," "plan," "goal," "potential," "estimate," "expect," "future," "will," "continue," derivatives of these words, and similar references are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various risks, uncertainties and other factors, including, but not limited to, risks associated with: the potential demand and market potential and acceptance of, as well as coverage and reimbursement related to, Auryxia, including estimates regarding the potential market opportunity; the competitive landscape for Auryxia, including potential generic entrants; the ability of Akebia to attract and retain qualified personnel; Akebia's ability to implement cost avoidance measures and reduce operating expenses; decisions made by health authorities, such as the FDA, with respect to regulatory filings, including the anticipated FDA decision on the NDA for vadadustat and the potential effects of a negative decision on Akebia's cash runway; the potential therapeutic benefits, safety profile, and effectiveness of vadadustat; the results of preclinical and clinical research; the direct or indirect impact of the COVID-19 pandemic on regulators and Akebia's business, operations, and the markets and communities in which Akebia and its partners, collaborators, vendors and customers operate; manufacturing, supply chain and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences; and early termination of any of Akebia's collaborations. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, and other filings that Akebia may make with the U.S. Securities and Exchange Commission in the future. These forward-looking statements (except as otherwise noted) speak only as of the date of this presentation, and, except as required by law, Akebia does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this presentation.

Built on foundation of scientific expertise, financial discipline and operational effectiveness

Auryxia® (ferric citrate)

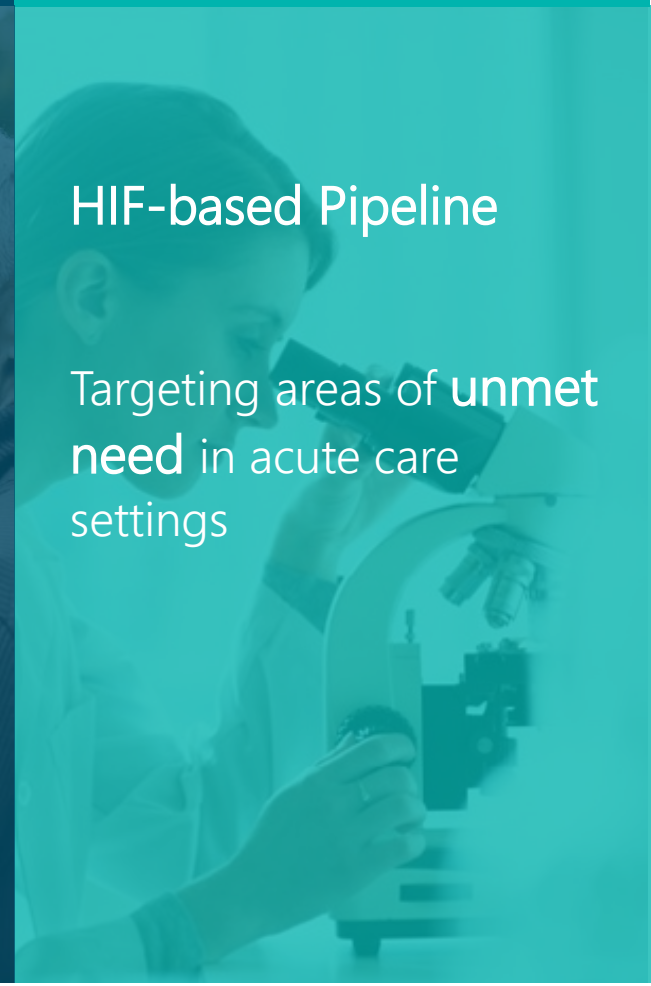
$170.0-$171.0 million in 2023 preliminary unaudited net product revenue with potential for growth in 2024



Vadadustat

March 27, 2024
U.S. PDUFA date

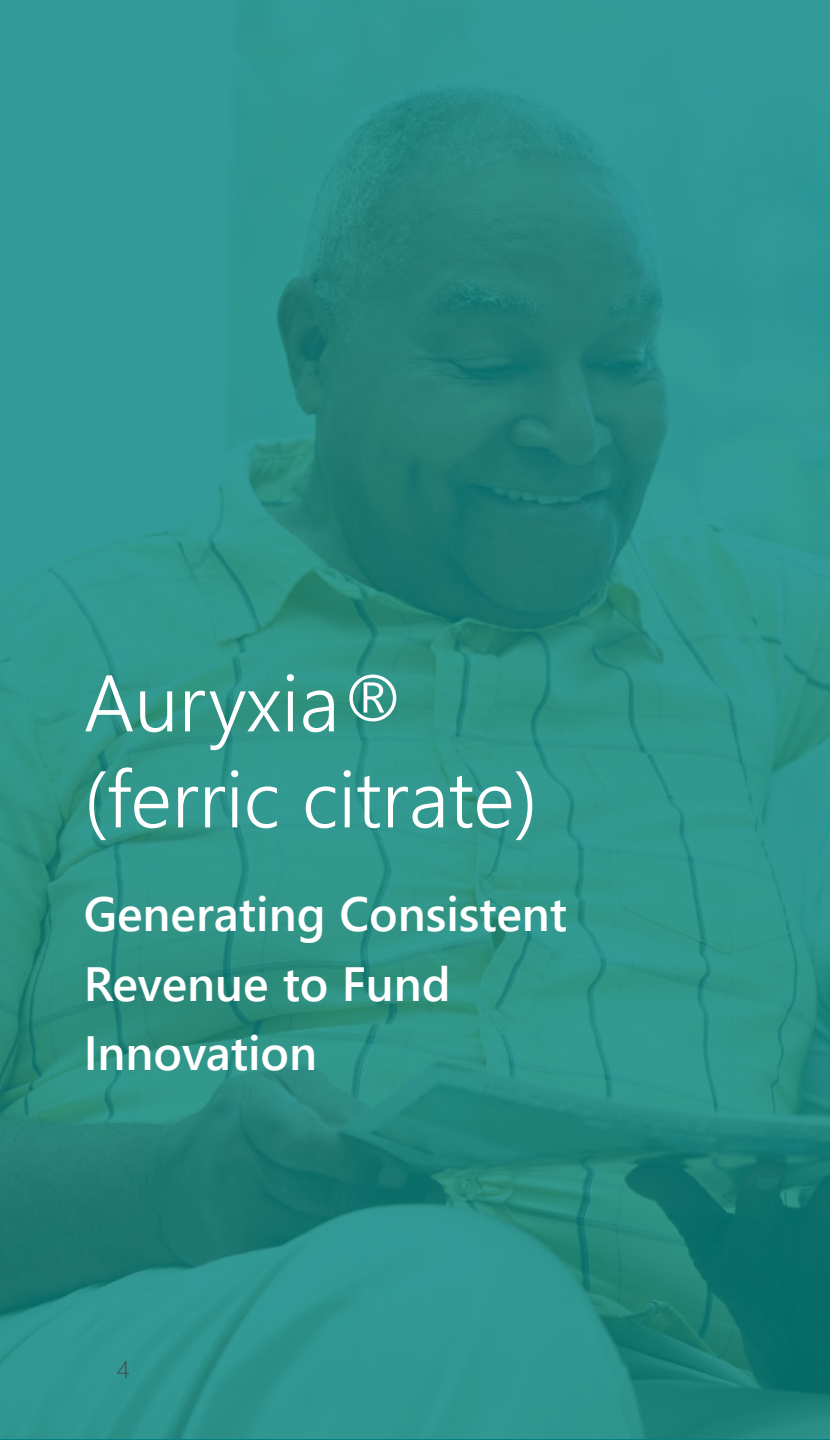
$1B[1] U.S. opportunity in dialysis, if approved



HIF-based Pipeline

Targeting areas of **unmet need** in acute care settings

PDUFA is Prescription Drug User Fee Act



Auryxia® (ferric citrate)

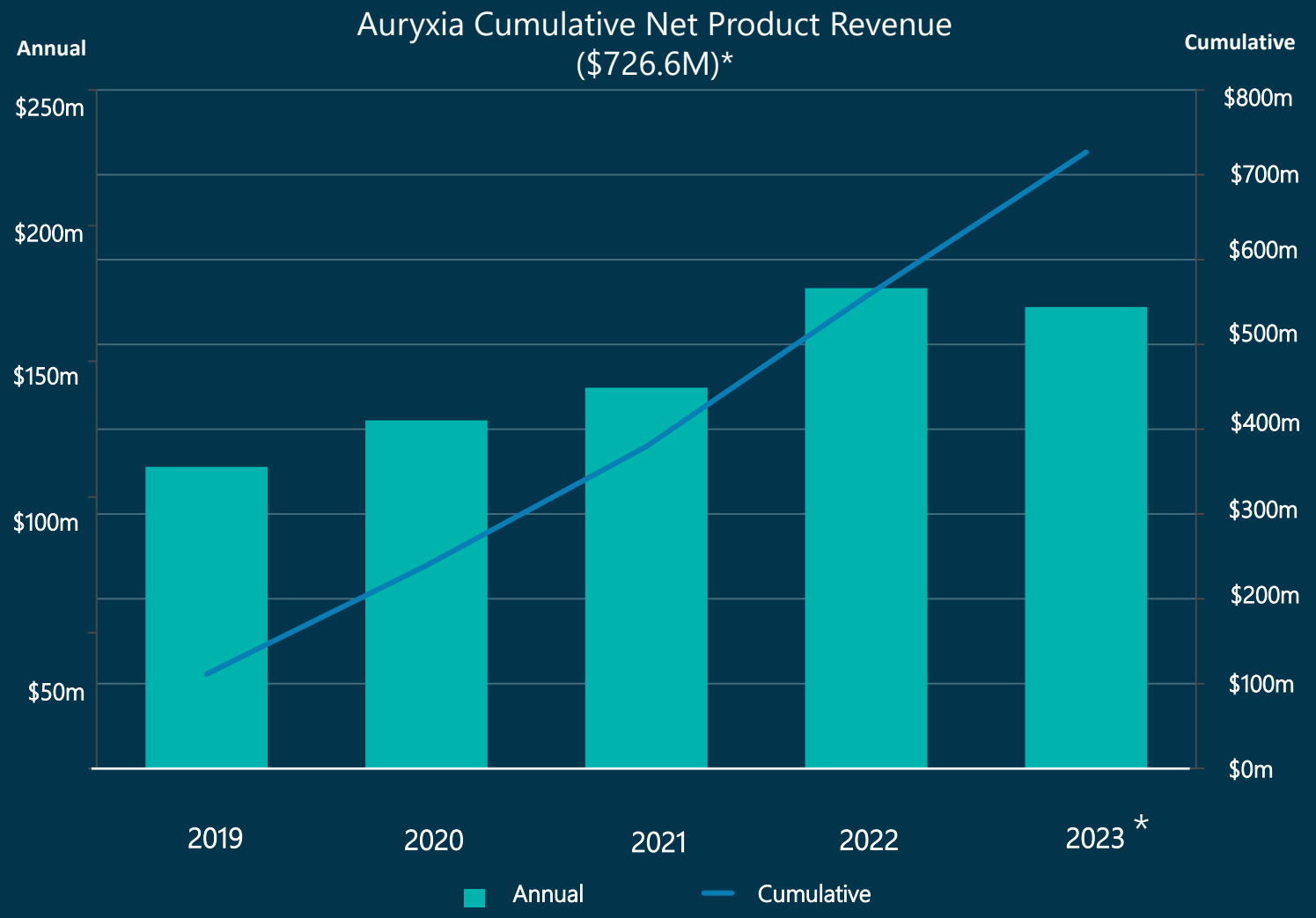
Generating Consistent Revenue to Fund Innovation

A medication FDA approved for:

Hyperphosphatemia in adult patients with chronic kidney disease (CKD) on dialysis (2014)

Iron deficiency anemia in adult patients with CKD not on dialysis (2017)

Auryxia Revenue Funds Innovation



Auryxia will continue to contribute meaningful near-term cash to business

- Expect revenue growth in 2024
- March 2025 loss of exclusivity
- Potential revenue upside in 2025 and 2026 due to phosphate binders being added to the bundle and eligible for Transitional Drug Add-on Payment Adjustment (TDAPA)

*Auryxia net product revenue for 2023 and cumulative are preliminary and unaudited

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Vadadustat*

Oral HIF prolyl-hydroxylase inhibitor (PHI) to treat anemia due to CKD

Unlocking the Power of the HIF Pathway

In low-oxygen environments, the body produces endogenous erythropoietin (EPO) and promotes iron utilization via the HIF pathway.

Leveraging HIF stabilization for anemia management enables a potential new standard of care

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Vadadustat as a treatment for anemia for adult dialysis dependent chronic kidney patients

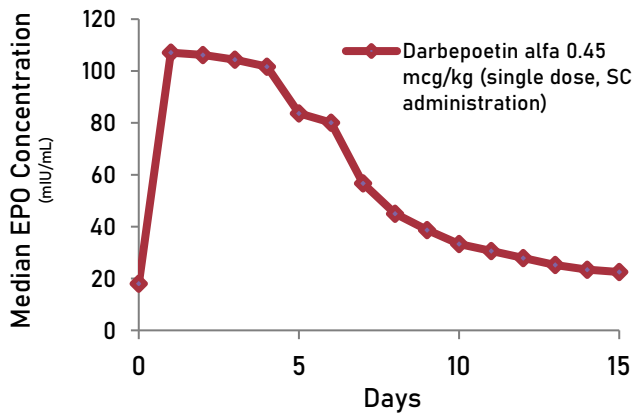
Approved for use in 36 countries
U.S. PDUFA date is March 27, 2024

*Vadadustat is not approved by the FDA.

Akebia THERAPEUTICS

Vadadustat Could Offer Providers and Patients a New Choice in Anemia Management

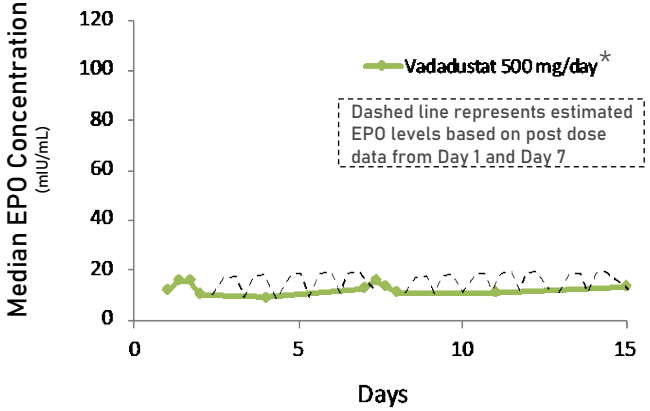
EPO vs Time with injectable ESAs[2]



EPO vs Time with vadadustat (Oral)

Phase 1 Study in Healthy Volunteers[3]

Not a head-to-head comparison



Highly differentiated new product positioned to deliver potential new oral standard of care if approved.

Clinical data showed vadadustat:

- Maintained EPO within physiologic range[3]
- Increased Hb in predictable and controlled manner[4]
- Resulted in fewer Hb excursions above target range with fewer dose adjustments than with ESAs[4]
- Provides convenient oral dosing to ease patient management

EPO is erythropoietin
Hb is hemoglobin

*Vadadustat was dosed once daily. Pre-dose EPO concentrations were evaluated on Days 1, 2, 4, 7, 8, 11, 15 and 22. Post-dose EPO concentrations were evaluated on Day 1 and Day 7 (8- and 16-hours post-dose).

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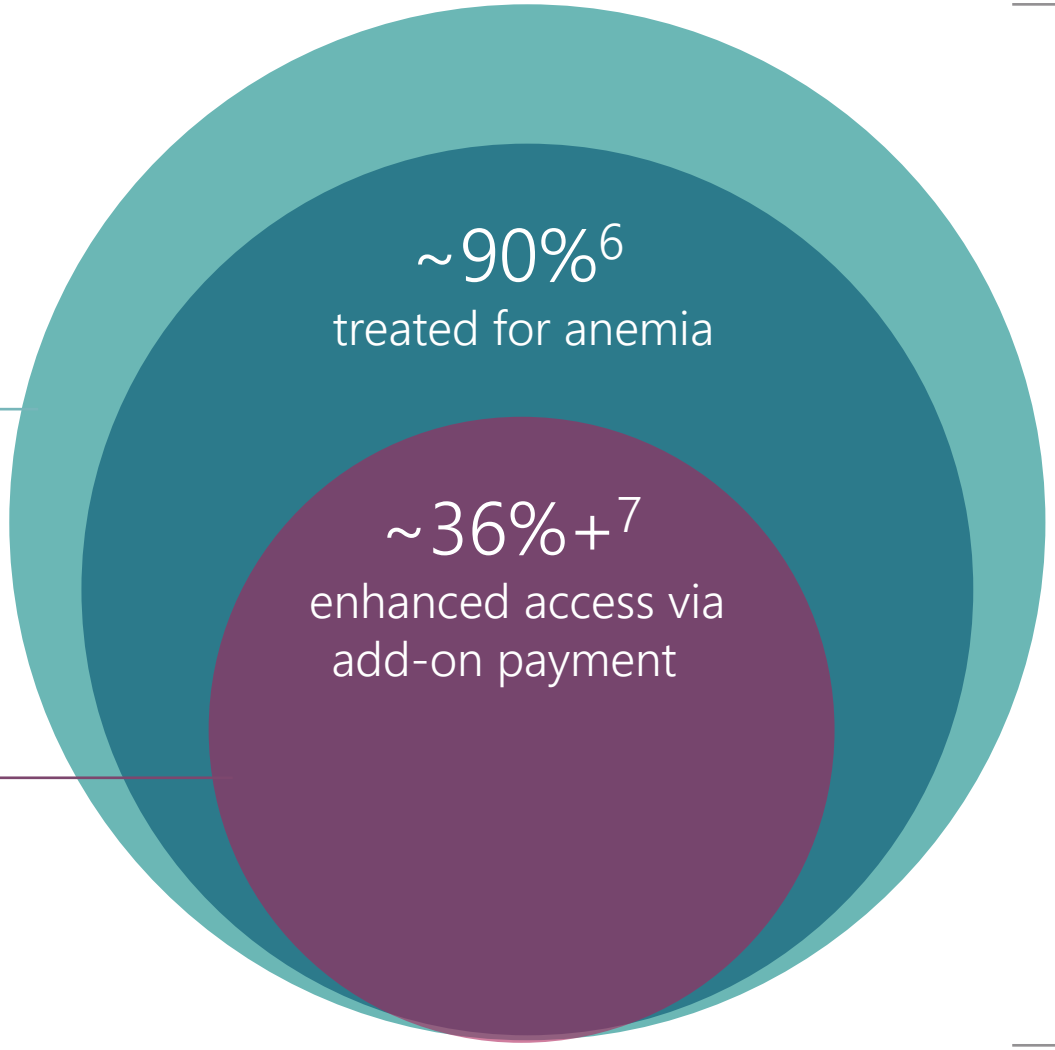
Significant U.S. Market Opportunity*

$1 Billion[1]

Payment for anemia management is included in bundled payment

A 2-year adjustment to TDAPA for medications used for dialysis patients



~558,000 CKD Patients on Dialysis[5]

Most patients on dialysis (Medicare and Medicare Advantage) are reimbursed through bundled payment

*If vadadustat is approved.

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Drive Toward a New Oral Standard of Care*

Opportunity to Differentiate Near Term to Drive Adoption

*If vadadustat is approved.

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Elements in Place for a Successful U.S. Launch*

U.S. PDUFA date is March 27, 2024

Expected TDAPA designation **expected 6 months** post-filing acceptance

Embedded Commercial Team

~30 key account managers supported by full operations team

Differentiated Renal Expertise

Deep leadership, Board and organizational experience and existing relationships with dialysis organizations

Commercial Partnership

CSL Vifor partnership provides potential access to up to 60% of market

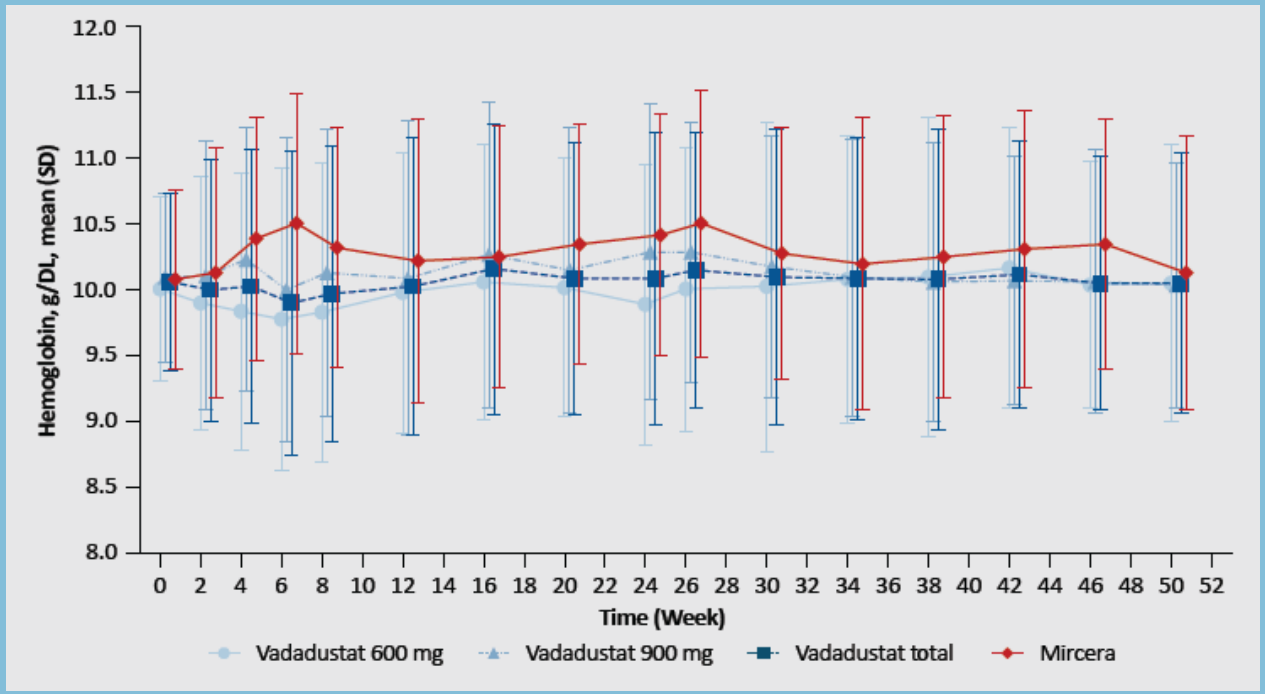
Supply Chain Readiness

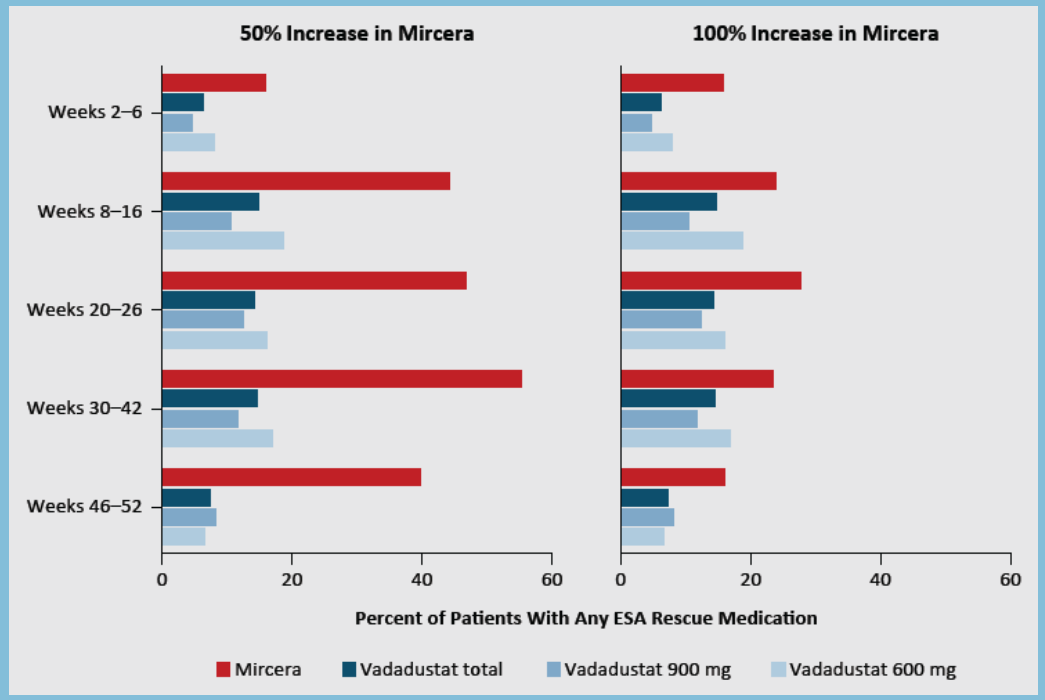
Adequate product manufactured and expected to supply launch

* If vadadustat is approved

Alternative Dosing Regimen

FOCUS Study: Safety and Efficacy of Vadadustat Thrice Weekly in Dialysis Patients with Anemia Due to Chronic Kidney Disease





- Vadadustat total (600mg and 900mg groups combined) was noninferior to Mircera for mean change in Hb from baseline to the primary evaluation period
- Vadadustat at 900 mg effectively maintained Hb levels above 10.0 g/dL for 52 weeks, while the vadadustat 600 mg group experienced a dip in Hb until Week 6, necessitating early dose increase in some patients

Post-Approval Label Expansion Opportunity

International Market Collaborations Provide Additional Upside

- Germany-based pharmaceutical company with extensive expertise in nephrology and dialysis
- Exclusive license agreement with Medice granting rights to market and sell Vafseo in European Economic Area, U.K., Switzerland and Australia
- At least 325,000 dialysis patients across Europe are currently treated for anemia due to CKD[11]
- Launch expected in first half 2024

- MTPC has exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries
- Vadadustat is approved for non-dialysis and dialysis adult patients in Japan and is marketed by MTPC under the trade name VAFSEO®

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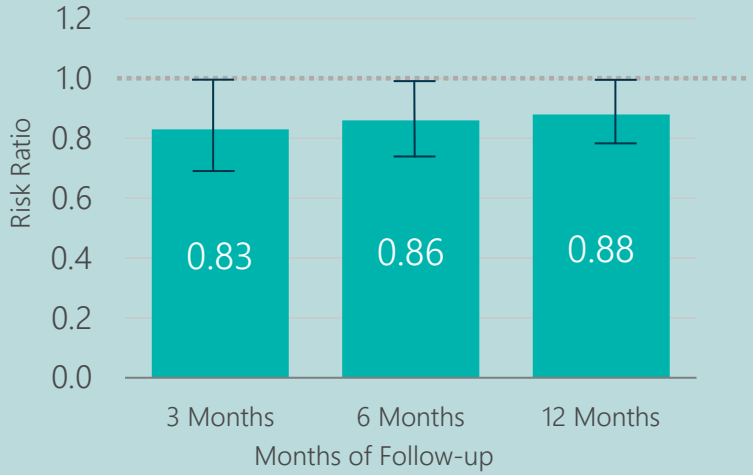
Non-Dialysis Dependent Patients

Anemia May Not Be Optimally Managed in Patients Transitioning to Dialysis

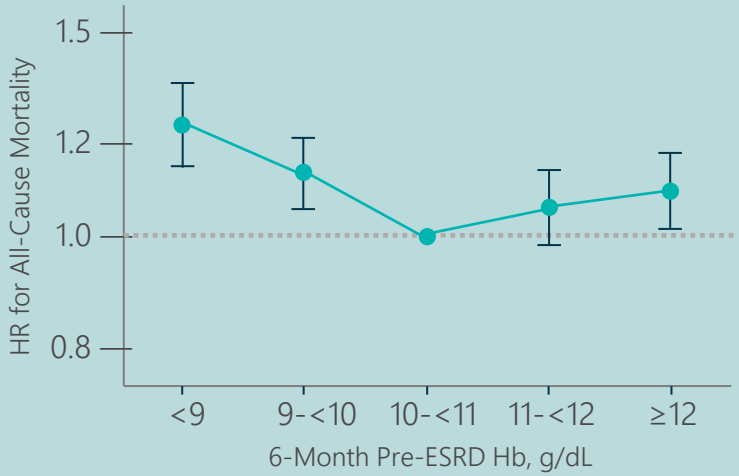
In patients with pre-hemodialysis Hb <9.0 g/dL (n=4855), 73.4% did not receive ESA pre-HD[12]

All-cause Mortality Risk in Patients With Pre-HD Hb ≥9.0 g/dL (n=3662) vs <9.0 g/dL (n=4461)[13]



- All-cause mortality risk was lower in patients with pre-HD Hb ≥9.0 g/dL vs <9.0 g/dL[13]
- Post-HD mean Hb levels were similar between patient groups[13]

Association of 6-Month Pre-ESRD Hb Levels With 12-month Post-ESRD All-cause Mortality (n=31,472)[14]



- All-cause mortality rate was higher in patients with Hb <10 g/dL vs Hb 10-<11 g/dL pre-ESRD[14]
- All Hb groups were corrected toward 11-12 g/dL within the first few months post-ESRD[14]

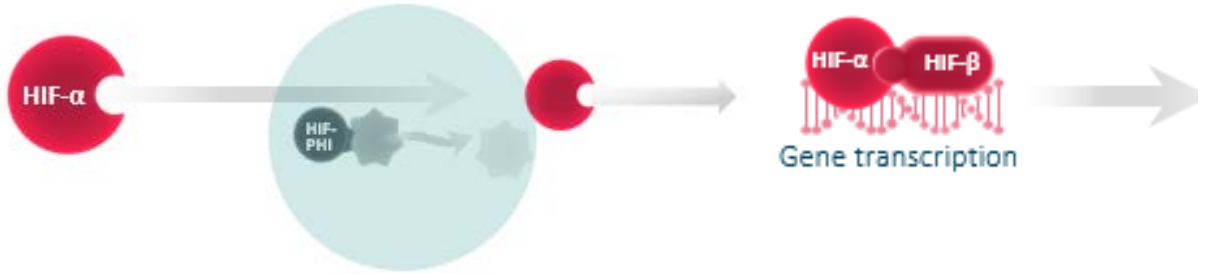
Potential to more than double patient population[14]

Post-Approval Label Expansion Opportunity

Novel HIF-Based Compounds

Acute care asset to enter clinic as early as 2025

HIF Stabilization in Acute Care Indications



- Angiogenesis
- Cell survival
- Glycolysis
- Gluconeogenesis
- Anti-inflammation

Pipeline targeting areas of high unmet need in acute care settings

AKB-9090
Acute Care Molecule

- Acute Kidney Injury (AKI)
- Acute Respiratory Distress Syndrome (ARDS)
- Other potential indications

AKB-10108
NICU Indication

- Retinopathy of Prematurity (ROP)
- Bronchopulmonary dysplasia (BPD)

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Acute Kidney Injury (AKI)

AKI is a sudden decline in the ability of kidneys to work and perform their normal functions.

- AKI occurs in 20-30% of ~2 million patients that undergo cardiac surgeries annually[15]
- No current treatments available for cardiovascular surgery-related associated AKI

The case for HIF-stabilization

Stabilization of HIF by prolyl hydroxylase inhibition (PHI) leads to the release of erythropoietin, a shift in anaerobic metabolism and decreased inflammatory responses that collectively lessen renal ischemia-reperfusion injury and ameliorate the decline in renal function.

Akebia has identified a novel HIF-PHI that is highly active in lessening the severity of AKI in an animal model of ischemia-reperfusion injury.

- **Plan to start a Phase 1 trial of AKB-9090 in AKI in 2025**

Acute Respiratory Distress Syndrome (ARDS)

ARDS is a life-threatening lung injury that results in low blood oxygen levels and difficulty breathing most commonly due to pneumonia, aspiration, or sepsis.

- ARDS caused 40% mortality in approximately 200,000 cases in the U.S. annually[16]
- No current treatments available for ARDS except for supportive care

The case for HIF-stabilization

Stabilization of HIF by prolyl hydroxylase inhibition leads to release of erythropoietin, increased extracellular adenosine signaling, increased glycolytic activity and decreased inflammation in lung epithelial cells that promote resolution of the lung injury.

Vadadustat lessened the severity of COVID-19 pneumonia in a clinical trial (NCT04478071) and improved outcomes in animal models of acute lung injury (ALI). Akebia has identified novel HIF-PHIs that are active in lessening the severity of ALI in an animal model.

- **Plan to start a Phase 2 trial with vadadustat in 2024 to validate this therapeutic approach**

Retinopathy of Prematurity (ROP)

The leading cause of blindness in preterm infants in the world that occurs due to abnormal blood vessel growth in the retina. ROP is caused by the high oxygen therapy used to treat preterm babies.

- ~100,000 new cases of infant blindness worldwide due to ROP[17]
- Targeting "prevention" indication for all low-birth-weigh (<1500 gm) preterm infants exposed to oxygen therapy

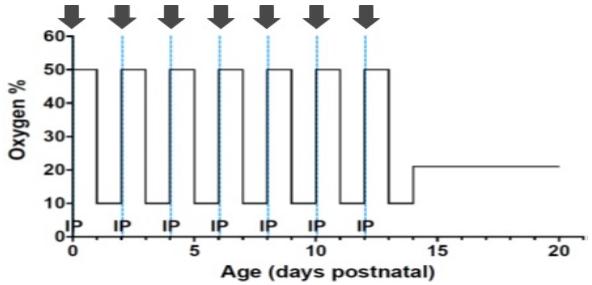
The case for HIF-stabilization

Hyperoxia can induce HIF1a degradation and prevent normal retinal development. HIF-PHIs can protect the retina by stabilizing HIF1a during hyperoxia, allowing normal retinal development and preventing aberrant neo-vascularization that can lead to scarring, retinal detachment, and blindness.

- **Continue pre-clinical development of AKB-10108 in 2024**

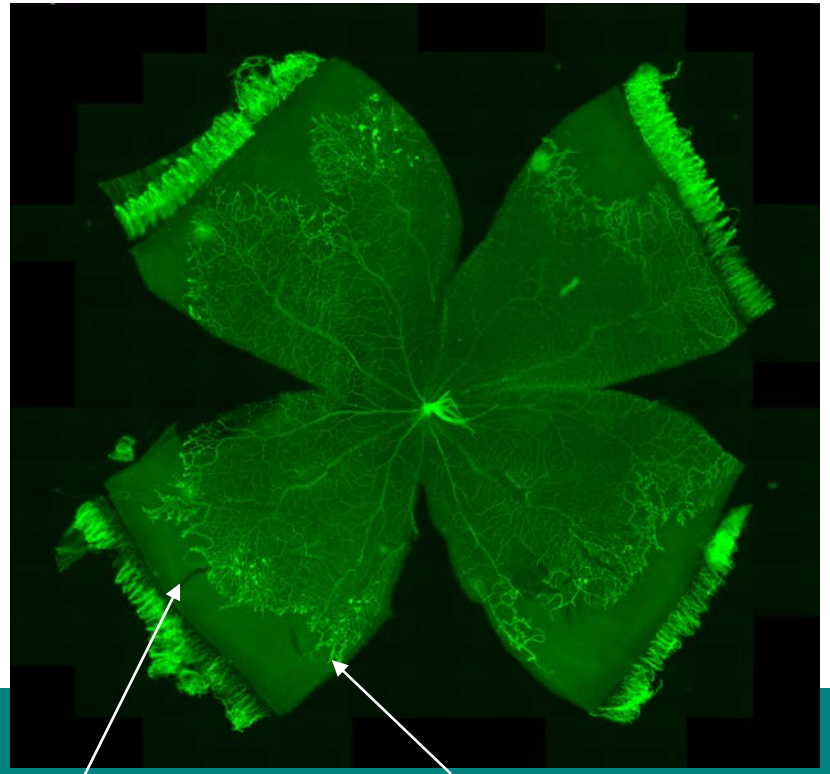
AKB-10108 Promoted Retinal Growth and Prevented Neovascularization*

Rat oxygen-induced retinopathy model



In mouse and rat models of ROP, AKB-10108 demonstrated a statistically significant, >50% reduction in retinal vaso-obliteration under hyperoxic conditions, as well as a statistically significant, >50% reduction in retinal neovascularization after returning to normal oxygen levels.

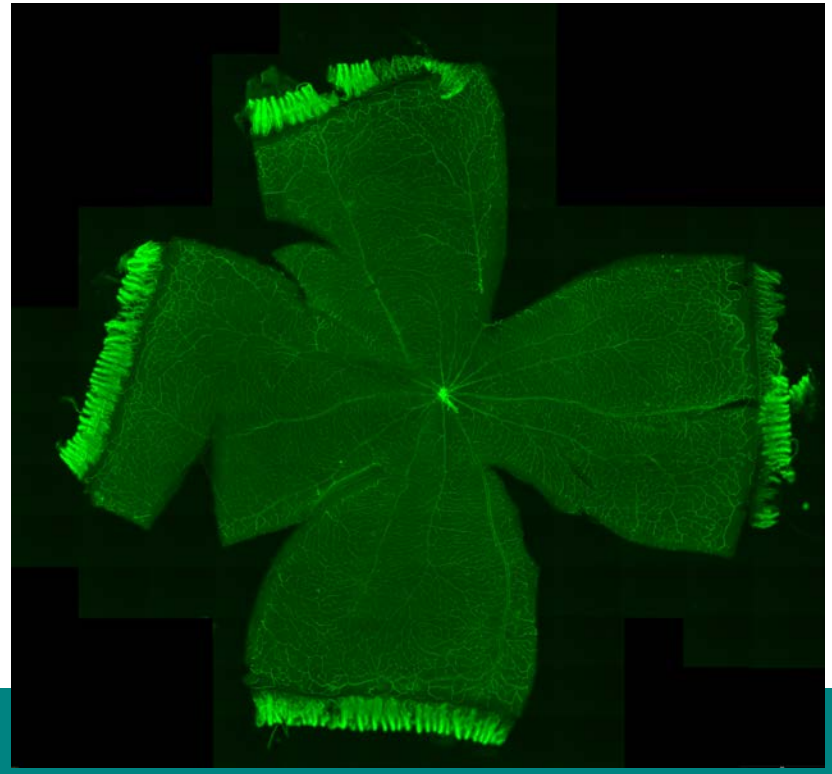
Vehicle Control



Peripheral avascular retina

Neo-vascularization

AKB-10108



*In preclinical studies

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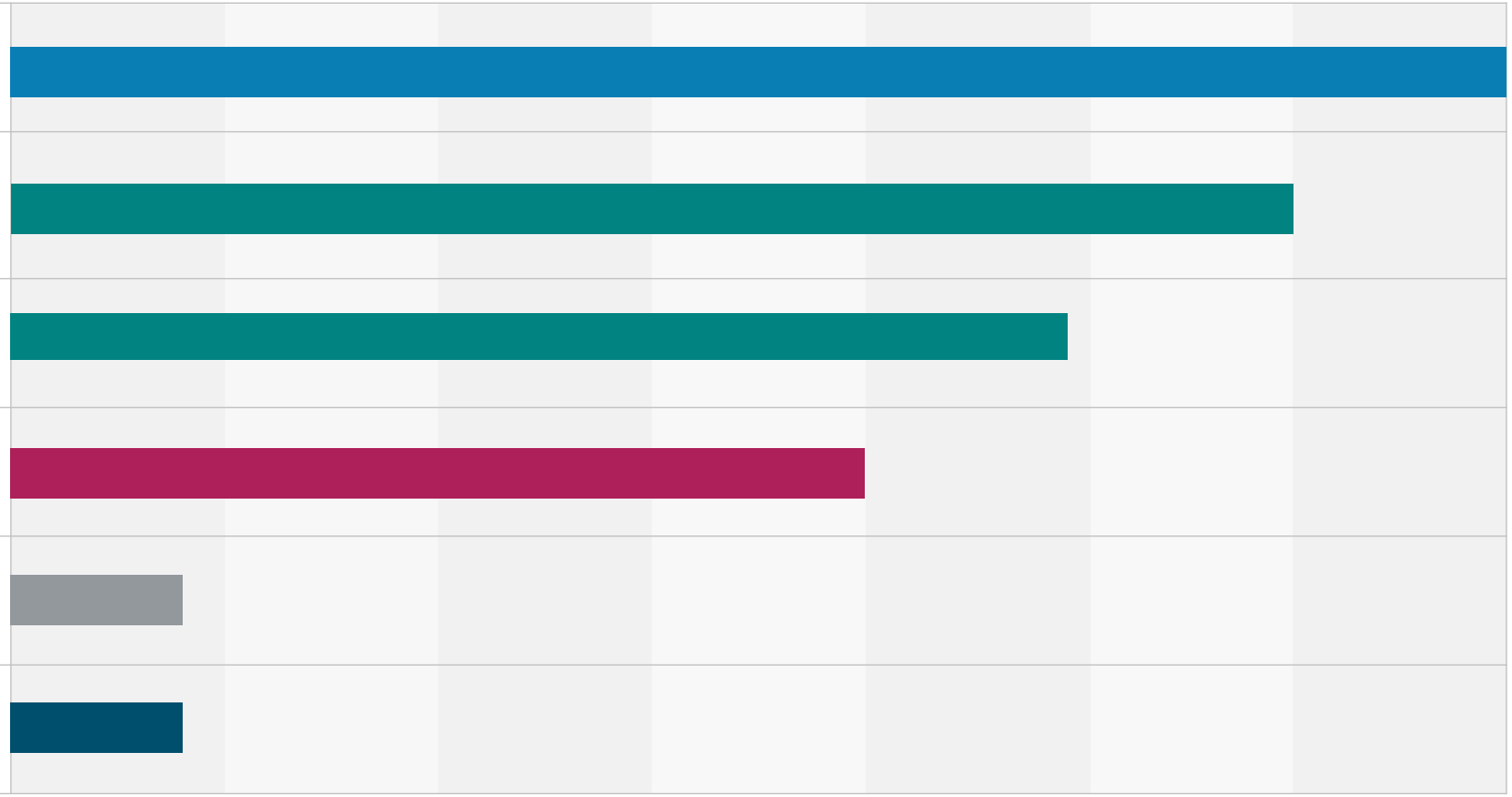
HIF Pipeline

	Indication	Region	Discovery	Phase 1	Phase 2	Phase 3	In Regulatory Review Process	Approved	In-Market
Vafseo	Anemia DD-CKD Anemia NDD-CKD	Japan[i]							
Vafseo	Anemia DD-CKD	EU,U.K., Switzerland Australia[ii] Taiwan, Korea[iii]							
Vadadustat	Anemia DD-CKD	United States							
Vadadustat	Anemia NDD-CKD	Global[iv]							
AKB-9090	AKI, ARDS	Global							
AKB-10108	ROP	Global							



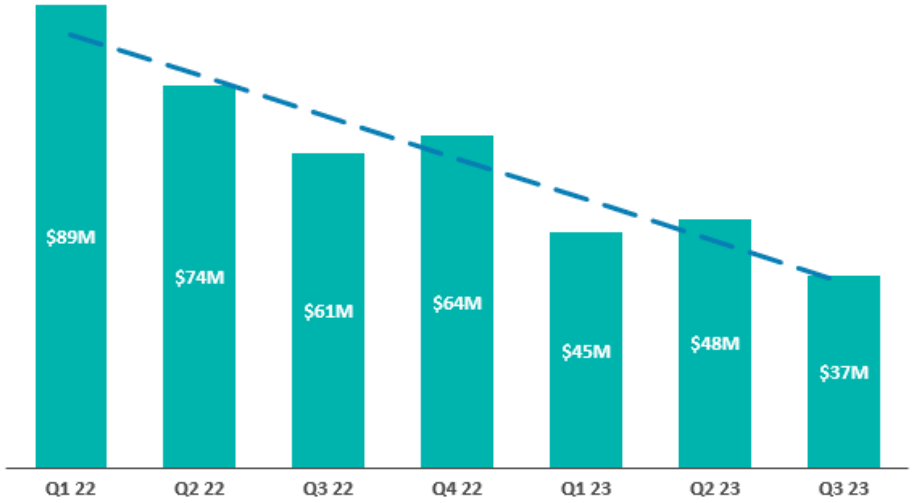
[i]Marketed by MTPC [ii]To be marketed by Medice [iii]To be marketed by MTPC [iv]MTPC and Medice have certain rights in their territories

Financial Outlook: Path to Expected Profitability

Product Revenue Growth

Auryxia 2023 preliminary unaudited net product revenue of $170.0-$171.0 million with potential for growth in 2024

Reduced Operating Expenses



Strengthening Balance Sheet

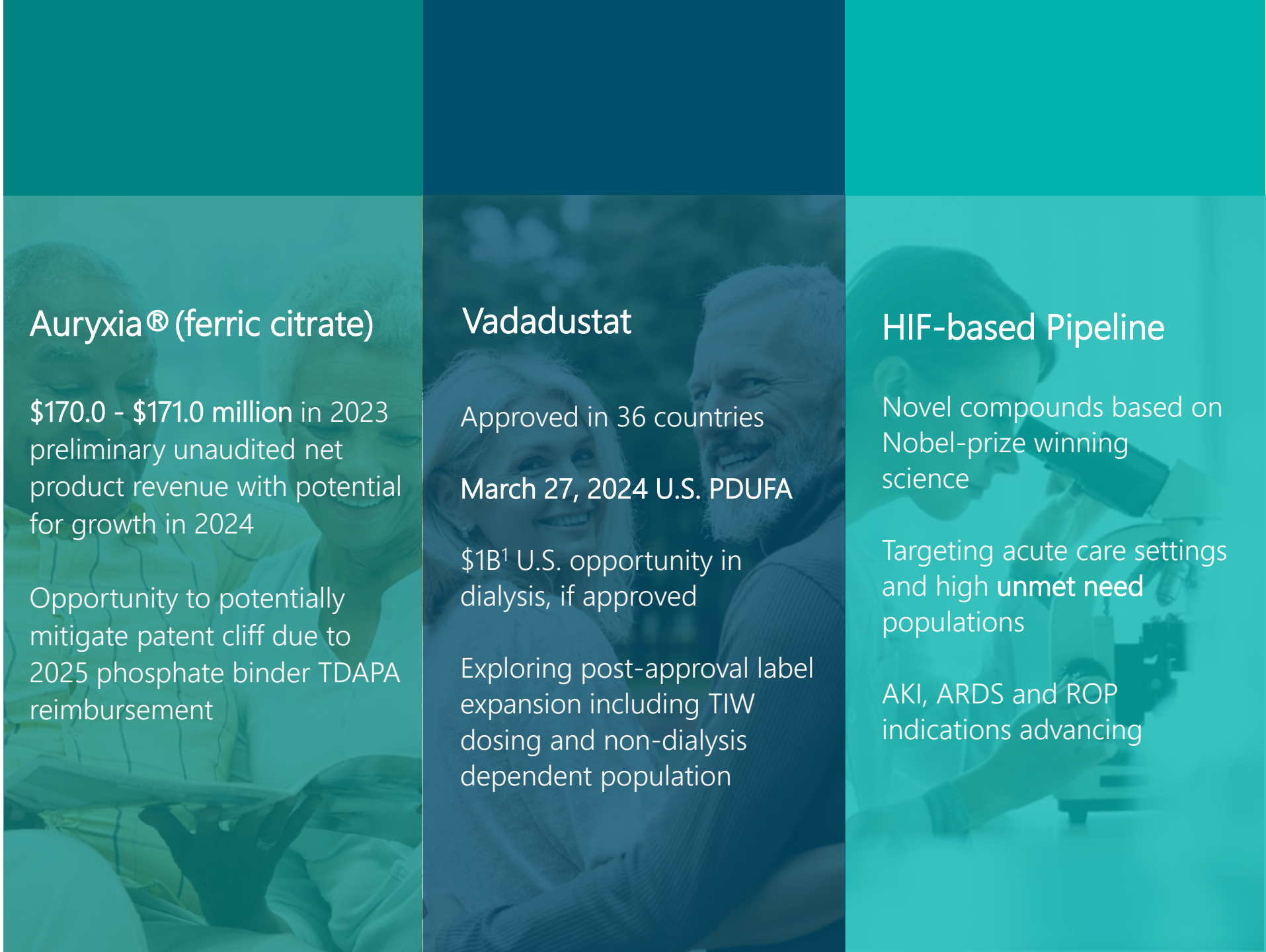
Amendment in October 2023 provides extension of maturity date through March 2025 and deferral of principal payments through October 2024 on the principal balance of $35.0 million

Continued financial discipline with improved operating margins and anticipated revenue from Auryxia are expected to provide a foundation to maximize value for vadadustat*.

*If vadadustat is approved.

Akebia THERAPEUTICS

Built on foundation of scientific expertise, financial discipline and operational effectiveness



Auryxia® (ferric citrate)

$170.0 - $171.0 million in 2023 preliminary unaudited net product revenue with potential for growth in 2024

Opportunity to potentially mitigate patent cliff due to 2025 phosphate binder TDAPA reimbursement

Vadadustat

Approved in 36 countries

March 27, 2024 U.S. PDUFA

$1B[1] U.S. opportunity in dialysis, if approved

Exploring post-approval label expansion including TIW dosing and non-dialysis dependent population

HIF-based Pipeline

Novel compounds based on Nobel-prize winning science

Targeting acute care settings and high **unmet need** populations

AKI, ARDS and ROP indications advancing

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SOURCES

[1]USRDS(https://usrds-adr.niddk.nih.gov/2022/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities);DOPPS (https://www.dopps.org/DPM/DPMSlideBrowser.aspx); Based on internal estimates and industry reports estimating ESA pricing

[2]Doshi S et al. Journal of Clinical Pharmacology, 2010;50:75S-90S. Original figure redrawn to depict darbepoetin alfa serum concentration (ng/mL/(mcg/kg)) converted to mU/mL. Data from 6 clinical studies conducted with extensive PK sampling in CKD patients following subcutaneous (SC) administration of a single dose or first dose of a monthly dosing regimen ranging from 0.4-0.6mcg/kg, dose normalized to 0.45 mcg/kg.

[3]Akebia Therapeutics, Inc. Data on File (2010). Data from Phase 1 study in healthy volunteers with vadadustat once daily dosing. Pre-dose EPO concentrations evaluated on Days 1, 2, 4, 7, 8, 11, 15 and 22. Post-dose data to assess acute rise in EPO following vadadustat dosing completed on Day 1 and Day 7 (8 and 16 hours post-dose). Dashed line represents estimated EPO levels based on post-dose data from Day 1 and Day

[4]Data from: Akebia's global INNO2VATE program which included two separate Phase 3 studies (Correction/Conversion and Conversion), and collectively enrolled 3,923 adult patients on dialysis with anemia due to CKD.

[5]United States Renal Data System. 2022 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2022

[6]Dopps.org: ESA use, last 3 months;

[7]Based on FMC patients' coverage as reported by FMC on Q4 2022 Earnings Call, Transcript and Akebia internal calculations

[8]FMC Capital Markets Day 2023 presentation, DaVita 2022 Annual Report and Akebia internal calculations

[9]DOPPS.org: Weekly IV epoetin dose received (30 day average)

[10]U.S. Department of Health and Human Services, "Advancing Kidney Health"

[11]EU5 for dialysis dependent patient population; CVRG CKD (2016-2025) & DRG (2018); Spherix RealWorld Dynamix, 2022

[12]Retrospective analysis of 20,454 patients who initiated HD from the 2012-2013 USRDS ESRD Database and CROWNWeb. Pre-HD ESA use is defined by data from Medicare Parts A and B claims, Medicare Part D claims, or the ESRD Medical Evidence Report. Post-HD ESA use was determined from ESRD monthly dialysis claims; .; Wetmore JB, et al. PLoS One. 2018;13(9):e0203767

[13]Retrospective analysis of 20,454 patients who initiated HD from the 2012-2013 USRDS ESRD Database and CROWNWeb. HR adjusted for demographic factors, primary cause of ESRD, duration of pre-dialysis nephrology care, and comorbid conditions. Patients with pre-HD Hb ≥9.0 g/dL received ESA pre- and post-HD; those with pre-HD Hb <9.0 g/dL received ESA post-HD and had increased Hb.; Wetmore JB, et al. PLoS One. 2018;13(9):e0203767

[14]Analysis of 31,472 veterans from the USRDS Special Study Center Transition of Care in CKD who transitioned to ESRD between October 2007 and March 2014. HR adjusted for case-mix and MICS.; Kleine CE, et al. Am J Nephrol. 2018;47:333-342

[15]Cheruku, SR, et al., Acute Kidney Injury after Cardiac Surgery: Prediction, Prevention, and Management, Anesthesiology. (2023)

[16]Matthay, M.A., Zemans, R.L. The Acute Respiratory Distress Syndrome: Pathogenesis and Treatment, (2011)

[17]Xanthi I. Couroucli, X.I. Oxidative stress in the retina: Implications for Retinopathy of Prematurity (2018)

Akebia THERAPEUTICS