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

Delivering Innovation for Patients with Chronic Kidney Disease (CKD)

June 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; Akebia's ability to enable a successful commercial launch of, and maximize the value of, Vafseo®, including statements regarding Vafseo'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; Akebia's expectations of the timing of Transitional Drug Add-on Payment Adjustment ("TDAPA') filing and designation and product availability of Vafseo the potential benefits related to TDAPA designation, and that the expectation of aligning product availability with TDAPA designation will maximize the revenue opportunity; Akebia's expectations regarding the spend needed to support such commercial launch, including the availability of sufficient supply; Akebia's plans with respect to Vafseo label expansion opportunities, including the potential market potential thereof and the expected timing of feedback from the FDA; statements regarding the beliefs about the benefits that Vafseo 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 revenue is expected to grow in 2024 and contribute meaningful near-term cash to business; Akebia's plans with respect to Vafseo as a treatment of anemia due to chronic kidney disease in patients on dialysis in the U.S., including statements regarding potential revenue from Vafseo in the U.S. and the potential market opportunity and near-term target patient populations; Akebia's ability to achieve anticipated catalysts in the timeframe expected, or at all; Akebia's early Hypoxia-Inducible Fact (HIF) research and the potential therapeutic applications of the hypoxia inducible factor pathway, including Akebia's ability to execute on its development plans and expectations on the timing of a clinical study; and Akebia's goals, objectives and expectations with respect to its operating plan, expenses, cash resources and sources of funding for its cash runway, including that its current cash position is anticipated to fund its operations for at least two years, and that ongoing financial discipline with improved operating margins and anticipated revenue from Auryxia are expected to provide a foundation to maximize value for Vafseo.

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: whether Vafseo will be commercially available when expected; the potential demand and market potential and acceptance of, as well as coverage and reimbursement related to, Auryxia and Vafseo, including estimates regarding the potential market opportunity; the competitive landscape for Auryxia and Vafseo, including potential generic entrants for Auryxia; 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; the potential therapeutic benefits, safety profile, and effectiveness of Vafseo; the results of preclinical and clinical research; manufacturing, supply chain and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences; Akebia's compliance with the covenants under its outstanding loan agreement; 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 March 31, 2024, 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 strength and operational effectiveness

Vafseo® (vadadustat) tablets

FDA approved for the treatment of anemia due to (CKD) in adults who have been receiving dialysis for at least three months

$1B[1] U.S. opportunity

Auryxia® (ferric citrate)

$170.3 million net product revenue in 2023 with growth expected in 2024

HIF-based Pipeline

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

Akebia® THERAPEUTICS

Vafseo® (vadadustat) Tablets

Overview

Vafseo® (vadadustat) Tablets

Akebia® THERAPEUTICS

Indication

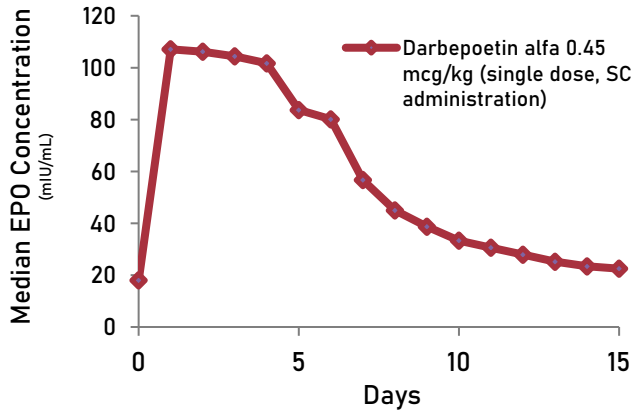
Vafseo® (vadadustat) Tablets for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months

- Hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor based on Nobel-prize winning science
- Once-daily oral tablet
- Activates the physiologic response to hypoxia to stimulate endogenous production of erythropoietin to treat anemia
- Now approved in 37 countries

Click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide.

A New Choice in Anemia Management

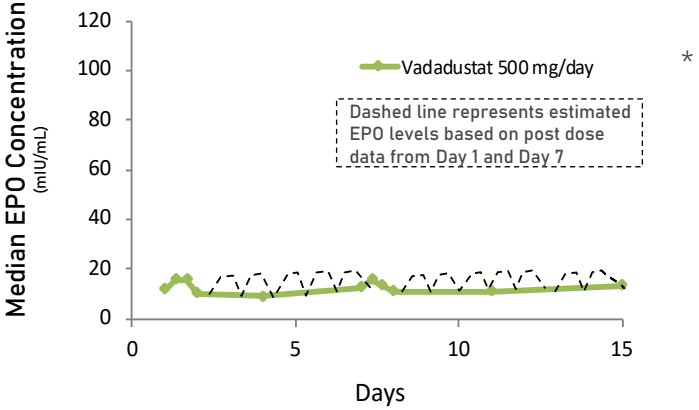
EPO vs Time with injectable ESAs[2]



EPO vs Time with vadadustat (Oral)

Phase 1 Study in Healthy Volunteers[3]

Not a head-to-head comparison



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

Clinical data showed vadadustat:

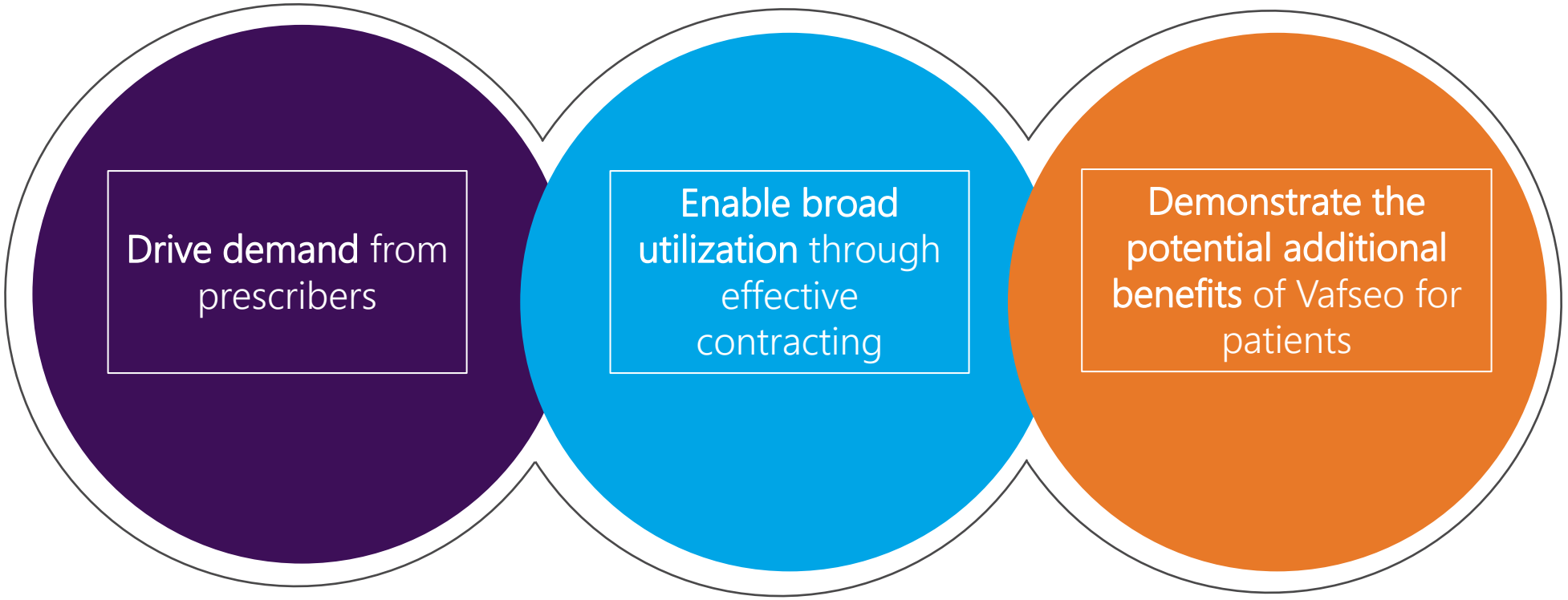
- Maintained EPO within physiologic range[3]
- Increased Hb in predictable and controlled manner[4]
- Resulted in fewer Hb excursions above target range with fewer dose adjustments than with ESAs[4]
- Provides convenient oral dosing to ease patient management

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).

Drive Toward a New Oral Standard of Care

Key Launch Initiatives through Product Availability in January 2025



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Elements in Place to Execute a Successful U.S. Launch

Embedded Commercial Team

~35 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

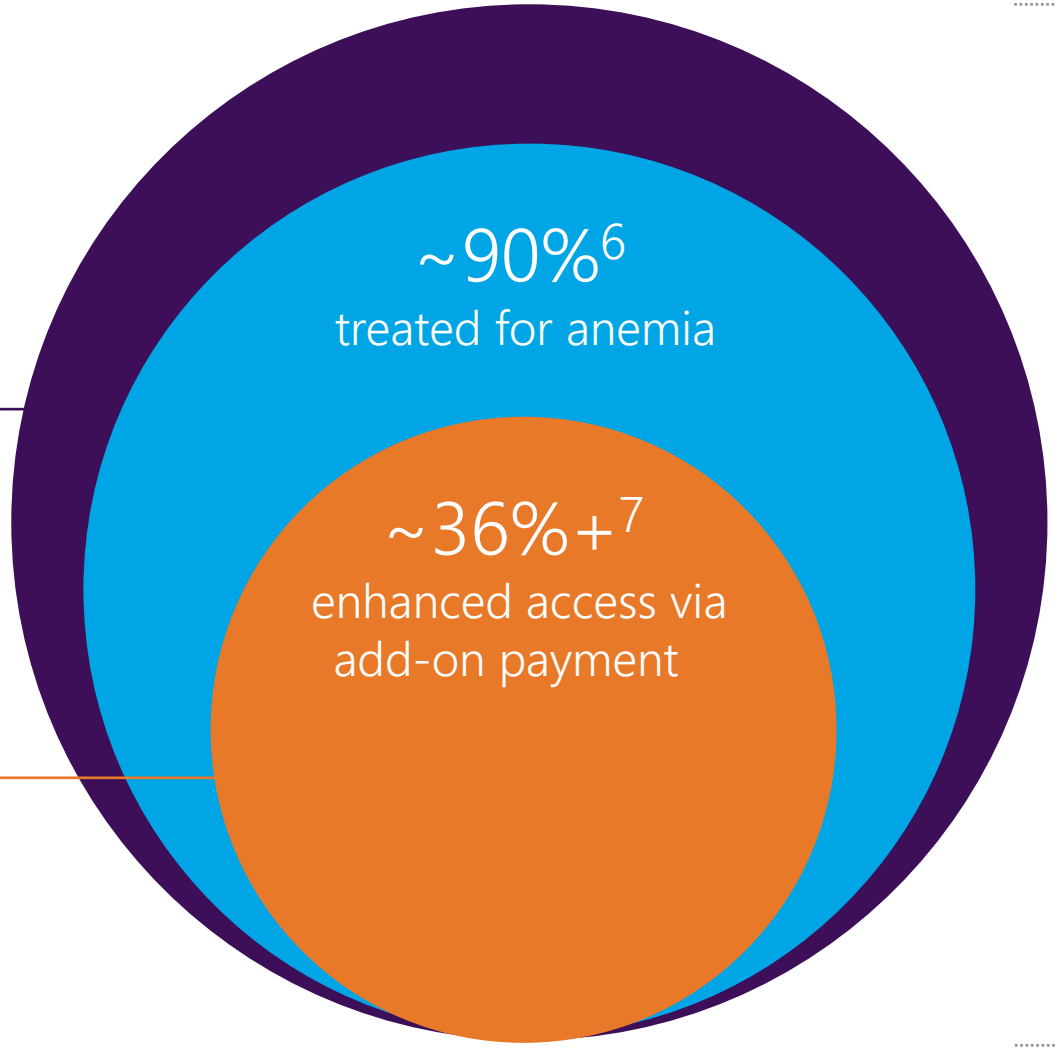
Supply Chain Readiness

Adequate product manufactured and expected to supply launch

$1 Billion[1] U.S. Market Opportunity

Payment for anemia management is included in bundled payment

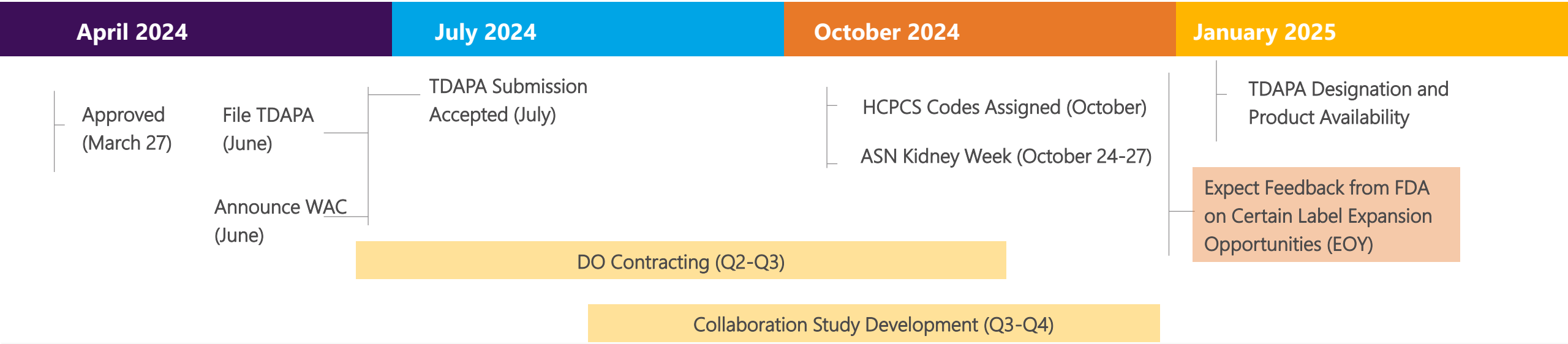
A 2-year adjustment to Transitional Drug Add-On Payment Adjustment (TDAPA) for medications used for dialysis patients



~541,000 Prevalent Dialysis CKD Patients[5]

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

Anticipated U.S. Launch Timeline



Launch Strategy and TDAPA Timing

Align product availability with TDAPA designation expected January 1, 2025, to maximize revenue opportunity

Vafseo® (vadadustat) Tablets

Akebia® THERAPEUTICS

Potential Near-Term Target Populations

>80,000
on home dialysis[8]

>150,000
patients on higher ESA doses[9]

Opportunity to Differentiate Near Term to Drive Adoption

Vafseo® (vadadustat) Tablets

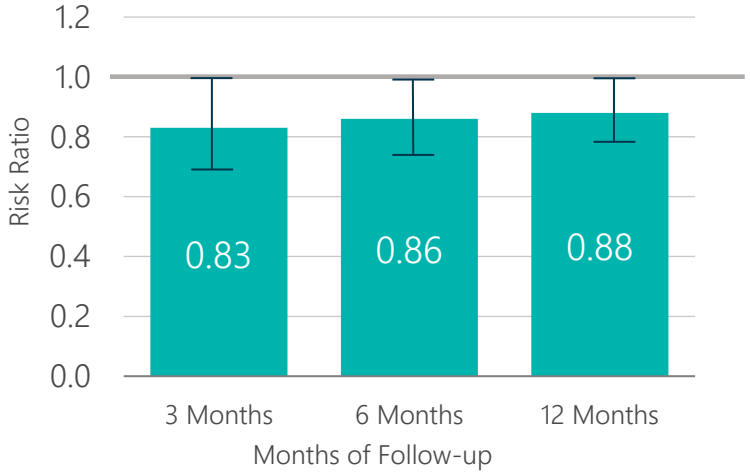
Label Expansion Opportunities

Non-Dialysis Dependent Patients

Anemia May Not Be Optimally Managed in Patients Transitioning to Dialysis

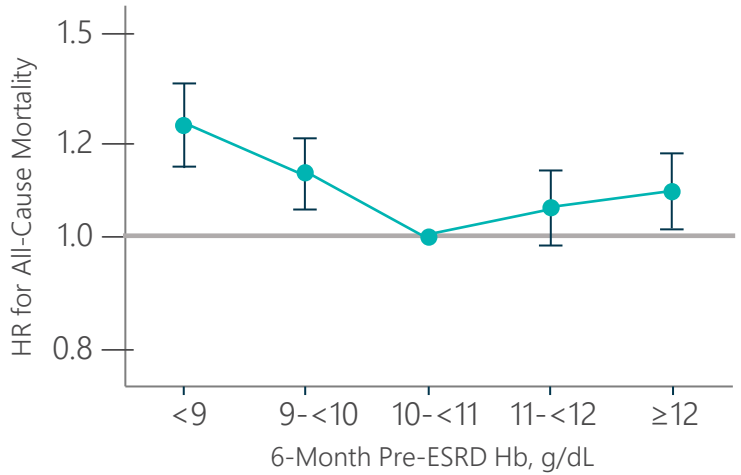
In patients with pre-hemodialysis Hb <9.0 g/dL (n=4855), 73.4% did not receive ESA pre-HD[10]

All-cause Mortality Risk in Patients With Pre-HD Hb ≥9.0 g/dL (n=3662) vs <9.0 g/dL (n=4461)[11]



- All-cause mortality risk was lower in patients with pre-HD Hb ≥9.0 g/dL vs <9.0 g/dL[11]
- Post-HD mean Hb levels were similar between patient groups[11]

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



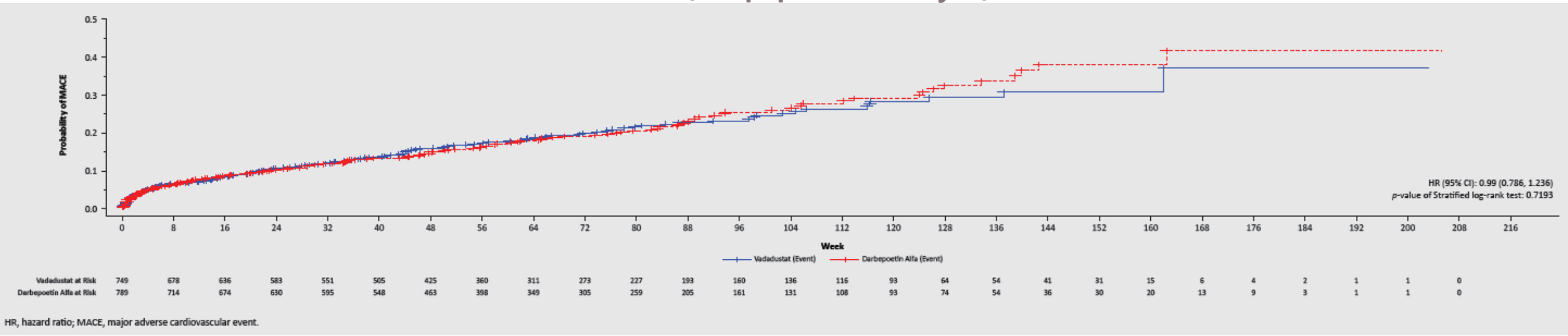
- All-cause mortality rate was higher in patients with Hb <10 g/dL vs Hb 10-<11 g/dL pre-ESRD[12]
- All Hb groups were corrected toward 11-12 g/dL within the first few months post-ESRD[12]

Label Expansion Opportunity

Incident Dialysis Patients

Studies of Cardiovascular Safety of Vadadustat Compared with Darbepoetin Alfa in Patients New to Dialysis with CKD-Related Anemia

Patients New to Dialysis from INNO$_2$VATE + PRO$_2$TECT Trials (sub population analysis)



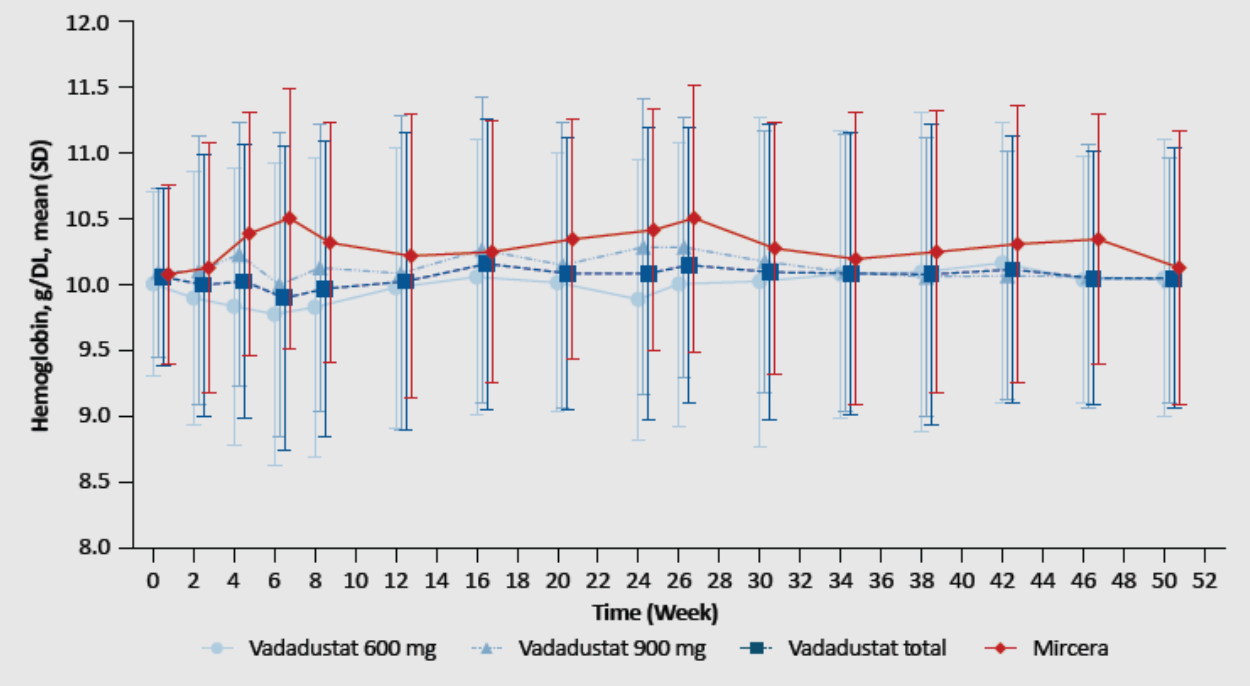
HR, hazard ratio; MACE, major adverse cardiovascular event.

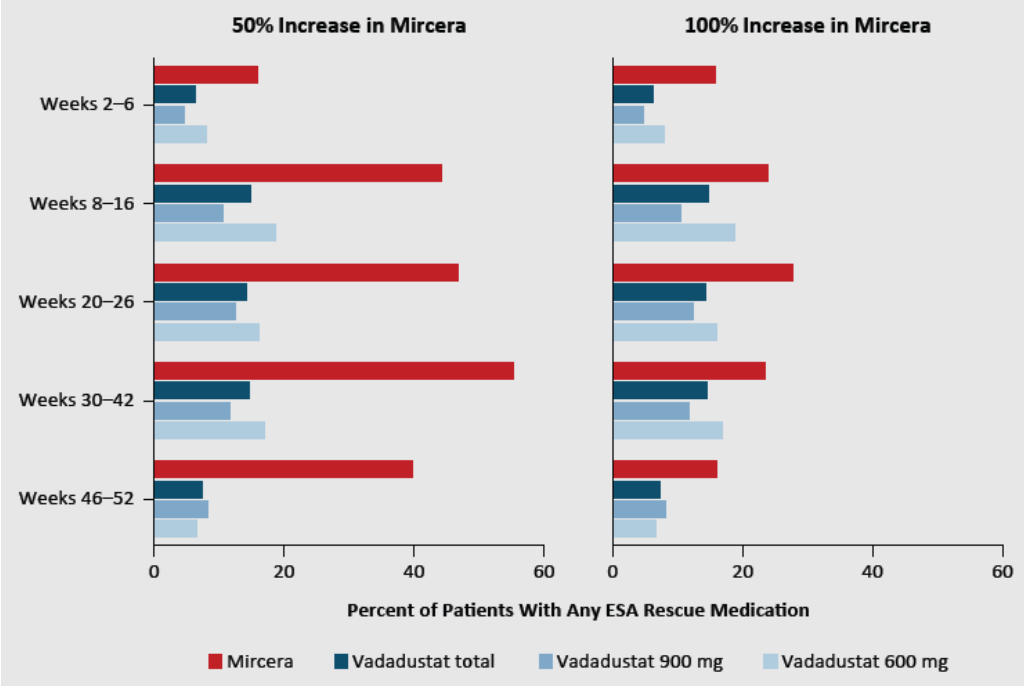
- The risk of MACE in patients new to dialysis treated with vadadustat was similar to the risk of MACE in patients new to dialysis treated with darbepoetin alfa.

Label Expansion Opportunity

Alternative Dosing Regimen

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



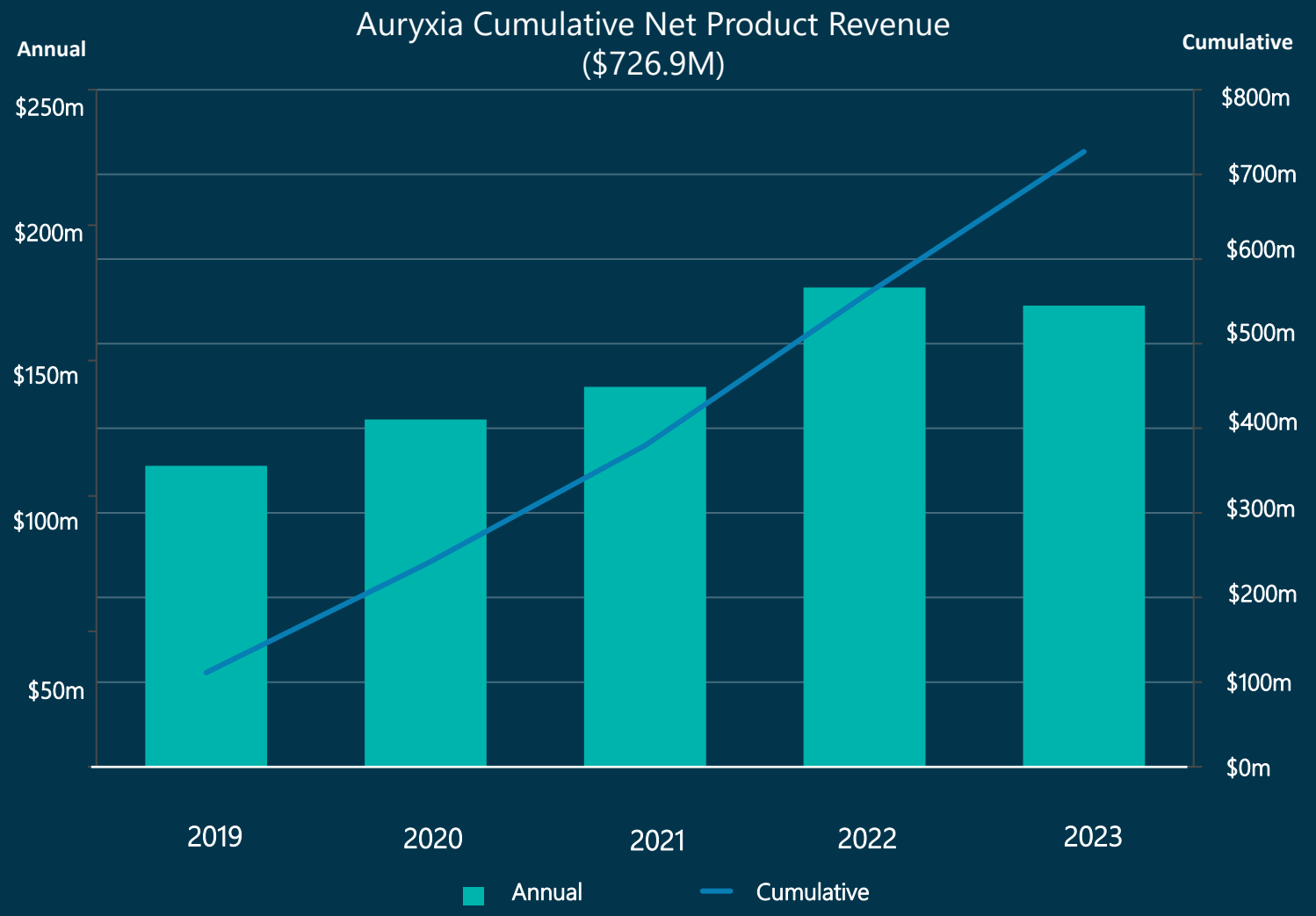


- Vadadustat total (600mg and 900mg groups combined) was noninferior to Mircera for mean change in Hb from baseline to the primary evaluation period
- Vadadustat at 900 mg maintained Hb levels above 10.0 g/dL for 52 weeks, while the vadadustat 600 mg group experienced a dip in Hb until Week 6, necessitating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

Label Expansion Opportunity

Auryxia® (ferric citrate)

Auryxia Revenue Funds Innovation



Auryxia is expected to contribute meaningful near-term cash to business

- Q1 2024 net produce revenue was $31 million.
- Expect revenue growth in 2024 with quarter revenue cadence similar to 2023
- March 2025 loss of exclusivity
- Potential revenue upside in 2025 and 2026 due to phosphate binders being added to the bundle and eligible for TDAPA

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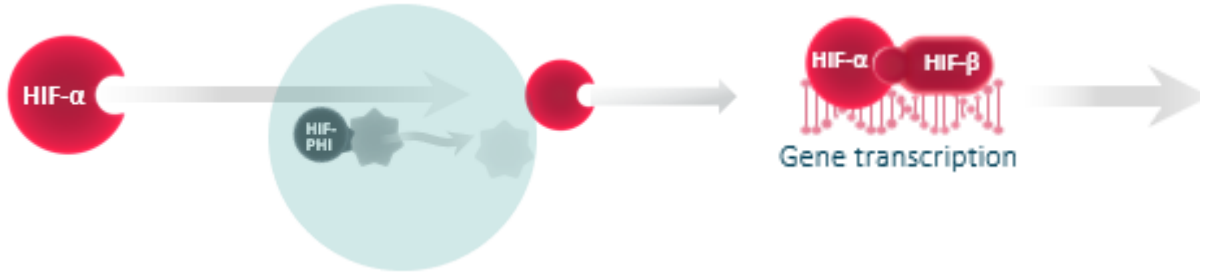
Pipeline

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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Financial Outlook

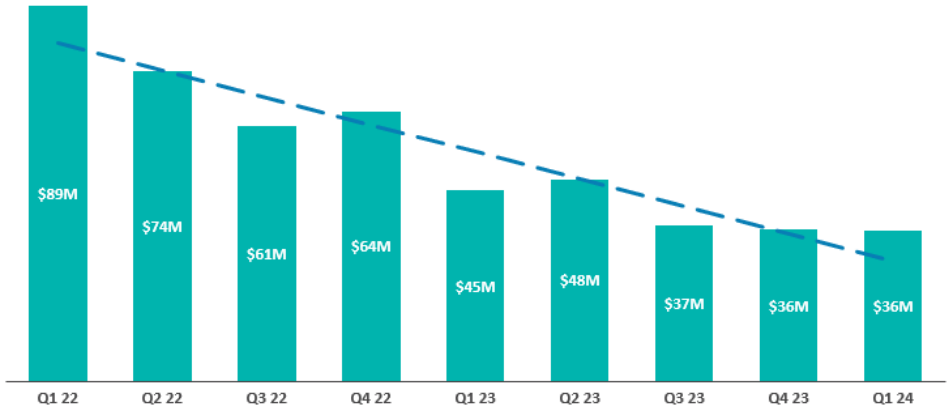
Strong Cash Position

Current Cash and Cash from Operations Anticipated to Fund Operations for at Least Two Years*

Product Revenue Growth

- Auryxia 2023 net product revenue of $170.3 million; expect growth in 2024
- Q1 2024 net product revenue was $31 million

Reduced Operating Expenses



Capital for Strategic Use

- Drew down second tranche of $55 million BlackRock debt facility and received net proceeds of $7.5 million.
- Cash and cash equivalents as of March 31, 2024, were approximately $42.0 million.

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

*As reported on May 9, 2024

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Important Safety Information

Sources

IMPORTANT SAFETY INFORMATION about VAFSEO (vadadustat) tablets

WARNING: INCREASED RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, and THROMBOSIS OF VASCULAR ACCESS.

See full prescribing information for complete boxed warning.

VAFSEO increases the risk of thrombotic vascular events, including major adverse cardiovascular events (MACE).

Targeting a hemoglobin level greater than 11 g/dL is expected to further increase the risk of death and arterial and venous thrombotic events, as occurs with erythropoietin stimulating agents (ESAs), which also increase erythropoietin levels.

No trial has identified a hemoglobin target level, dose of VAFSEO, or dosing strategy that does not increase these risks.

Use the lowest dose of VAFSEO sufficient to reduce the need for red blood cell transfusions.

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IMPORTANT SAFETY INFORMATION about VAFSEO (vadadustat) tablets (continued)

CONTRAINDICATIONS

- Known hypersensitivity to VAFSEO or any of its components
- Uncontrolled hypertension

WARNINGS AND PRECAUTIONS

- **Increased Risk of Death, Myocardial Infarction, Stroke, Venous Thromboembolism, and Thrombosis of Vascular Access**

  A rise in hemoglobin (Hb) levels greater than 1 g/dL over 2 weeks can increase these risks. Avoid use in patients with a history of myocardial infarction, cerebrovascular event, or acute coronary syndrome within the 3 months prior to starting VAFSEO. Targeting a Hb level of greater than 11g/dL is expected to further increase the risk of death and arterial and venous thrombotic events, as occurs with ESAs, which also increase erythropoietin levels. No specific Hb target level, dose of VAFSEO, or dosing strategy has been identified to avoid these risks. Use the lowest effective dose and adhere to dosing and Hb monitoring recommendations to avoid excessive erythropoiesis.

  Advise patients to seek immediate medical attention if they develop signs or symptoms of myocardial infarction, stroke, venous thromboembolism, or thrombosis of vascular access. Evaluate and manage promptly if these occur.
- **Hepatotoxicity**

  Hepatocellular injury attributed to VAFSEO was reported in less than 1% of patients, including one severe case with jaundice. All events were asymptomatic and resolved after discontinuation of VAFSEO. The time to onset was generally within the first 3 months of treatment. Elevated serum ALT, AST, and bilirubin levels were observed in 1.8%, 1.8%, and 0.3% of CKD patients treated with VAFSEO, respectively. Measure ALT, AST, and bilirubin before treatment and monthly for the first 6 months, then as clinically indicated. Discontinue VAFSEO if ALT or AST is persistently elevated or accompanied by elevated bilirubin. Not recommended in patients with cirrhosis or active, acute liver disease.
- **Hypertension**

  Worsening of hypertension was reported in 14% (9.4 per 100 person-years [PY]) of patients receiving VAFSEO and 17% (11.8 per 100 PY) of patients receiving darbepoetin alfa. Serious worsening of hypertension was reported in 2.7% (1.7 per 100 PY) of patients receiving VAFSEO and 3% (1.8 per 100 PY) of patients receiving darbepoetin alfa. Cases of hypertensive crisis including hypertensive encephalopathy and seizures have also been reported in patients receiving VAFSEO. Monitor blood pressure. Adjust anti-hypertensive therapy as needed.
- **Seizures**

  Seizures occurred in 1.6% (1.0 per 100 PY) of patients who received VAFSEO and 1.6% (1.0 per 100 PY) of patients who received darbepoetin alfa. Following initiation of VAFSEO, monitor patients closely for premonitory neurologic symptoms. Monitor for new-onset seizures, premonitory symptoms, or change in seizure frequency.

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IMPORTANT SAFETY INFORMATION about VAFSEO (vadadustat) tablets (continued)

- **Gastrointestinal Erosion**
  Gastric or esophageal erosions occurred in 6.4% (4.0 per 100 PY) of patients receiving VAFSEO and 5.3% (3.3 per 100 PY) of darbepoetin alfa-treated patients. Serious gastrointestinal (GI) erosions, including GI bleeding and the need for red blood cell transfusions were reported in 3.4% (2.1 per 100 PY) and 3.3% (2.0 per 100 PY) of those receiving VAFSEO and darbepoetin alfa, respectively. Consider the risk of GI erosion in high-risk patients, including those with a history of GI erosion, peptic ulcer disease, and tobacco or alcohol use.
  Advise patients of the signs and symptoms of erosions and GI bleeding and urge them to seek prompt medical care if present.
- **Serious Adverse Reactions in Patients with Anemia Due to Chronic Kidney Disease and Not on Dialysis**
  The safety of VAFSEO has not been established for the treatment of anemia due to CKD in adults not on dialysis and its use is not recommended in this setting. In large clinical trials in adults with anemia of CKD who were not on dialysis, an increased risk of mortality, stroke, myocardial infarction, serious acute kidney injury, serious hepatic injury, and serious GI erosions was observed in patients treated with VAFSEO compared to darbepoetin alfa.
- **Malignancy**
  VAFSEO has not been studied and is not recommended in patients with active malignancies. Malignancies were observed in 2.2% (1.3 per 100 PY) of patients treated with VAFSEO and 3.0% (1.8 per 100 PY) of patients treated with darbepoetin alfa. No evidence of increased carcinogenicity was observed in animal studies.

ADVERSE REACTIONS

- The most common adverse reactions (occurring at ≥ 10%) were hypertension and diarrhea.

DRUG INTERACTIONS

Iron supplements and iron-containing phosphate binders: Administer VAFSEO at least 1 hour before products containing iron.
Non-iron-containing phosphate binders: Administer VAFSEO at least 1 hour before or 2 hours after non-iron-containing phosphate binders.
BCRP substrates: Monitor for signs of substrate adverse reactions and consider dose reduction.
Statins: Monitor for statin-related adverse reactions. Limit the daily dose of simvastatin (20 mg) and rosuvastatin (5 mg).

USE IN SPECIFIC POPULATIONS

Pregnancy: May cause fetal harm.
Lactation: Breastfeeding not recommended until two days after the final dose.
Hepatic Impairment: Not recommended for use in patients with cirrhosis or active, acute liver disease.

Please note that this information is not comprehensive. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide.

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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]NIH. 2023 Annual report: End stage renal disease. Accessed April 24, 2024. https://usrds-adr.niddk.nih.gov/2023/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities

[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]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

[11]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

[12]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

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