Akebia Receives FDA Approval of Vafseo® (vadadustat) Tablets for the Treatment of Anemia due to Chronic Kidney Disease in Adult Patients on Dialysis

March 28, 2024

Once-Daily Oral HIF-PH Inhibitor Activates Physiologic Response to Manage Anemia

Akebia's Launch Strategy Developed to Drive Toward a Potential New Oral Standard of Care

Company to Host Conference Call on Thursday, March 28 at 8:00 AM ET

CAMBRIDGE, Mass., March 27, 2024 /PRNewswire/ -- Akebia Therapeutics®, Inc. (Nasdaq: AKBA), a biopharmaceutical company with the purpose to better the lives of people impacted by kidney disease, today announced that the U.S. Food and Drug Administration (FDA) has approved 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. Vafseo is a once-daily oral hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor that activates the physiologic response to hypoxia to stimulate endogenous production of erythropoietin to manage anemia. Vafseo is now approved in 37 countries.

"With the approval of Vafseo in the U.S., we're proud to deliver an alternative treatment option for the hundreds of thousands of Americans on dialysis who are diagnosed with anemia due to CKD," said John P. Butler, Chief Executive Officer of Akebia. "At Akebia we are committed to kidney patients, a dedication that has driven our team to achieve this milestone. We believe this commitment uniquely positions the company to execute a successful launch designed to drive toward a potential new oral standard of care for dialysis patients."

The approval of Vafseo for the treatment of anemia due to CKD in adults who have been receiving dialysis for at least three months is based on efficacy and safety data from the INNO$_2$VATE program and an assessment of post marketing safety data from Japan where VAFSEO was launched in August 2020. Results from the INNO$_2$VATE program were published in the New England Journal of Medicine: (N Engl J Med 2021; 384:1601-1612); (N Engl J Med 2021; 384:1589-1600). See the Important Safety Information section below, including BOXED WARNING regarding increased risk of death, myocardial infarction, stroke, venous thromboembolism and thrombosis of vascular access.

Approximately 500,000 adult patients in the U.S. on dialysis suffer from anemia due to CKD[1], which may be associated with many adverse clinical outcomes. The burden of managing uncontrolled anemia in CKD patients can be substantial, both in terms of healthcare costs and the impact on patients, healthcare providers and caregivers. Today, most CKD patients are treated for anemia with injectable erythropoiesis-stimulating agents mostly administered at dialysis centers. "Patients receiving maintenance dialysis would benefit from additional therapeutic options that can effectively increase and maintain hemoglobin concentrations within guideline-recommended target ranges," said Glenn M. Chertow, M.D., M.P.H., Professor of Medicine, Division of Nephrology at Stanford University and Co-Chair of the independent Executive Steering Committee for PRO$_2$TECT and INNO$_2$VATE, the global Phase 3 clinical development programs for Vafseo.

Lori Hartwell, who has had kidney disease since she was a young child, is the Founder and President of the Renal Support Network. She expressed her support of this new therapy for adults with anemia due to chronic kidney disease on dialysis by stating, "Anemia is a debilitating condition that significantly impacts our daily lives. It is promising to see the introduction of innovative treatment options for people fighting anemia."

Akebia intends to commercialize Vafseo in the U.S. with its established commercial team that has deep renal experience and by leveraging its relationship with CSL Vifor, an industry leader in bringing innovative therapies to U.S. dialysis organizations. In line with the approved label, Akebia will execute a launch strategy to drive Vafseo toward the goal of becoming a new oral standard of care for adult dialysis patients.

Mr. Butler added, "We are tremendously grateful for the patients, physicians, investigators, and site coordinators who participated in our clinical trials that led to this important approval. This milestone is the culmination of years of perseverance by Akebia employees and partners committed to bettering the lives of people impacted by kidney disease."

Conference Call
Akebia will host a conference call on Thursday, March 28 at 8:00 a.m. Eastern Time to discuss the approval and planned next steps for launch. To access the call, please register by clicking on this Registration Link (https://register.vevent.com/register/BI8d947513ebdd4e32bf2fbc68d973108f), and you will be provided with dial in details. To avoid delays and ensure timely connection, we encourage dialing into the conference call 15 minutes ahead of the scheduled start time.

A live webcast of the conference call will be available via the "Investors" section of Akebia's website at: https://ir.akebia.com/. An online archive of the webcast can be accessed via the Investors section of Akebia's website at https://ir.akebia.com approximately two hours after the event.

About Akebia Therapeutics
Akebia Therapeutics, Inc. is a fully integrated biopharmaceutical company with the purpose to better the lives of people impacted by kidney disease. Akebia was founded in 2007 and is headquartered in Cambridge, Massachusetts. For more information, please visit our website at www.akebia.com, which does not form a part of this release.

About Anemia due to Chronic Kidney Disease (CKD)
Anemia is a condition in which a person lacks enough healthy red blood cells to carry adequate oxygen to the body's tissues. It commonly occurs in people with CKD because their kidneys do not produce enough erythropoietin, a hormone that helps regulate production of red blood cells. Anemia due to CKD can have a profound impact on a person's quality of life[2] as it can cause fatigue, dizziness, shortness of breath and cognitive dysfunction. Left untreated, anemia leads to deterioration in health and is associated with increased mortality[3] in people with CKD.

About Vafseo® (vadadustat) Tablets
Vafseo® (vadadustat) tablets is a once-daily oral hypoxia-inducible factor prolyl hydroxylase inhibitor that activates the physiologic response to hypoxia to stimulate endogenous production of erythropoietin, increasing hemoglobin and red blood cell production to manage anemia. Vafseo is approved for use in 37 countries.

INDICATION

VAFSEO is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months.

Limitations of Use

- VAFSEO has not been shown to improve quality of life, fatigue, or patient well-being.
- VAFSEO is not indicated for use:
  - As a substitute for red blood cell transfusions in patients who require immediate correction of anemia.
  - In patients with anemia due to CKD not on dialysis.

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.

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 month 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 VASFEO, 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.
- **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.

Forward-Looking Statements

Statements in this press release 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 ability to execute a successful commercial launch of Vafseo; and Akebia's plans with respect to commercializing Vafseo, including Vafseo's potential to become a new oral standard of care; and timing of commercial availability of Vafseo. The terms "intend," "believe," "plan," "goal," "potential," "anticipate, "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; 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; the direct or indirect impact of the COVID-19 pandemic on 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 Annual Report on Form 10-K for the fiscal year ended December 31, 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 press release, and, except as required by law, Akebia does not undertake, and

specifically disclaims, any obligation to update any forward-looking statements contained in this press release.

Akebia Therapeutics®, Auryxia® and Vafseo® are registered trademarks of Akebia Therapeutics, Inc. and its affiliates.

Sources:

[1]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; Dopps.org

[2]Eriksson D, et al. BMC Nephrol. 2016;17:97; Finkelstein FO, et al. Clin J Am Soc Nephrol. 2009;4:33-38; Farag YM, et al. Clin Nephrol. 2011;75:524-533

[3] Portolés J, et al. BMC Nephrol. 2013;14:2. 3. NICE. Clinical Guideline: Anaemia Management in Chronic Kidney Disease: Partial Update 2015. 4. Silverberg DS, et al. Clin Lab Haematol. 2001;23:1-6. 5. Herzog CA, et al. J Card Fail. 2004;10:467-472

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