Akebia Therapeutics and U.S. Renal Care Initiate the VOICE Trial of Vafseo® (vadadustat) for Patients on Dialysis

September 5, 2024

- *Outcomes study will assess mortality and hospitalization in patients treated with Vafseo compared to current standard of care*
- *Trial aims to build a body of real-world evidence to understand the potential benefits of treating patients with Vafseo*

CAMBRIDGE, Mass., Sept. 5, 2024 /PRNewswire/ -- Akebia Therapeutics®, Inc. (Nasdaq: AKBA), a biopharmaceutical company with the purpose to better the lives of people impacted by kidney disease, and U.S. Renal Care (USRC), the nation's largest privately held and fastest-growing kidney care provider, today announced plans to begin a collaborative clinical trial of recently approved Vafseo. The first patient in this trial is expected to be enrolled this year.

The Vafseo Outcomes In-Center Experience (VOICE) trial intends to enroll approximately 2,200 patients who will be randomized to oral Vafseo 300 mg tablets administered three times per week or standard-of-care erythropoiesis-stimulating agents. The trial will end approximately 18 months after the last patient is randomized. The primary endpoint is all-cause mortality and the secondary endpoint is all-cause hospitalization. The trial was powered to demonstrate non-inferiority for all-cause mortality and superiority for a 10% reduction in all-cause hospitalization. More information about the VOICE trial can be found here.

"We are pleased to be collaborating with the prominent kidney care provider, U.S. Renal Care, on this important trial. Akebia has already established a robust body of evidence with respect to the safety and efficacy of Vafseo in dialysis patients with the INNO$_2$VATE clinical trial program, as well as its MO$_2$DIFY and FO$_2$CUS studies," said Steven K. Burke, M.D., Chief Medical Officer of Akebia. "Given what we have learned, we are excited to collaborate with U.S. Renal Care on the VOICE trial to further investigate the safety of Vafseo when dosed three times a week to align with patients' current dialysis schedule. We continue to focus on helping those kidney patients who may benefit from an orally-administered treatment for anemia that leads to enhanced hemoglobin stability."

"U.S. Renal Care is proud to be spearheading the first Vafseo patient experience trial in our dialysis centers," noted Geoffrey A. Block, M.D., FASN, Associate Chief Medical Officer and Senior Vice President, Clinical Research & Medical Affairs for U.S. Renal Care. "This innovative product has the potential to become the new standard of care for treating anemia due to chronic kidney disease and it is important to build the body of real-world evidence to understand the potential benefits and risks of treating patients with Vafseo, providing valuable insights for our treating physicians and patient community."

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 U.S. Renal Care
U.S. Renal Care, the largest privately held and fastest-growing dialysis provider in the nation, partners with nephrologists to care for more than 36,000 people living with kidney disease across 32 states in the U.S. Since 2000, U.S. Renal Care has been a leader in clinical quality, innovation, and operational excellence – delivering the best experience and outcomes for our patients. Visit USRenalCare.com to learn more.

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.

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 (MI), 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 in patients with a history of MI, cerebrovascular event, or acute coronary syndrome within the 3 months prior to starting VAFSEO. Targeting a Hb level of greater than 11 g/dL is expected to further increase the risk of death and arterial and venous thrombotic events. Use the lowest effective dose to reduce the need for red blood cell (RBC) transfusions. Adhere to dosing and Hb monitoring recommendations to avoid excessive erythropoiesis.

- **Hepatotoxicity**
  Hepatocellular injury attributed to VAFSEO was reported in less than 1% of patients, including one severe case with jaundice. 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% of VAFSEO and 17% of darbepoetin alfa patients. Serious worsening of hypertension was reported in 2.7% of VAFSEO and 3% of darbepoetin alfa patients. 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% of VAFSEO and 1.6% of darbepoetin alfa patients. Monitor for new-onset seizures, premonitory symptoms, or change in seizure frequency.

- **Gastrointestinal (GI) Erosion**
  Gastric or esophageal erosions occurred in 6.4% of VAFSEO and 5.3% of darbepoetin alfa patients. Serious GI erosions, including GI bleeding and the need for RBC transfusions, were reported in 3.4% of VAFSEO and 3.3% of darbepoetin alfa patients. Consider this risk in patients at increased risk of GI erosion. Advise patients about signs of erosions and GI bleeding and urge them to seek prompt medical care if present.

- **Serious Adverse Reactions in Patients with Anemia Due to CKD 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, MI, 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% of VAFSEO and 3.0% of darbepoetin alfa patients. 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 to 20 mg and rosuvastatin to 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 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 expectations regarding the VOICE trial, including the ability to build on the body of real-world evidence to understand the potential benefits of treating patients with Vafseo and the timing of enrollment of patients; expectations as to the potential benefits and risks of Vafseo when dosed three times a week in dialysis patients, including enhanced hemoglobin stability; and Vafseo's potential to become the new standard of care for treating anemia due to chronic kidney disease. 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, including the VOICE trial; 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 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 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.

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