Vadadustat U.S. Patient Data from Global Phase 3 Clinical Program Published in Journal of the American Society of Nephrology

June 4, 2025

Akebia continues to publish important, clinically relevant data to further physicians' understanding of Vafseo® (vadadustat)

CAMBRIDGE, Mass., June 04, 2025 (GLOBE NEWSWIRE) -- 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 *Journal of the American Society of Nephrology* (JASN) has published pre-specified analyses for the U.S. and non-U.S. patient subgroups from the vadadustat global phase 3 clinical program, which included two trials in patients with dialysis-dependent chronic kidney disease (DD-CKD; INNO$_2$VATE) and two trials in patients with non–dialysis-dependent CKD (NDD-CKD; PRO$_2$TECT).

The vadadustat global phase 3 clinical trials were open-label, randomized, noninferiority trials that compared the safety and efficacy of vadadustat with darbepoetin alfa in adult patients with CKD-related anemia. Data from the pre-specified analyses for the U.S. patient subgroup demonstrate that among patients with DD-CKD, safety and efficacy of vadadustat and darbepoetin alfa in the U.S. and outside the U.S. were similar. Among the U.S. patient subgroup with NDD-CKD, safety and efficacy outcomes were similar, but the risk for major adverse cardiovascular event (MACE) with vadadustat was higher than darbepoetin alfa outside the United States. In these analyses, safety was measured by time to first MACE and efficacy was measured by mean change in hemoglobin. The article titled, "*Safety and Efficacy of Vadadustat for the Treatment of CKD-Related Anemia within and outside the United States*," is available here.

Vafseo® (vadadustat) was approved by the U.S. Food and Drug Administration in March 2024 for the treatment of anemia due to chronic kidney disease in adults who have been receiving dialysis for at least three months. Vafseo has been available in the U.S. since January 2025.

"Geographic-specific pre-specified analyses of the vadadustat global phase 3 clinical program are important data as physicians in the U.S. are making care decisions for patients with CKD-related anemia," said Steven K. Burke, M.D., Senior Vice President, Research & Development and Chief Medical Officer of Akebia. "The analyses reflect how regional differences in clinical trial patient baseline characteristics, hemoglobin targets, and access to health care services and other regional clinical practices can ultimately contribute to differing outcomes in a global trial."

Full results of the vadadustat global clinical phase 3 clinical program were previously published in the New England Journal of Medicine: INNO$_2$VATE, PRO$_2$TECT.

The *Journal of the American Society of Nephrology*, an official publication of the American Society of Nephrology (ASN), publishes high-impact research to advance the understanding and treatment of kidney diseases, including physiology, pathobiology, and person-centered care. *JASN* publishes original research advancing the understanding and care of kidney diseases through laboratory, translational, and clinical studies.

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 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 importance of the vadadustat global phase 3 clinical data, including that the geographic-specific pre-specified analyses are important data as physicians in the U.S. are making care decisions for patients with CKD-related anemia; and Akebia's ability to continue to publish important, clinically relevant data to further physicians' understanding of Vafseo.

The terms "intend," "believe," "plan," "goal," "potential," "anticipate, "estimate," "expect," "future," "will," "continue," "could", 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 commercial availability of Vafseo; the potential demand and market potential and acceptance of, as well as coverage and reimbursement related to Vafseo, including estimates regarding the potential market opportunity; the competitive landscape for Vafseo, including generic entrants and the timing thereof; the ability of Akebia to attract and retain qualified personnel; Akebia's ability to achieve and maintain profitability and to maintain operating expenses consistent with its operating plan; decisions made by health authorities, such as the FDA, with respect to regulatory filings and other interactions; 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; early termination of any of Akebia's collaborations; and changes in the geopolitical environment and uncertainty surrounding U.S. trade policy on tariffs. 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, 2025, 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 Contact

Mercedes Carrasco
mcarrasco@akebia.com

Source: Akebia Therapeutics, Inc.