Vafseo® (vadadustat) Dialysis Dependent Patient Post Hoc Data Analysis: Composite of All-Cause Mortality and Hospitalization Outcomes Statistically More Favorable for Patients Receiving Vadadustat vs. ESAs

November 6, 2025

Win-Odds Analysis Presented at American Society of Nephrology Kidney Week 2025

CAMBRIDGE, Mass., Nov. 06, 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 the presentation of a post-hoc win odds analysis of all-cause mortality and hospitalization from the Phase 3 INNO$_2$VATE trials of vadadustat at the American Society of Nephrology Kidney Week 2025 (ASN Kidney Week). The presentation entitled, "*Win-Odds Analysis of Deaths and Hospitalization in Patients taking Vadadustat or Darbepoetin Alfa for CKD-Related Anemia Undergoing Dialysis,*" demonstrated favorable and statistically significant effects of Vafseo relative to the erythropoiesis-stimulating agent (ESA) darbepoetin alfa on the composite endpoint of death or hospitalization.

Vafseo® (vadadustat) is approved for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months. Vafseo has been available in the U.S. since January 2025.

"The win-odds statistical method is a useful tool to prioritize clinically meaningful endpoints and account for all events in the order of clinical importance," said Glenn M. Chertow, M.D., M.P.H., Professor of Medicine, Stanford University School of Medicine. "This analysis showed that patients randomized to vadadustat experienced a lower risk of death or hospitalization compared with patients randomized to darbepoetin alfa. Physicians can consider these findings when selecting medications for the treatment of anemia in patients receiving maintenance dialysis."

"As we work toward our goal to make Vafseo standard of care for the treatment of CKD-related anemia in patients receiving dialysis, we recognize the value of sharing new analysis of data on well-accepted outcomes like all-cause mortality and hospitalization that can inform care decisions," said Steven Burke, MD, Senior Vice President and Chief Research & Development Officer at Akebia. "We are also actively advancing multiple trials of Vafseo in real-world clinical settings, including VOICE, a collaborative clinical trial of Vafseo, also designed to measure mortality and hospitalizations. We are grateful to our partners within dialysis organizations and various academic settings, including Dr. Chertow and his team, who clearly share our commitment to persons living with kidney disease."

Study Details:

The post-hoc win-odds analysis was based on data from two global Phase 3, open-label, randomized (1:1), noninferiority trials (INNO$_2$VATE) comparing vadadustat treatment vs darbepoetin alfa in adults with anemia associated with incident or prevalent dialysis-dependent chronic kidney disease. The primary safety endpoint in the primary analysis was time to first adjudicated MACE (a composite endpoint of death from any cause, non-fatal myocardial infarction, or non-fatal stroke).

In this post-hoc win-odds analysis of INNO$_2$VATE data, the hierarchical composite of 1) all-cause mortality and 2) hospitalizations was statistically significantly lower for those patients receiving vadadustat compared to darbepoetin alfa.

Study Analysis:

- **On study analysis:** Inverted win-odds 0.93, 95% CI (0.87-0.99); *P*=0.03 (vada loss count+ 0.5*ties)/ (vada win count + 0.5*ties)
- **On treatment + 28 days post last dose:** Inverted win-odds ratio 0.86, 95% CI (0.81, 0.95); *p* <0.0001

A win-odds analysis is a statistical method used to analyze clinical trial data to evaluate the effectiveness of treatments. It provides a novel way to measure treatment effect by comparing the number of wins and losses for the treatment and control groups, which can be easily used in studies with prioritized multiple outcomes.

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 about a win odds analysis of all-cause mortality and hospitalization from the Phase 3 INNO$_2$VATE trials of vadadustat, including that such analysis demonstrates favorable and statistically significant effects of Vafseo relative to the ESA darbepoetin alfa on the composite endpoint of death or hospitalization; Akebia's beliefs that physicians can consider these findings when selecting medications for the treatment of anemia in patients receiving maintenance dialysis; Akebia's plans to work toward its goal to make Vafseo standard of care for the treatment of CKD-related anemia in patients receiving dialysis; Akebia's beliefs that sharing new analysis of data can inform care decisions; and Akebia's plans to actively advance multiple trials of Vafseo in real-world clinical settings, including VOICE. 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: the potential therapeutic benefits, safety profile, and effectiveness of Vafseo; the results of preclinical and clinical research; decisions made by health authorities, such as the FDA, with respect to regulatory filings and other interactions; 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; 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 June 30, 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.

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