Akebia Therapeutics Announces Positive Top-Line Results from Vadadustat Alternative Dosing Study

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- Data demonstrated that vadadustat met the primary and secondary efficacy endpoints and was non-inferior to an ESA as a treatment for anemia due to chronic kidney disease when administered three times a week at the time of dialysis
- Vadadustat demonstrated a similar safety profile to long-acting ESA when used three times a week

CAMBRIDGE, Mass., April 3, 2023 /PRNewswire/ -- Akebia Therapeutics®, Inc. (Nasdaq: AKBA), a biopharmaceutical company with the purpose to better the lives of people impacted by kidney disease, today announced positive top-line results from FO_2CUS, a study evaluating the efficacy and safety of vadadustat, an oral hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor, in hemodialysis patients who were converted from a long-acting erythropoiesis-stimulating agent (ESA) to three times weekly oral vadadustat dosing for the maintenance treatment of anemia. The data demonstrated that vadadustat met the primary and secondary efficacy endpoints and was non-inferior to an ESA in the treatment of anemia due to chronic kidney disease in patients on hemodialysis when used three times a week at the time of dialysis and with a comparable safety profile to the current standard of care.

FO_2CUS was an open-label, active-controlled, sponsor-blinded study that evaluated 456 hemodialysis patients who were randomized (1:1:1) into vadadustat 600mg, vadadustat 900mg, or a long-acting ESA (Mircera®) treatment arms. The primary efficacy endpoint was the mean change in hemoglobin (Hb) between baseline and the primary evaluation period (weeks 20-26). The secondary efficacy endpoint was the mean change in Hb between baseline and the secondary evaluation period (weeks 46-52).

"The FO_2CUS study demonstrated that vadadustat managed hemoglobin levels in patients on hemodialysis when administered three times a week, which we believe is important as the dosing schedule aligns with dialysis visits and has the potential, if approved, to provide an oral alternative to the standard of care," said Steven K. Burke, M.D., Senior Vice President, Research & Development and Chief Medical Officer of Akebia. "We continue to believe in the potential benefit vadadustat could deliver to patients on dialysis if approved and recognize that even with available treatments many dialysis patients do not stay within target hemoglobin range. The FO_2CUS study has been a tremendous undertaking, and we're pleased the data support that vadadustat was non-inferior to, and had a comparable safety profile to, an ESA. We would like to extend our sincere appreciation to everyone involved in this study including the patients, physicians, investigators, and site coordinators."

Primary and Secondary Efficacy Endpoint Results
In the FO_2CUS study, each vadadustat dosing regimen (600mg, 900mg) and the combined vadadustat-treated group achieved the primary efficacy endpoint of the mean change in Hb between baseline and the primary evaluation period compared to Mircera in adult patients on hemodialysis, demonstrating non-inferiority to Mircera based on a non-inferiority margin of -0.75 g/dL. Similarly, each dosing regimen of vadadustat and the combined vadadustat-treated group achieved the secondary efficacy endpoint of the mean change in Hb between baseline and the secondary evaluation period.

In the FO_2CUS study in hemodialysis patients (n=456):

- **Primary Efficacy Endpoint Results**: Vadadustat was non-inferior to Mircera. The least square mean difference in Hb was -0.43 g/dL (-0.67, -0.20) for the vadadustat 600 mg-treated group, -0.23 g/dL (-0.46, 0.01) for the vadadustat 900 mg-treated group, and -0.33 g/dL (-0.53, -0.13) for the combined vadadustat-treated group, achieving the pre-specified non-inferiority margin of -0.75 g/dL. The mean Hb level during the primary evaluation period was 10.11 (0.061) g/dL for the combined vadadustat-treated group compared to 10.41 (0.068) g/dL for Mircera-treated group.

- **Secondary Efficacy Endpoint Results:** Vadadustat was non-inferior to Mircera. The least square mean difference in Hb was -0.27 g/dL (-0.54, -0.00) for the vadadustat 600 mg-treated group, -0.38 g/dL (-0.67, -0.10) for the vadadustat 900 mg-treated group, and -0.33 g/dL (-0.56, -0.09) for the combined vadadustat-treated group. The mean Hb level during the secondary evaluation period was 10.03 (0.066) g/dL for the combined vadadustat-treated group compared to 10.28 (0.076) g/dL for the Mircera-treated group.

Safety Results
In the FO_2CUS study, a total of 78.7% patients experienced any TEAEs in the combined vadadustat-treated group, and 75.3% experienced any TEAEs in the Mircera-treated group. The data demonstrated that 44.5% of patients experienced any treatment-emergent SAEs in the combined vadadustat-treated group, and 44.7% of patients experienced any treatment-emergent SAEs in the Mircera-treated group. During the study, the most

common TEAEs reported in vadadustat-/Mircera- treated patients were COVID-19 (14.6%/16.0%), diarrhea (12.3%/8.0%) and hyperkalaemia (9.0%/10.7%).

Akebia expects to present full study results at an upcoming medical conference or in a peer-reviewed journal this year.

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. The Company 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 Vadadustat

Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, which can lead to increased red blood cell production and improved oxygen delivery to tissues. Vadadustat is an investigational new drug and is not approved by the U.S. Food and Drug Administration (FDA). On March 29, 2022, the FDA issued a complete response letter to Akebia's New Drug Application for vadadustat for the treatment of anemia due to chronic kidney disease (CKD). In November 2022, Akebia submitted a Formal Dispute Resolution Request focused on the favorable balance of the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis. Vadadustat is currently under review by the European Medicines Agency for the treatment of anemia due to CKD in adults. In Japan vadadustat is approved as a treatment for anemia due to CKD in both dialysis-dependent and non-dialysis dependent adult patients.

Forward Looking Statement
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 beliefs in the benefits of vadadustat as an oral treatment for patients on dialysis with anemia due to chronic kidney disease; Akebia's expectations on the timing of presenting full study results. The terms "expect," "intend," "believe," "plan," "goal," "potential," "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: decisions made by health authorities, such as the FDA and the European Medicines Agency, with respect to regulatory filings, including the New Drug Application for vadadustat and the Formal Dispute Resolution Request for vadadustat; the potential therapeutic benefits, safety profile, and effectiveness of vadadustat; the direct or indirect impact of the COVID-19 pandemic on regulators and Akebia's business, operations, and 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; early termination of any of Akebia's collaborations; and the competitive landscape for vadadustat, if approved. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's Annual Report on Form 10-K for the year ended December 31, 2022, 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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