Akebia Therapeutics Announces Positive Top-Line Results from Two Pivotal Phase 3 Studies of Vadadustat in Japanese Patients with Anemia Due to Chronic Kidney Disease

March 12, 2019

– Each Study Met Its Primary Endpoint –

– Regulatory Submission in Japan Expected in 2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 12, 2019-- Akebia Therapeutics, Inc. (Nasdaq:AKBA) today announced positive top-line results from two phase 3 active-controlled pivotal studies evaluating vadadustat, an investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), in Japanese subjects with anemia due to chronic kidney disease (CKD). These studies were conducted by Akebia's development and commercialization collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation (MTPC). Each study, one in non-dialysis dependent subjects and one in hemodialysis-dependent subjects, met its primary endpoint. In addition, results from two phase 3 single-arm studies conducted by MTPC in peritoneal dialysis subjects and hemodialysis subjects further support vadadustat's potential in these indications. MTPC expects to submit a Japanese New Drug Application in 2019.

"Collectively, these data provide further confirmation of vadadustat's potential to meaningfully transform the treatment paradigm for patients with anemia due to CKD," said John P. Butler, President and Chief Executive Officer of Akebia. "These results add to our dataset demonstrating the potential for vadadustat to effectively manage hemoglobin levels in both dialysis-dependent and non-dialysis dependent patients, including those who convert from erythropoiesis stimulating agents."

Top-Line Results from the Pivotal Phase 3 Study in Non-Dialysis Dependent CKD Subjects (J01 Study)

- The phase 3 randomized, open-label, active-controlled correction and conversion study assessed the efficacy and safety of vadadustat compared to darbepoetin alfa, an erythropoiesis stimulating agent (ESA), in 304 Japanese non-dialysis dependent subjects with anemia due to CKD, with a treatment duration of 52 weeks. Data from the planned analysis at 24 weeks are provided. The study met its primary endpoint, with the mean hemoglobin (Hb) level at week 20 and week 24 at 11.66 g/dL (95% CI 11.49, 11.84 g/dL) for vadadustat-treated subjects compared to 11.93 g/dL (95% CI 11.76, 12.10 g/dL) for darbepoetin alfa-treated subjects. The difference in mean Hb was -0.26 g/dL (95% CI -0.50, -0.02 g/dL), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The incidence of adverse events (AEs) was 72.2% in the vadadustat-treated group compared to 73.2% in the darbepoetin alfa-treated group. The most common AEs reported in vadadustat-treated subjects were nasopharyngitis (14.6%), diarrhea (10.6%), constipation (5.3%), and contusion (5.3%). The incidence of serious adverse events (SAEs) was 13.9% in the vadadustat-treated group compared to 14.4% in the darbepoetin alfa-treated group; no SAE was considered related to study drug. No deaths were reported in the vadadustat-treated group, and one fatal myocardial infarction was reported in the darbepoetin alfa-treated group, which was assessed as not related to study drug.

Top-Line Results from the Pivotal Phase 3 Study in Dialysis-Dependent CKD Subjects (J03 Study)

- The phase 3 randomized, double-blind, active-controlled conversion study assessed the efficacy and safety of vadadustat compared to darbepoetin alfa in 323 Japanese hemodialysis subjects with anemia due to CKD who had been receiving ESA therapy prior to study screening, with a treatment duration of 52 weeks. Group level data at 24 weeks from this ongoing double-blind study are provided. The study met its primary endpoint, with the mean Hb level at week 20 and week 24 at 10.61 g/dL (95% CI 10.45, 10.76 g/dL) for vadadustat-treated subjects compared to 10.65 g/dL (95% CI 10.50, 10.80 g/dL) for darbepoetin alfa-treated subjects. The difference in mean Hb was -0.05 g/dL (95% CI -0.26, 0.17 g/dL), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The incidence of AEs was 89.5% in the vadadustat-treated group compared to 88.2% in the darbepoetin alfa-treated group. The most common AEs reported in vadadustat-treated subjects were nasopharyngitis (19.8%), diarrhea (10.5%), and shunt stenosis (8.0%). The incidence of SAEs was 13.0% in the vadadustat-treated group compared to 10.6% in the darbepoetin alfa-treated group; no SAE was considered related to study drug.

Top-Line Results from Two Phase 3, Single-Arm Studies in Dialysis-Dependent CKD Subjects (J02 Study and J04 Study)

- The phase 3 open-label, single-arm J02 study assessed the efficacy and safety of vadadustat in 42 Japanese peritoneal dialysis subjects with anemia due to CKD, with a treatment duration of 24 weeks. The mean Hb level at week 20 and week

24 was 11.35 g/dL (95% CI 10.99, 11.70 g/dL) for vadadustat-treated subjects. Thirty-eight subjects (90.5%) experienced an AE and twelve (28.6%) experienced an SAE. One SAE of fatal myocardial ischemia was assessed as possibly related to vadadustat by the investigator.

- The phase 3 open-label, single-arm J04 correction study evaluated the safety and efficacy of vadadustat, with a treatment duration of 24 weeks, in 24 Japanese hemodialysis subjects with anemia due to CKD who had not been receiving ESA therapy prior to study screening or who underwent ESA washout during screening. The mean Hb level at week 20 and week 24 was 10.75 g/dL (95% CI 10.35, 11.14 g/dL) for vadadustat-treated subjects. Twenty-three subjects (95.8%) experienced an AE, and seven (29.2%) experienced an SAE. No SAE was assessed as related to study drug, and no deaths were reported.

Akebia will discuss these findings on its previously announced fourth quarter and full-year 2018 investor update call on Monday, March 18, 2019 at 4:30 p.m. Eastern Time. Additional data from the studies are expected be presented by MTPC at an upcoming medical meeting.

In Japan, an estimated 13 million people are afflicted with advanced stages of CKD. Anemia is common in patients with CKD and its prevalence increases as CKD progresses. Injectable ESAs are currently the standard of care. Vadadustat, if approved for marketing, would provide patients with a once-daily oral treatment option and has the potential to set a new standard of care for the treatment of anemia due to CKD.

About Vadadustat

Vadadustat is an oral hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor currently in global phase 3 development for the treatment of anemia due to chronic kidney disease. Vadadustat's proposed mechanism of action is designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with increased production of HIF, which coordinates the interdependent processes of iron mobilization and erythropoietin production to increase red blood cell production and, ultimately, improve oxygen delivery. Vadadustat is an investigational therapy and is not approved by the U.S. Food and Drug Administration or any other regulatory authority.

About Akebia Therapeutics

Akebia Therapeutics, Inc. is a fully integrated biopharmaceutical company focused on the development and commercialization of therapeutics for patients with 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.

Forward-Looking Statements

This document contains forward-looking statements within the meaning of the federal securities laws. Such statements are based upon current plans, estimates and expectations that are subject to various risks and uncertainties. The inclusion of forward-looking statements should not be regarded as a representation that such plans, estimates and expectations will be achieved. Words such as "anticipate," "create," "expect," "project," "intend," "believe," "may," "will," "should," "plan," "could," "target," "contemplate," "estimate," "position," "predict," "potential," "opportunity," "working to," "look forward" and words and terms of similar substance used in connection with any discussion of future plans, actions or events identify forward-looking statements. All statements, other than historical facts, including regarding plans for regulatory submissions, the potential to set a new standard of care, and market and growth opportunity and potential, are forward-looking statements. Important factors that could cause actual results to differ materially from Akebia's plans, estimates or expectations could include, but are not limited to: whether the data from the phase 3 clinical trials of vadadustat in Japanese subjects will warrant a Japanese New Drug Application (JNDA) submission on the timeline expected, or at all, and whether any such JNDA will be approved; the timing and content of interactions with and decisions made by regulatory authorities; and success of others in developing competing products. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's most recently filed Quarterly Report on Form 10-Q, and other filings that Akebia may make with the U.S. Securities and Exchange Commission in the future. Akebia does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this press release.

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