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Akebia Announces Publication of Phase 2b Data for Vadadustat in Non-Dialysis Patients with Anemia Related to Chronic Kidney Disease

-- Data Showed That Vadadustat Controlled Hemoglobin Levels While Improving Iron Metabolism --

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Akebia Therapeutics, Inc. (NASDAQ: AKBA), a biopharmaceutical company focused on delivering innovative therapies to patients with kidney disease through the biology of hypoxia-inducible factor (HIF), today announced the publication of positive results from a Phase 2b study of vadadustat, a once-daily oral HIF stabilizer, in development for the treatment of anemia related to chronic kidney disease (CKD). The study demonstrated that vadadustat increased and maintained hemoglobin levels in patients throughout the 20-week study in a predictable and controlled manner. The peer-reviewed paper, titled "Vadadustat, a novel oral HIF stabilizer, provides effective anemia treatment in non-dialysis-dependent chronic kidney disease," was published online by *Kidney International*, the official journal of the International Society of Nephrology.

"Treatment of anemia related to CKD with the current standard of care, erythropoiesis-stimulating agents, can lead to substantial hemoglobin increases above the desired target range," said Pablo Pergola, M.D., Ph.D., Renal Associates PA, and University of Texas Health Science Center at San Antonio. "These results demonstrate that vadadustat raised and maintained hemoglobin levels while minimizing hemoglobin excursions and improving iron mobilization, and may offer patients an effective alternative therapy for treating renal anemia."

The multicenter, randomized, double-blind, placebo-controlled study assessed the ability of oral, once-daily vadadustat to correct anemia in patients with stages 3a-5 non-dialysis dependent chronic kidney disease. Patients initiated treatment with either 450 mg of vadadustat or matching placebo, administered once daily for 20 weeks. The initial 450 mg daily dose of vadadustat was adjusted in accordance with the patient's hemoglobin (Hb) response using a dose titration algorithm designed to minimize Hb excursions above 13.0 g/dL. Patients were assigned to one of three study groups: recombinant erythropoietin stimulating agents (rESAs) treatment naïve, rESAs previously treated, or rESAs actively treated. Within each group, patients were randomized 2:1 to receive vadadustat or placebo and were stratified according to CKD stage and the presence or absence of diabetes mellitus. The full manuscript is available on the *Kidney International* website at: http://www.kidney-international.org/article/S0085-2538(16)30357-X/fulltext.

Findings from the study include:

- Vadadustat increased and maintained Hb levels in patients throughout the study when compared to placebo; by week two, mean Hb levels in the vadadustat group had increased significantly compared to placebo, plateaued by week six to week eight and were sustained throughout the 20 weeks of treatment, with limited Hb excursions and dose adjustments;
- Vadadustat improved iron mobilization compared to the placebo group, as measured by significant decreases in hepcidin and ferritin, as well as a significant increase in total iron binding capacity; and
- There was no difference between the vadadustat and placebo groups in the mean change from baseline in vascular endothelial growth factor (VEGF) levels at week 12 or end of treatment.

Vadadustat was generally well tolerated in the Phase 2b trial and overall adverse events were balanced between the treatment and placebo groups.

"The positive results from our Phase 2b study provided a strong foundation for our vadadustat global Phase 3 program, which continues to enroll dialysis-dependent and non-dialysis patients with anemia related to chronic kidney disease," said Brad Maroni, M.D., Chief Medical Officer at Akebia. "We will continue to publish the results from the more than 15 clinical studies of vadadustat, and look forward to reporting key findings from our Phase 3 program following the completion of those trials."

About Vadadustat

Vadadustat is an oral hypoxia-inducible factor (HIF) stabilizer with best-in-class potential for the treatment of anemia related to chronic kidney disease. Vadadustat, currently in development, exploits the same mechanism of action used by the body to naturally adapt to lower oxygen availability associated with a moderate increase in altitude. 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.

About Anemia Related to CKD

Approximately 30 million people in the U.S. have chronic kidney disease (CKD), with an estimated 1.8 million of these patients suffering from anemia. Anemia results from the body's inability to coordinate red blood cell production in response to lower oxygen levels due to the progressive loss of kidney function, which occurs in patients with CKD. Left untreated, anemia significantly accelerates patients' overall deterioration of health with increased morbidity and mortality. Renal anemia is currently treated with injectable recombinant erythropoiesis stimulating agents, which are associated with inconsistent hemoglobin responses and well-documented safety risks.

About Akebia Therapeutics

Akebia Therapeutics, Inc. is a biopharmaceutical company headquartered in Cambridge, Massachusetts, focused on delivering innovative therapies to patients with kidney disease through hypoxia-inducible factor biology. Akebia's lead product candidate, vadadustat, is an oral therapy in development for the treatment of anemia related to chronic kidney disease in both non-dialysis and dialysis patients. Akebia has commenced its vadadustat Phase 3 Program, which includes the PRO$_2$TECT studies for non-dialysis patients with anemia secondary to chronic kidney disease and INNO$_2$VATE studies for dialysis-dependent patients. For more information, please visit our website at www.akebia.com.

Forward-Looking Statements

This press release includes forward-looking statements. Such forward-looking statements include those about Akebia's strategy, future plans and prospects, including statements regarding the potential indications and benefits of vadadustat, clinical development plans and publication plans. The words "anticipate," "appear," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement, including the risk that existing preclinical and clinical data may not be predictive of the results of ongoing or later clinical trials; the ability of Akebia to successfully complete the clinical development of vadadustat; the funding required to develop Akebia's product candidates and operate the company, and the actual expenses associated therewith; the cost of the Phase 3 studies of vadadustat and the availability of financing to cover such costs; the timing and content of decisions made by the FDA and other regulatory authorities; the rate of enrollment in clinical studies of vadadustat; the actual time it takes to initiate and complete clinical studies; the success of competitors in developing product candidates for diseases for which Akebia is currently developing its product candidates; and Akebia's ability to obtain, maintain and enforce patent and other intellectual property protection for vadadustat. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's Annual Report on Form 10-Q for the quarter ended June 30, 2016, and other filings that Akebia may make with the 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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Akebia Contact:
AJ Gosselin, 617-844-6130
Manager, Corporate Communications
agosselin@akebia.com

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