Akebia Therapeutics Announces Initial Findings from Investigator-Sponsored Clinical Study Evaluating Vadadustat for the Prevention and Treatment of Acute Respiratory Distress Syndrome (ARDS) in Subjects with COVID-19 and Hypoxemia (VSTAT)

August 4, 2022

CAMBRIDGE, Mass., Aug. 4, 2022 /PRNewswire/ -- Akebia Therapeutics®, Inc. (Nasdaq: AKBA), a biopharmaceutical company with the purpose to better the lives of people impacted by kidney disease, today announced initial findings from an investigator-sponsored study evaluating vadadustat, Akebia's investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), for the prevention and treatment of ARDS in clinical trial subjects with COVID-19 and hypoxemia (O2 saturation ≤94%). The VSTAT trial (Vadadustat for the Prevention and Treatment of ARDS in Hospitalized Patients with Coronavirus Disease 2019) was a phase 2, randomized, double-blind, placebo-controlled trial, conducted by The University of Texas Health Science Center at Houston (UTHealth) in Houston, Texas and partially funded by Akebia.

The trial enrolled 449 adult subjects at five hospitals who were randomized 1:1 to vadadustat 900 mg or placebo once per day orally for up to 14 days while hospitalized. The VSTAT trial measured the proportion of subjects with either 6 (non-invasive ventilation or high flow oxygen devices), 7 (invasive mechanical ventilation or extracorporeal membrane oxygenation), or 8 (death) on the National Institute of Allergy and Infectious Disease Ordinal Scale (NIAID-OS) at Day 7 and Day 14 (primary). While a smaller proportion of subjects in the vadadustat group had a score of 6, 7, or 8 on the NIAID-OS than in the placebo group at Day 14, the trial failed to meet its primary superiority threshold of >95% probability. Those receiving vadadustat; however, did demonstrate 94% probability for conferring benefit on the NIAID-OS at Day 14.

At Day 14, the proportions of subjects who had a 6, 7 or 8 on the NIAID-OS were 13.3% (9.6%, 17.7%; 2.5, 97.5 percentiles from Bayesian simulations) for vadadustat versus 16.9% (12.6%, 22.0%) for placebo with a relative risk of 0.79 and 94% probability that vadadustat was superior to placebo. In a pre-specified analysis at Day 7, the proportions of subjects who had a 6, 7 or 8 on the NIAID-OS were 25.4% (20.7%, 30.5%) for vadadustat versus 29.7% (24.5%, 35.3%) for placebo with a relative risk of 0.86 and 97% probability that vadadustat was superior to placebo.

The incidence of treatment emergent adverse events was 78.6% in the vadadustat group and 76.2% in the placebo group. The most common treatment emergent adverse events reported in vadadustat/placebo subjects were alanine aminotransferase increase (34.4%/28.7%), COVID-19 pneumonia (19.5%/27.4%), anemia (14.0%/17.0%), aspartate aminotransferase increase (14.0%/14.8%), hyponatremia (10.7%/15.7%), septic shock (11.6%/10.8%), hyperkalemia (10.2%/10.8%), and hypermagnesemia (7.0%/13.9%). The incidence of serious treatment emergent adverse events was 27.9% in the vadadustat group and 32.7% in the placebo group. The most common serious treatment emergent adverse events reported in vadadustat/placebo subjects were COVID-19 pneumonia (19.5%/27.4%) and septic shock (11.6%/10.8%).

"While the trial missed its prespecified primary endpoint at Day14, we are extremely encouraged by the data and believe they support further developing vadadustat as a treatment for ARDS due to COVID-19 or other causes," said John P. Butler, Chief Executive Officer of Akebia. "I want to thank UTHealth for delivering a well-executed clinical trial during this difficult period. We also want to thank the patients who participated in the trial. We will now work to review the full data set more thoroughly, consult with experts in the field and ultimately consult FDA on a potential path forward."

Akebia is working with UTHealth Houston on publication of the full trial results and determining next steps in developing vadadustat as a potential treatment for ARDS due to COVID-19 or other causes.

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). 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 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 development plans for vadadustat and evaluation of vadadustat as a potential treatment for ARDS due to COVID-19 or other causes. The terms "believe," "plan," "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: vadadustat may not be an effective treatment to treat ARDS or other causes or be approved for marketing by the FDA; 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; the risk that clinical trials may not be successful; manufacturing risks; risks associated with management and key personnel changes and transitional periods; the actual costs incurred in the clinical trials of vadadustat and the availability of financing to cover such costs; the risk that clinical trials are discontinued or delayed for any reason, including for safety, tolerability, enrollment, manufacturing or economic reasons; market acceptance and coverage and reimbursement of vadadustat, if approved; the risks associated with potential generic entrants; the timing and content of decisions made by regulatory authorities; the competitive landscape; the scope, timing, and outcome of any legal, regulatory and administrative proceedings; the actual time it takes to initiate and complete preclinical and clinical studies; changes in the economic and financial conditions of the businesses of Akebia and its partners; and Akebia's and its partners' ability to obtain, maintain and enforce patent and other intellectual property protection. 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, 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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