FDA Provides Akebia Therapeutics a Path Forward for Vadadustat

May 30, 2023

- FDA denies formal dispute resolution, but outlines path to resubmit NDA for dialysis-dependent patients without new clinical studies
- Akebia plans to request Type A meeting and then resubmit NDA
- Akebia will host a conference call on Tuesday, May 30 at 8:30 a.m. ET

CAMBRIDGE, Mass., May 30, 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 that the company received a written response from the Office of New Drugs (OND) of the U.S. Food and Drug Administration (FDA) to Akebia's Formal Dispute Resolution Request (FDRR) regarding the Complete Response Letter (CRL) received in March 2022 for vadadustat. The letter from the OND stated the company's appeal was denied; however, the letter provided a path forward for the company to resubmit the new drug application (NDA) for vadadustat for the treatment of anemia due to chronic kidney disease (CKD) for dialysis dependent patients. The letter addressed issues outlined in the CRL, provided feedback and conclusions on those issues, and outlined information to be included in an NDA resubmission, which did not include the generation of additional clinical data.

The CRL raised a concern regarding the increased risk of thromboembolic events, driven by vascular access thrombosis (VAT). While not dismissing the potential safety signal, the OND indicated that the extent of the increase in potential risk is not large and it may be a reasonable conclusion that the increase in VAT events can be managed as a labeling issue.

The CRL noted a concern about the risk for drug-induced liver injury (DILI) and concern that ongoing monitoring would be less uniformly implemented once commercially available than in the clinical trial. The OND concluded that while DILI remains a concern, the DILI signal appears modest in intensity and is potentially manageable with appropriate monitoring. The OND also acknowledged Akebia's comments that such monitoring is routine among dialysis patients, and therefore rigorous testing consistent with labeled recommendations is likely to be fully implemented. The OND letter states that commercial experience would be highly valuable in considering that DILI can be handled through labeling and that DILI will be an unusual event post-approval. It further advises that data from commercial experience in Japan may prove valuable in further assessing the risk of DILI. Accordingly, Akebia plans to include post-approval data from Japan in the NDA resubmission, where tens of thousands of Japanese patients with CKD have been exposed to vadadustat to date. Notably, based on the safety data the company has received from its partner in Japan, Mitsubishi Tanabe Pharma Corporation, there have been no reports of DILI in the more than two years that vadadustat has been in the market in Japan.

"We are extremely pleased with this outcome. The OND's letter provides guidance on a path for the resubmission of our NDA and potential approval of vadadustat for dialysis dependent patients in the U.S. without suggesting the need to generate additional clinical data. We appreciate the FDA's engagement with us throughout the appeal process," said John P. Butler, Chief Executive Officer of Akebia.

The OND suggested that Akebia request a Type A meeting with the Division to ensure alignment on the contents of the NDA resubmission. Akebia plans to request this meeting as soon as possible and expects to resubmit the NDA in the second half of 2023.

John Butler added, "Our team will quickly prepare for a Type A meeting with the Division and in parallel continue to prepare our resubmission. We anticipate the Division would conduct a 6-month review of our resubmission. We remain committed to patients impacted by kidney disease and believe in the favorable balance of the benefits and risks of vadadustat as a treatment for anemia due to chronic kidney disease."

Vadadustat is currently approved for use in 33 countries. In April 2023 and May 2023 respectively, the European Commission and the United Kingdom Medicines and Healthcare products Regulatory Agency granted marketing authorization for Vafseo® (vadadustat), for the treatment of symptomatic anemia associated with chronic kidney disease in adults on chronic maintenance dialysis. Also in May 2023, Akebia entered into an exclusive license agreement with Germany-based Medice, granting Medice the rights to market and sell Vafseo in the European Economic Area in addition to the United Kingdom, Switzerland and Australia. A launch of Vafseo is expected in Europe by the end of 2023. Vafseo is marketed in Japan by Mitsubishi Tanabe Pharma Corporation.

Conference Call

Akebia will host a conference call on Tuesday, May 30 at 8:30 a.m. ET to discuss the response to the FDRR and anticipated next steps. To access the call, please register by clicking on this Registration Link, and then you will be provided with dial in details. To avoid delays, we encourage dialing into the conference call fifteen minutes ahead of the scheduled start time.

A live webcast of the conference call will be available via the Investors section of Akebia's website at: **https://ir.akebia.com/**. An online archive of the webcast can be accessed via the Investors section of Akebia's website at **http://ir.akebia.com** approximately two hours after the event.

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 not approved by the U.S. Food and Drug Administration (FDA). Vadadustat is approved in Europe for the treatment of symptomatic anemia due to CKD in adult patients on chronic maintenance dialysis. In Japan, vadadustat is approved as a treatment for anemia due to CKD in both dialysis-dependent and non-dialysis dependent adult patients.

Important Safety Information

For safety information, view the European Summary of Product Characteristics (SPC/SmPC) for Vafseo® (vadadustat) at https://ec.europa.eu/health/documents/community-register/2023/20230424158854/anx_158854_en.pdf and https://products.mhra.gov.uk/.

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 plans to request a Type A meeting and then resubmit its NDA for vadadustat, including the timing thereof and data to be included therein; Akebia's expectations on the timing of review of its NDA once resubmitted; Akebia's plans and expectations with respect to commercializing Vafseo in Europe, including the timing thereof; and statements regarding the beliefs about the benefits that vadadustat could provide to patients. 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, with respect to regulatory filings; the potential demand and market potential and acceptance of, as well as coverage and reimbursement related to, vadadustat; the results of preclinical and clinical research; 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, 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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