KalVista Pharmaceuticals Announces New England Journal of Medicine Publishes Oral Sebetralstat Phase 3 Data Demonstrating its Potential to Transform the Treatment Landscape for People with Hereditary Angioedema

May 31, 2024

– Late-breaking data from phase 3 KONFIDENT trial of sebetralstat published in NEJM and presented concurrently at the European Academy of Allergy and Clinical Immunology Congress 2024 –

– Interim data from KONFIDENT-S open-label trial show median time to treatment of 9 minutes and median time to beginning of symptom relief for laryngeal attacks 1.3 hours –

CAMBRIDGE, Mass. & SALISBURY, England--(BUSINESS WIRE)--May 31, 2024-- KalVista Pharmaceuticals, Inc. (NASDAQ: KALV), today announced that late-breaking data from the pivotal phase 3 KONFIDENT trial and open label KONFIDENT-S extension trial evaluating the efficacy and safety of sebetralstat were presented as late-breaking presentations at the European Academy of Allergy and Clinical Immunology Congress 2024. The results of KONFIDENT were simultaneously published in *The New England Journal of Medicine*.

“The phase 3 KONFIDENT results represent a major advance for people living with HAE and reinforce our commitment to addressing critical gaps in the current standard of care,” said Paul Audhya, MD, MBA, KalVista’s Chief Medical Officer. “The efficacy and safety data presented as a late-breaker at EAACI and simultaneously published in *The New England Journal of Medicine* support the potential of sebetralstat as the first new treatment approach for the on-demand treatment of HAE in more than a decade, and the first potential oral therapy for this indication.”

As presented and published, the KONFIDENT trial met its primary and key secondary endpoints and demonstrated a safety profile no different from placebo.

Phase 3 KONFIDENT Trial Results

- Median time from attack onset to treatment was 41 min (Q1, 6; Q3, 140) with 55.7% of participants treating in less than 1 hour
- 42.8% of attacks treated when still mild

Primary endpoint:

- Time to beginning of symptom relief was significantly faster than placebo (p<0.0001 for 300 mg sebetralstat, p=0.0013 for 600 mg sebetralstat)
- Median time to beginning of symptom relief was 1.61 hours with sebetralstat 300 mg (IQR, 0.78-7.04), 1.79 hours with sebetralstat 600 mg (IQR, 1.02-3.79), and 6.72 hours with placebo (IQR, 1.34->12)

Key secondary endpoints:

- Significantly faster time to a reduction in attack severity from baseline compared to placebo (p=0.0036 for 300 mg sebetralstat, p=0.0032 for 600 mg sebetralstat)
- Significantly faster time to complete attack resolution compared to placebo (p=0.0022 for 300 mg sebetralstat, p<0.0001 for 600 mg sebetralstat)

Primary and key secondary endpoints were analyzed in a fixed, hierarchical sequence and adjusted for multiplicity. Subgroup analyses showed a consistency of treatment effect in among attacks regardless of attack severity, attack location, use of long-term prophylaxis, or geography.

The safety of sebetralstat at both dose levels was no different than placebo. There were no patient withdrawals due to any adverse events and no treatment-related serious adverse events (SAEs) were observed. Treatment-related adverse event rates were 2.3% for 300 mg sebetralstat, 3.2% for 600 mg sebetralstat, and 4.8% for placebo.

“For many years, HAE patients and their caregivers have sought an oral on-demand treatment option that would allow them to effectively and safely manage their attacks and take control of their disease. The KONFIDENT results demonstrate that sebetralstat has the potential to meet that need,” said Danny Cohn, MD, PhD, Department of Vascular Medicine, Amsterdam University Medical Centre, and principal investigator for the KONFIDENT phase 3 trial. “Sebetralstat provided rapid symptom relief with a safety profile no different from placebo. It was also encouraging to see that efficacy was consistent regardless of attack severity, anatomic location or the use of long-term prophylaxis. These data reinforce that, if approved, sebetralstat would have the potential to transform the treatment landscape.”

Phase 3 KONFIDENT-S Open-Label Extension Trial Interim Results (as of February 2, 2024)

- 112 participants enrolled (Europe 50.0%, US 27.7%, other 22.3%)
  - 15.2% aged 12-<18 years, 81.3% aged 18-<65 years, and 2.7% aged ≥65 years
  - 68.8% receiving on-demand treatment only; 31.3% receiving stable long-term prophylaxis
- 649 attacks treated with sebetralstat; median 5.0 attacks treated per participant (range, 1-39)
- Median time from attack onset to treatment was 9 minutes (IQR 1-69)

- Median time to beginning of symptom relief was 1.8 hours
- Median times to reduction in attack severity (6.57 hours [IQR 1.61->12]) and complete attack resolution (21.0 hours [IQR 7.22->24]) were consistent with results in the KONFIDENT Trial. KONFIDENT and KONFIDENT-S are the first and only clinical trials ever to include complete symptom relief as an endpoint; all other trials use near-complete relief, which is a much lower standard that does not capture the entire attack sequence in the same manner.
- Laryngeal attack subgroup (n=14), median time to beginning of symptom relief was 1.3 hours

“Compared to KONFIDENT, which is a placebo-controlled crossover trial, KONFIDENT-S has many real-world elements which enabled patients to treat attacks even earlier as evidenced by a median time to treatment of 9 minutes. These results further validate the promise of an oral on-demand treatment. By acting quickly, patients may halt the progression of attacks before they become severe and thereby minimize the burden of their attacks and the time to improvement and resolution of their symptoms,” said Henriette Farkas, MD, PhD, Hungarian Angioedema Center of Reference and Excellence, Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary. “Importantly, we also learned that sebetralstat’s effect in laryngeal attacks was consistent with the results in all other attack locations.”

“We want to thank the trial participants, their families, their advocates, and the investigator teams around the world who supported KONFIDENT and continue to support KONFIDENT-S. As reported at EAACI, as of May 7, 2024, KONFIDENT-S participants have treated over 1000 attacks with sebetralstat (including 24 laryngeal attacks). We look forward to submitting a new drug application for sebetralstat to the US FDA in June 2024 and in the EU and Japan later this year,” said Ben Palleiko, Chief Executive Officer of KalVista.

The publication abstract can be found at the below link:

https://www.nejm.org/doi/full/10.1056/NEJMoa2314192

Links to all posters and presentations can be found on the KalVista website under “Publications”.

About the KONFIDENT Phase 3 Trial

The KONFIDENT phase 3 trial was a randomized, double blind, event-driven, crossover clinical trial evaluating the efficacy and safety of sebetralstat 300 mg and 600 mg versus placebo for the on-demand treatment of HAE. The trial enrolled a total of 136 adult and adolescent HAE patients from 66 clinical sites across 20 countries, making it the largest clinical trial ever conducted in HAE. In the trial, patients treated each eligible attack with up to two doses of study drug, and each patient could treat up to three attacks over the course of the study. The trial included type 1 and type 2 HAE patients who had at least two attacks in 90 days prior to enrollment.

About the KONFIDENT-S Trial

The KONFIDENT-S trial is an open label extension study evaluating the long-term safety of sebetralstat for on-demand treatment of HAE attacks in adolescents (aged 12-17) and adult patients with HAE Type I or Type II. The trial is also evaluating sebetralstat for use as a short-term prophylaxis treatment prior to medical procedures.

About Sebetralstat

Discovered by KalVista, sebetralstat is an investigational novel, oral plasma kallikrein inhibitor for the on-demand treatment of hereditary angioedema (HAE). Sebetralstat received Fast Track and Orphan Drug designations from the U.S. FDA, as well as Orphan Drug Designation and an approved Pediatric Investigational Plan from the European Medicines Agency (EMA).

About Hereditary Angioedema

Hereditary angioedema (HAE) is a rare genetic disease resulting in deficiency or dysfunction in the C1 esterase inhibitor (C1INH) protein and subsequent uncontrolled activation of the kallikrein-kinin system. People living with HAE experience painful and debilitating attacks of tissue swelling in various locations of the body that can be life-threatening depending on the location affected. All currently approved on-demand treatment options require either intravenous or subcutaneous administration.

About KalVista Pharmaceuticals, Inc.

KalVista Pharmaceuticals, Inc. is a global pharmaceutical company focused on the development and delivery of oral medicines for diseases with significant unmet need. KalVista disclosed positive phase 3 data for the KONFIDENT trial for its oral, on-demand therapy sebetralstat in February 2024. The Company anticipates submitting a new drug application to the U.S. Food and Drug Administration (FDA) for sebetralstat in June 2024 and expects to file for approval in the UK, Europe, and Japan later in 2024.

For more information about KalVista, please visit www.kalvista.com.

Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties that could cause actual results to differ materially from what we expect. Examples of forward-looking statements include, among others, timing or outcomes of communications with the FDA or other international regulatory agencies, our expectations about safety and efficacy of our product candidates, our ability to obtain regulatory approvals for sebetralstat and other candidates in development within our expected timelines or at all, our success in engaging with potential commercial partners, the success of any efforts to commercialize sebetralstat, the ability of sebetralstat and other candidates in development to treat HAE or other diseases, our ability to commence pediatric trials of sebetralstat and develop an ODT formulation, the future progress and potential success of our oral Factor XIIa program, our ability to reduce spending on discovery and preclinical activities, and our expectation to become cash flow positive. Further information on potential risk factors that could affect our business and financial results are detailed in our filings with the Securities and Exchange Commission, including in our annual report on Form 10-K for the year ended April 30, 2023, our quarterly reports on Form 10-Q, and our other reports that we may make from time to time with the Securities and Exchange Commission. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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