Zevra Therapeutics Announces Top-Line Data from the Phase 2 Clinical Trial of KP1077 for Idiopathic Hypersomnia

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KP1077 demonstrates clinically meaningful benefits for key IH symptoms

Top-line data provide key information for the design of a Phase 3 study

CELEBRATION, Fla., March 26, 2024 (GLOBE NEWSWIRE) -- Zevra Therapeutics, Inc. (NasdaqGS: ZVRA) (Zevra, or the Company) a rare disease therapeutics company, today announced top-line data from its placebo-controlled, double-blind Phase 2 clinical trial (NCT05668754) evaluating the safety and tolerability of KP1077 (serdexmethylphenidate, or SDX) in patients with idiopathic hypersomnia (IH). This proof-of-concept study was not powered to demonstrate statistical significance. The data gathered for several secondary and exploratory endpoints, including the Epworth Sleepiness Scale (ESS), Idiopathic Hypersomnia Severity Scale (IHSS) and Sleep Inertia Visual Analog Scale (SIVAS) will inform the Phase 3 study design.

"Zevra's Phase 2 trial evaluating KP1077 as a treatment for IH demonstrated clinically meaningful impact and encouraging outcomes on both clinical safety and efficacy," stated Christopher Drake, PhD, FAASM, DBSM, Principal Investigator of the study. "During the open-label dose titration period, patients showed robust improvements in IH symptom severity, including excessive daytime sleepiness that were maintained during the double-blind withdrawal period. At the end of the study, patients randomized into the KP1077 treatment group also demonstrated improvements in patient reported IH specific outcomes. We look forward to presenting the final results of the Phase 2 trial at the upcoming SLEEP 2024 annual meeting."

"We're thankful to the patients in the Phase 2 clinical trial for their participation in advancing the investigational treatment, KP1077, for IH," said Neil McFarlane, Chief Executive Officer of Zevra. "We believe KP1077 has strong potential to alleviate the immense burden of key IH symptoms, including excessive daytime sleepiness, sleep inertia and brain fog, and could provide a differentiated treatment option for patients underserved by currently available therapies. We would also like to thank our IH-focused patient advocacy group partners and supporters for making this clinical trial possible. Their partnership in raising awareness for this study and supporting trial enrollment has been crucial for its success."

The positive top-line results of the Phase 2 trial support the safety and tolerability of KP1077 as measured by the primary endpoint of the study. The study also successfully fulfilled the objectives of providing key information for the design of a potentially pivotal efficacy trial, and the results of the secondary efficacy endpoints were supportive of initiating a Phase 3 trial of KP1077.

KP1077 was shown to be well-tolerated at all dose levels evaluated in the trial, including the highest dose of 320 mg daily, regardless of dosing regimen (once or twice daily). The most common adverse events were insomnia, headache, anxiety, nausea, and decreased appetite. Due to its unique pharmacokinetic profile, adverse events were mostly mild in severity despite higher overall exposure levels when compared to both immediate and long-acting methylphenidate products currently used off-label for the treatment of IH.

Topline results of the Phase 2 study include:

- KP1077 produced clinically meaningful improvement in excessive daytime sleepiness (EDS), as assessed by change from baseline in the Epworth Sleepiness Scale (ESS), that was maintained during both the five-week open-label titration period and throughout the 2-week double-blind withdrawal period for both dosing regimens.
- Patients administered KP1077 showed benefits in change from baseline for the IH Severity Scale (IHSS), Sleep Inertia Visual Analog Scale (SIVAS) and Brain Fog severity Scale (BFS) at the end of the open-label dose titration, and at the end of the double-blind withdrawal period.
- The results from the completed Phase 2 trial provide key information for the design of a potentially pivotal Phase 3 trial of KP1077 in patients with IH.

The Company plans to request an end-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration to seek guidance on the Phase 3 clinical trial design.

About the KP1077 Phase 2 Trial

The Phase 2 clinical trial was a double-blind, placebo-controlled, randomized-withdrawal, dose-optimizing, multi-center study that evaluated the safety and efficacy of KP1077 for the treatment of IH. Part 1 of the trial consisted of a five-week open-label dose titration phase during which patients were optimized to one of four doses of KP1077 (80, 160, 240, or 320 mg/day). Part 2 of the

trial entailed a two-week randomized, double-blind, withdrawal phase, during which two-thirds of the trial participants continued to receive their optimized dose while the remaining one-third received placebo. Participants were assigned into two evenly divided cohorts. The first cohort received a single daily dose just before bedtime, and the second cohort received half the daily dose shortly after awakening and the second half prior to bedtime. Zevra enrolled 66 adult patients with IH in 24 centers in the U.S into the open-label titration phase of the study and 50 of those patients continued into the double-blind phase.

The primary endpoint was the safety and tolerability of KP1077. The major secondary efficacy endpoint was the change in Epworth Sleepiness Scale (ESS) total score. Additional secondary endpoints included the IH Severity Scale (IHSS), the Sleep Inertia Visual Analog Scale (SIVAS), and a new scale to assess the symptoms and severity of brain fog.

About Idiopathic Hypersomnia (IH)

Idiopathic hypersomnia (IH) is a rare sleep disorder characterized by excessive daytime sleepiness (EDS). Patients with IH experience daytime lapses into sleep, or an irrepressible need to sleep that persists even with adequate or prolonged nighttime sleep. Additionally, those with IH have extreme difficulty waking, otherwise known as sleep inertia, severe brain fog, and often fall asleep unintentionally or at inappropriate times. These symptoms of IH often lead to further, even more debilitating problems such as memory lapses, difficulty maintaining focus, and depression.

It is estimated, based on claims data, that approximately 37,000 patients in the United States are currently diagnosed with IH, although the total patient population may be much larger due to some patients who have not yet been diagnosed, have been misdiagnosed, or are not currently seeking treatment.

About KP1077

KP1077 (serdexmethylphenidate or SDX) is Zevra's proprietary prodrug of d-methylphenidate (d-MPH) and its sole active pharmaceutical ingredient (API). KP1077 has been granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) for the treatment of IH, and the U.S. Drug Enforcement Agency (DEA) has classified SDX, the sole API in KP1077, as a Schedule IV controlled substance based on evidence suggesting SDX has a lower potential for abuse when compared to d-MPH, a Schedule II controlled substance.

About Zevra Therapeutics

Zevra Therapeutics is a rare disease company combining science, data, and patient needs to create transformational therapies for diseases with limited or no treatment options. Our mission is to bring life-changing therapeutics to people living with rare diseases. With unique, data-driven development and commercialization strategies, the Company is overcoming complex drug development challenges to make new therapies available to the rare disease community.

For more information, please visit www.zevra.com or follow us on X (formerly Twitter) and LinkedIn.

Caution Concerning Forward-Looking Statements

This press release may contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include all statements that do not relate solely to historical or current facts, including without limitation statements regarding the promise and potential impact of our preclinical or clinical trial data; the design, initiation, timing and results of any clinical trials or readouts; interpretations of trial data outcomes on clinical safety and efficacy; Zevra's reports regarding or presentation of trial data, including at conferences, or the timing thereof; the promise and potential impact of any of our products or product candidates for any specific disease indication or at any dosage; Zevra's plans to request an end-of-Phase 2 (EOP2) meeting; the potential launch or commercialization of any of product candidates or products, and our strategic and product development objectives, including with respect to becoming a leading, commercially focused rare disease company. Forward-looking statements are based on information currently available to Zevra and its current plans or expectations. They are subject to several known and unknown uncertainties, risks, and other important factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. These and other important factors are described in detail in the "Risk Factors" section of Zevra's Annual Report on Form 10-K for the year ended December 31, 2022, as updated in Zevra's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, and Zevra's other filings with the Securities and Exchange Commission. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Although we believe the expectations reflected in such forward-looking statements are reasonable, we cannot assure that such expectations will prove correct. These forward-looking statements should not be relied upon as representing our views as of any date after the date of this press release.

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