Zevra Therapeutics Announces Positive Final Results from Phase 2 Clinical Trial of KP1077 for Idiopathic Hypersomnia at SLEEP 2024 Annual Meeting

June 3, 2024 3:00 PM EDT

KP1077 was well tolerated and showed meaningful clinical improvements in patient-reported assessments of daytime sleepiness, sleep inertia, and brain fog

Additional data presented on pharmacokinetics of morning and nighttime doses of KP1077

European Commission has granted Orphan Drug Designation for KP1077 for the treatment of idiopathic hypersomnia

CELEBRATION, Fla., June 03, 2024 (GLOBE NEWSWIRE) -- Zevra Therapeutics, Inc. (NasdaqGS: ZVRA) (Zevra, or the Company), a rare disease therapeutics company, today announced that final positive results 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) were presented in a poster at SLEEP 2024, the 38th annual joint meeting of the American Academy of Sleep Medicine and the Sleep Research Society, held in Houston, TX, June 1-5, 2024. In addition, a second poster describing the pharmacokinetics of SDX when administered in the morning and at night was also presented.

"We are encouraged by the positive results of the Phase 2 clinical trial, which serve as further support of KP1077 as a strong candidate to treat patients struggling with idiopathic hypersomnia," said Adrian Quartel, MD, FFPM, Chief Medical Officer of Zevra. "We believe that KP1077 has great potential to provide a differentiated treatment option for patients underserved by currently available therapies."

This proof-of-concept study was designed to demonstrate safety and tolerability and was not powered to demonstrate statistical significance. However, the trial included several important secondary and exploratory endpoints, such as change in Epworth Sleepiness Scale (ESS) total score, 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. These data gathered from the secondary endpoints will help inform the study design for a potential Phase 3 clinical trial of KP1077.

"The results of the Phase 2 clinical trial support the safety and tolerability of KP1077 as measured by the primary endpoint of the study," stated Christopher Drake, PhD, FAASM, DBSM, Principal Investigator of the study. "The clinically meaningful impact for both the safety and efficacy were well demonstrated by patients showing significant improvements in IH symptom severity such as sleep inertia, excessive daytime sleepiness (EDS), and patient-reported IH-specific outcomes."

Key Takeaways from Phase 2 Clinical Trial of KP1077 for Idiopathic Hypersomnia:

- KP1077 was well tolerated at all dose levels evaluated in the trial, including the highest dose of 320 mg daily, regardless of the dosing regimen: once daily (QD) or twice daily (BID).
  - Adverse events (AEs) were similar to other methylphenidate products
  - Most common AEs included insomnia, headache, anxiety, decreased appetite, and nausea
  - Most AEs occurred during the titration period, were mild, and did not lead to early discontinuation
- KP1077 produced clinically meaningful improvements in EDS as assessed by change from baseline in the ESS during both the 5-week open-label (OL) titration period which was maintained during the 2-week double-blind withdrawal period for both dosing regimens.
  - Mean total ESS scores decreased by approximately 9 points after 5 weeks of OL treatment.
- At the end of 7 weeks of treatment, patients administered KP1077 showed clinically meaningful benefits in change from baseline for the ESS, IHSS, SIVAS, and Brain Fog Scale (BFS):
  - Mean total ESS score decreased by 9.4 (QD) and 8.8 (BID)
  - Mean total IHSS score decreased by 16.1 (QD) and 12.3 (BID)
  - Mean SIVAS score decreased by 25.9 (QD) and 17.2 (BID)
  - Mean total BFS symptom score decreased by 23.8 (QD) and 22.3 (BID)

- The study successfully fulfilled the objectives of providing key information for the design of a pivotal efficacy trial, and the results of the secondary efficacy endpoints were supportive of initiating a Phase 3 trial of KP1077.

Separately, the pharmacokinetics of morning and nighttime dose of KP1077 was studied. These data are also being presented in a poster at SLEEP 2024.

Key Takeaways from Pharmacokinetics of Morning and Nighttime Doses of KP1077

Based on the Phase 2 trial results, the Company believes that:

- Peak exposure of SDX-derived d-MPH after a nighttime dose of SDX occurs during the next morning leading to higher exposure at awakening compared to a morning dose.
- The delay in exposure is likely due to a longer intestinal transit time and lower intestinal activity during the nighttime sleeping hours.
- The delay in exposure supports nighttime dosing of SDX in patients with IH who suffer from EDS and sleep inertia (difficulty waking up in the morning).

The results from each study were discussed during two poster presentations in Hall A3, Poster Presentation Session P-13:

- **Title:** *Safety and Efficacy of KP1077 in a Phase 2, Double-blind, Randomized Trial in Patients with Idiopathic Hypersomnia*
  Date/Time: June 3, *2*024, 10 a.m. to 11:45 a.m. CDT

- **Title:** *Pharmacokinetics of Morning and Nighttime Doses of KP1077, an Investigational Treatment for Idiopathic Hypersomnia*
  Date/Time: June 3, 2024, 10 a.m. to 11:45 a.m. CDT

Representatives from Zevra Therapeutics are also available during exhibit hours at Booth #1421 for additional discussion. Zevra proudly supports the *Hypersomnia Foundation's* mission to raise awareness, educate, and uplift the voices of those living with idiopathic hypersomnia and was proud to participate in the inaugural *Idiopathic Hypersomnia* Day (IH Day) on June 1, 2024. IH Day, held in Houston during the Hypersomnia Foundation's *BeyondSleepy Conference*, served as the kickoff to *Idiopathic Hypersomnia Awareness Week*, which runs through June 7, 2024.

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 5-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
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), and by the European Commission, for the treatment of IH. 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. In addition, KP1077 has intellectual property protection through 2037 and potentially beyond.

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.

Expanded access programs are made available by Zevra Therapeutics and its affiliates and are subject to the Company's Expanded Access Program

(EAP) policy as published on its website. Participation in these programs is subject to the laws and regulations of each jurisdiction under which each respective program is operated. Eligibility for participation in any such program is at the treating physician's discretion.

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

About American Academy of Sleep Medicine
Established in 1975 as the Association of Sleep Disorders Centers, the American Academy of Sleep Medicine (AASM) is the only professional society dedicated exclusively to the medical subspecialty of sleep medicine. As the leading voice in the sleep field, the AASM sets standards and promotes excellence in sleep medicine health care, education, and research. The AASM has a combined membership of 11,000 accredited member sleep centers and individual members, including physicians, scientists, and other health care professionals.

About the Sleep Research Society
The Sleep Research Society (SRS) is an organization for scientific investigators who educate and research sleep and circadian science. The SRS serves its members and the field of sleep research through training and education, and by providing forums for the collaboration and the exchange of ideas.

Cautionary Note 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 initiation, timing, design, or results of any clinical trials or readouts, the potential benefits of any of our products or product candidates for any specific disease indication or at any dosage, and upcoming events or Zevra's participation at such events. 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, 2023, Zevra's quarterly report for the three months ended March 31, 2024, 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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