Zevra Therapeutics Presented New Data for Arimoclomol and OLPRUVA® (Sodium Phenylbutyrate) at the Society for the Study of Inborn Errors of Metabolism (SSIEM) 2024 Annual Symposium

September 6, 2024

New clinical efficacy and safety data for arimoclomol as a possible treatment for Niemann-Pick disease type C, including from long-term and real-world settings, demonstrate clinically meaningful reduction in disease progression

Arimoclomol was well tolerated during the Open Label Extension trial and Early Access Program with no safety signals identified

PK modeling studies showed that administration of OLPRUVA while fasting vs fed results in higher drug exposure which may allow for lower effective dosages when taken without food

CELEBRATION, Fla., Sept. 06, 2024 (GLOBE NEWSWIRE) -- Zevra Therapeutics, Inc. (NasdaqGS: ZVRA) (Zevra, or the Company), a rare disease therapeutics company, today announced the presentation of five posters at the Society for the Study of Inborn Errors of Metabolism (SSIEM) 2024 Annual Symposium. Four posters focused on data from multiple studies showing the efficacy and safety of arimoclomol as a treatment for people living with Niemann-Pick disease type C (NPC), and one poster highlighted data from pharmacokinetic modeling studies of OLPRUVA®, a therapy for the long-term management of certain adult and pediatric patients with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC) or argininosuccinic acid synthetase (AS).

"The data collected during the Phase 2/3 study of arimoclomol, including long-term data from Open Label Extension (OLE) and Early Access Program (EAP) participants, add to the large body of evidence that demonstrates arimoclomol's clinical efficacy and safety as a treatment for people living with NPC," said Adrian Quartel, M.D., FFPM, Chief Medical Officer of Zevra. "Additionally, we presented PK modeling data from OLPRUVA in both adult and pediatric virtual patients, showing an increase in drug exposure under fasting conditions."

Presentation Details

The data for arimoclomol presented at SSIEM is summarized below:

Poster Number: 21260

Title: Efficacy Results from a 12-month Double-blind Randomized Trial of Arimoclomol for Treatment of Niemann Pick Disease Type C – presenting an improved 4-Domain NPC Clinical Severity Scale

Authors: Marc Patterson, Sven Guenther and Christine i Dali

Summary: The treatment effect of arimoclomol was evaluated in a 12-month, double-blind, placebo-controlled clinical trial (NCT02612129) using the original 5-domain Niemann pick type C clinical severity scale (5DNPCCSS) and the modified 4-domain Niemann Pick type C clinical severity scale (4DNPCCSS). A statistically significant treatment effect was shown using the modified 4DNPCCSS and the prespecified 5DNPCCSS primary endpoint in the 12-month clinical trial, representing a clinically meaningful reduction in disease progression with arimoclomol treatment compared to placebo.

Poster Number: 21271

Title: Long-term Efficacy and Safety Evaluation of Arimoclomol Treatment in Patients with Niemann Pick Type C – Data from 48 Months Open Label Trial

Authors: Marc Patterson, Eugene Mengel, Sven Guenther and Christine i Dali

Summary: The long-term safety and efficacy of arimoclomol in the 12-month double-blind, and 48-month open-label extension (OLE) portion of the clinical trial (NCT02612129) were presented using the 4-Domain Niemann Pick Type C Clinical Severity scale (4DNPCCSS) which evaluates ambulation, speech, swallowing and fine motor skills. For those patients transitioning from placebo to arimoclomol at the start of the open-label extension

period, the mean annual rate of disease progression reduced from an annual rate of change of 1.9 points during the double-blind phase, to a rate of 0.3 in the first 12 months of treatment, remained numerically smaller for the rest of the trial, and was comparable between the double-blind phase of the trial and the open-label extension phase of the trial. Additionally, arimoclomol was well tolerated with no new safety signals observed.

Poster Number: PO-212

Title: Arimoclomol for the Treatment of NPC in a Real-World Setting: Long-term Outcomes from an Expanded Access Program in the USA

Authors: Walla Al-Hertani, Elizabeth M. Berry-Kravis, Raymond Wang, Marc Patterson, Can Ficicioglu, Loren Pena, Kristina Julich, Damara Ortiz, Paula Schleifer, Caroline Hastings, Paul Hillman, Ronan O'Reilly, Christine Dali and Daniel Gallo

Summary: The long-term safety and efficacy of arimoclomol in a real-world setting were evaluated in a total of 56 adult and pediatric patients in the U.S. arimoclomol expanded access program (EAP) trial (NCT04316637). Data presented included over 3 years of U.S. EAP clinical outcomes and demonstrated that adult and pediatric patients treated with arimoclomol, including those with and without miglustat as a component of their routine clinical care, experienced relatively stable disease as measured by the 5DNPCCSS and 4DNPCCSS and show that arimoclomol was well tolerated.

Poster Number: 20950

Title: Arimoclomol safety profile in the treatment of NPC in a Real-World setting: Long-term data from an Expanded Access program in the USA

Authors: Can Ficicioglu, Elizabeth M. Berry-Kravis, Walla Al-Hertani, Raymond Wang, Marc Patterson, Loren Pena, Kristina Julich, Damara Ortiz, Paula Schleifer, Paul Hillman, Caroline Hastings, Ronan O'Reilly, Christine Dali and Daniel Gallo

Summary: Safety data from 94 adult and pediatric participants in the arimoclomol US EAP were presented. Safety outcomes reported from exposure periods spanning as much as 46 months of treatment, demonstrated a safety profile consistent with the published clinical trial experience of arimoclomol in NPC.

The data for OLPRUVA presented at SSIEM is summarized below:

Poster Number: PO-609

Title: Modeling the Pharmacokinetics of Phenylbutyrate in Fed and Fasted States

Authors: Steiner, Rebecca Baillie, Tongli Zhang, Christina Friedrich, Meredith Hart, Mike Reed

Summary: Pharmacokinetic modeling evaluating whether sodium phenylbutyrate (NaPBA) could be safely and effectively administered while fasting showed greater absorption and bioavailability with increased drug exposure in fasted administration of NaPBA compared to fed administration of NaPBA and glycerol phenylbutyrate (GPB) in both adult and child virtual patients, which is predicted to increase efficacy in proportion to increased drug exposure, theoretically allowing for a 30% dose decrease compared to fed conditions.

About the SSIEM 2024 Annual Symposium

The Society for the Study of Inborn Errors of Metabolism (SSIEM) 2024 Annual Symposium took place September 3-6, 2024, in Porto, Portugal. The annual symposium is intended to foster the study of inherited metabolic disorders and promote the exchange of ideas between professionals in different disciplines who are researching inborn errors of metabolism (IEM).

About Niemann-Pick Disease Type C (NPC)

Niemann-Pick disease type C (NPC) is an ultra-rare, progressive, and neurodegenerative lysosomal storage disorder characterized by an inability of the body to transport cholesterol and other lipids within the cell, leading to an accumulation of these substances in various tissue areas, including brain tissue. The disease is caused by mutations in the NPC1 or NPC2 genes, which are responsible for making lysosomal proteins. Both children and adults can be affected by NPC with varying clinical presentations. Those living with NPC lose independence due to physical and cognitive limitations, with key neurological

impairments presenting in speech, cognition, swallowing, ambulation, and fine motor skills. Disease progression is irreversible and can be fatal within months or take years to be diagnosed and advance in severity.

About Arimoclomol

Arimoclomol, Zevra's orally-delivered, investigational drug product candidate for the treatment of NPC, has been granted Orphan Drug designation, Fast Track designation, Breakthrough Therapy designation, and Rare Pediatric Disease designation by the FDA, and Orphan Medicinal Product designation for the treatment of NPC by the European Medicines Agency (EMA). The FDA has accepted the resubmission of the NDA for arimoclomol and has set a user fee action date (PDUFA date) of September 21, 2024.

About Urea Cycle Disorders

UCDs are a group of rare, genetic disorders that can cause harmful ammonia to build up in the blood, potentially resulting in brain damage and neurocognitive impairments if ammonia levels are not controlled. Any increase in ammonia over time is serious. Therefore, it is important to adhere to any dietary protein restrictions and have alternative medication options to help control ammonia levels.

About OLPRUVA®

OLPRUVA (sodium phenylbutyrate) was approved for the treatment of certain UCDs in December 2022 and has recently been marketed under the brand name, OLPRUVA®. OLPRUVA (sodium phenylbutyrate) for oral suspension is a prescription medicine used along with certain therapies, including changes in diet, for the long-term management of adults and children weighing 44 pounds (20 kg) or greater and with a body surface area (BSA) of 1.2 m^2 or greater, with UCDs, involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). OLPRUVA is not used to treat rapid increase of ammonia in the blood (acute hyperammonemia), which can be life-threatening and requires emergency medical treatment. For more information, please visit www.OLPRUVA.com.

Important Safety Information

Certain medicines may increase the level of ammonia in your blood or cause serious side effects when taken during treatment with OLPRUVA. Tell your doctor about all the medicines you or your child take, especially if you or your child take corticosteroids, valproic acid, haloperidol, and/or probenecid.

OLPRUVA can cause serious side effects, including: 1) nervous system problems (neurotoxicity). Symptoms include sleepiness, tiredness, lightheadedness, vomiting, nausea, headache, confusion, 2) low potassium levels in your blood (hypokalemia) and 3) conditions related to swelling (edema). OLPRUVA contains salt (sodium), which can cause swelling from salt and water retention. Tell your doctor right away if you or your child get any of these symptoms. Your doctor may do certain blood tests to check for side effects during treatment with OLPRUVA. If you have certain medical conditions such as heart, liver or kidney problems, are pregnant/planning to get pregnant or breast-feeding, your doctor will decide if OLPRUVA is right for you.

The most common side effects of OLPRUVA include absent or irregular menstrual periods, decreased appetite, body odor, bad taste or avoiding foods you ate prior to getting sick (taste aversion). These are not all of the possible side effects of OLPRUVA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

About Zevra Therapeutics, Inc.

Zevra Therapeutics, Inc. 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 and its affiliates and are subject to the Company's Expanded Access Program (EAP) policy as published on its website at www.zevra.com. 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.

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 zpotential impact of our preclinical or clinical trial data; the initiation, timing and results of any clinical trials or readouts, the content, information used for, timing or results of any NDA submissions or resubmissions for arimoclomol or any other product candidates for any specific disease indication or at any dosage; the potential benefits of any of our products or product candidates for any specific disease or at any dosage; our strategic and product development objectives, including with respect to becoming a leading, commercially focused rare disease company; potential revenues from our arimoclomol expanded access program; the potential for royalty and milestone contributions, the presentation of

data at conferences; and the timing of any of the foregoing. 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 on Form 10-Q for the three months ended June 30, 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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