Zevra Therapeutics' MIPLYFFA™ (arimoclomol) Receives U.S. FDA Approval as Treatment for Niemann-Pick Disease Type C

September 20, 2024

MIPLYFFA is the first FDA-approved treatment for Niemann-Pick disease type C (NPC), an ultra-rare and progressive neurodegenerative disease

MIPLYFFA is indicated for use in combination with miglustat for the treatment of neurological manifestations of NPC in adults and pediatric patients 2 years of age and older

Zevra receives rare pediatric disease priority review voucher in conjunction with approval

Company launches AmplifyAssist™ patient support program

Conference call and webcast set for 8:00 a.m. EDT on Monday, Sept. 23, 2024

CELEBRATION, Fla., Sept. 20, 2024 (GLOBE NEWSWIRE) -- Zevra Therapeutics, Inc. (NasdaqGS: ZVRA) (Zevra, or the Company), a commercial-stage rare disease therapeutics company, today announced that the U.S. Food and Drug Administration (FDA) has approved MIPLYFFA™ (MY-PLY-FAH) (arimoclomol) capsules as an orally delivered treatment for Niemann-Pick disease type C (NPC). The first NPC drug approved by the FDA, MIPLYFFA is indicated for use in combination with miglustat for the treatment of neurological manifestations of NPC in adult and pediatric patients 2 years of age and older. In addition, the Company announced that it has received a rare pediatric disease priority review voucher (PRV) in conjunction with the approval.

"NPC is an ultra-rare, relentlessly progressive, degenerative, and fatal disease for which there were no FDA-approved treatment options until today," said Neil F. McFarlane, President and Chief Executive Officer of Zevra Therapeutics, Inc. "The approval of MIPLYFFA is a monumental milestone for NPC patients and their family members in the U.S. We are immensely grateful for the unwavering support we have received over the years from the families and individuals impacted by NPC as well as the collaborative efforts of advocacy groups, researchers, and clinicians."

In the U.S., it is estimated that 900 people are living with NPC, of which approximately one-third have been diagnosed with this ultra-rare, relentlessly progressive, and fatal neurodegenerative disease.[i] Both children and adults can be affected by NPC with varying clinical presentations. Characteristically, those living with NPC experience progressive physical and cognitive limitations, with key neurological impairments presenting in speech, cognition, swallowing, ambulation, and fine motor skills.

"Until now, those living with NPC have had no FDA-approved treatment to combat this devastating disease," said Laurie Turner, Family Services Manager, National Niemann-Pick Disease Foundation (NNPDF). "For more than 30 years, NNPDF and the community have been working to find treatments for NPC, and we are grateful for the diligence and commitment of the researchers, clinicians, families and Zevra for making this approval possible."

"The FDA approval of MIPLYFFA marks a significant moment for those living with NPC and the global NPC community," *stated Dr. Elizabeth Berry-Kravis, Professor, Departments of Pediatrics, Neurological Sciences, Anatomy and Cell Biology, Director, RUSH Pediatric Neurosciences F.A.S.T. Center for Translational Research at Rush University Medical Center,* "Effective management of NPC requires multiple treatment options due to the complexity of the disease. Until today, there were no approved therapies in the U.S. for NPC. With this labeled indication, patients will now have more access to treatments to tackle this devastating disease."

The approval of MIPLYFFA for the treatment of NPC is based on the totality of the data in the New Drug Application (NDA), which included additional evidence supporting trial endpoints, FDA-preferred analyses, and additional confirmatory evidence, both clinical and nonclinical. The safety and effectiveness of MIPLYFFA were studied in a 12-month multicenter, randomized, double-blind, placebo-controlled trial in patients with NPC between two and 19 years of age. In this trial, 76% of patients in the MIPLYFFA group and 81% of those in the placebo group received miglustat as part of their routine care. The effectiveness of MIPLYFFA was evaluated using the rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS). Results from this trial demonstrated:

- MIPLYFFA, in combination with miglustat, halted disease progression through 12 months of treatment, as demonstrated by a decrease of 0.2 points from baseline on the R4DNPCCSS compared to 1.9 points of progression for patients treated with miglustat alone.

Additional confirmatory evidence included data from a 48-month open-label extension study which suggested improved outcomes when compared to a matched National Institutes of Health NPC natural history cohort.

MIPLYFFA is administered orally, three times a day with or without food, with the exact dosage ranging from 47 mg to 124 mg dependent on body weight, by appropriate patients or caregivers with follow-up from a healthcare provider. Healthcare providers and patients/caregivers should refer to the Full Prescribing Information and Instructions for Use for information on the proper administration of MIPLYFFA.

Zevra will immediately initiate its launch activities for MIPLYFFA, which is expected to be commercially available in the U.S. in eight to 12 weeks.

Launch of AmplifyAssist™ —Comprehensive Support for Patients

Zevra is committed to assisting those whose lives are affected by NPC to overcome the barriers and challenges that may impact their treatment journey. The Company today launched AmplifyAssist, Zevra's comprehensive patient support program. The mission of the program is to support the individual needs of eligible patients and those who care for them. Available resources include personalized insurance coverage education and support, copay and alternate funding identification assistance for eligible patients, product needs, disease state information and therapy management counseling, and ongoing interactions to address barriers while facilitating timely prescription refills. Information about the program is available at MIPLYFFA.com or via telephone. The AmplifyAssist team can be reached toll-free at (888) 668-4198 from 8 a.m. CT to 6 p.m. CT Monday through Friday. Healthcare providers who want to submit prescriptions can visit MIPLYFFA.com to complete the prescription enrollment form that initiates the process for accessing the treatment.

Conference Call and Webcast Information

Zevra Therapeutics, Inc. will host a conference call and audio webcast at 8 a.m. ET on Monday, September 23, 2024, to discuss FDA approval of MIPLYFFA. A link to the audio webcast will be accessible via the Investor Relations section of the Company's website, https://investors.zevra.com/. To join the meeting by conference call, use the dial-in information below:

(800) 267-6316 (U.S.)
+1 (203) 518- 9783 (International)
Conference ID: ZVRA0923

An archive of the webcast will be available for ninety (90) days beginning at approximately 9 a.m. ET, on September 23, 2024, at https://investors.zevra.com/.

About MIPLYFFA™ (arimoclomol)

MIPLYFFA (arimoclomol) increases the activation of the transcription factors EB (TFEB) and E3 (TFE3) resulting in the upregulation of coordinated lysosomal expression and regulation (CLEAR) genes. MIPLYFFA has also been shown to reduce unesterified cholesterol in the lysosomes of human NPC fibroblasts. The clinical significance of these findings is not fully understood. MIPLYFFA was granted Breakthrough Therapy designation, Rare Pediatric Disease designation, Orphan Drug designation, and Fast Track designation by the FDA for the treatment of NPC. MIPLYFFA was further granted Orphan Medicinal Product designation by the European Medicines Agency (EMA) for the treatment of NPC.

INDICATIONS AND USAGE

MIPLYFFA is indicated for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older.

IMPORTANT SAFETY INFORMATION

Hypersensitivity Reactions:

Hypersensitivity reactions such as urticaria and angioedema have been reported in patients treated with MIPLYFFA during Trial 1: two patients reported both urticaria and angioedema (6%) and one patient (3%) experienced urticaria alone within the first two months of treatment. Discontinue MIPLYFFA in patients who develop severe hypersensitivity reactions. If a mild or moderate hypersensitivity reaction occurs, stop MIPLYFFA and treat promptly. Monitor the patient until signs and symptoms resolve.

Embryofetal Toxicity:

MIPLYFFA may cause embryofetal harm when administered during pregnancy based on findings from animal reproduction studies. Advise pregnant females of the potential risk to the fetus and consider pregnancy planning and prevention for females of reproductive potential.

Increased Creatinine without Affecting Glomerular Function:
Across clinical trials of MIPLYFFA, mean increases in serum creatinine of 10% to 20% compared to baseline were reported. These increases occurred mostly in the first month of MIPLYFFA treatment and were not associated with changes in glomerular function.

During MIPLYFFA treatment, use alternative measures that are not based on creatinine to assess renal function. Increases in creatinine reversed upon MIPLYFFA discontinuation.

The most common adverse reactions in Trial 1 (≥15%) in MIPLYFFA-treated patients who also received miglustat were upper respiratory tract infection, diarrhea, and decreased weight.

Three (6%) of the MIPLYFFA-treated patients had the following adverse reactions that led to withdrawal from Trial 1: increased serum creatinine (one patient), and progressive urticaria and angioedema (two patients). Serious adverse reactions reported in MIPLYFFA-treated patients were hypersensitivity reactions including urticaria and angioedema.

To report SUSPECTED ADVERSE REACTIONS, contact Zevra Therapeutics, Inc. at toll-free phone 1-844-600-2237 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interaction(s):
Arimoclomol is an inhibitor of the organic cationic transporter 2 (OCT2) transporter and may increase the exposure of drugs that are OCT2 substrates. When MIPLYFFA is used concomitantly with OCT2 substrates, monitor for adverse reactions and reduce the dosage of the OCT2 substrate.

Use in Females and Males of Reproductive Potential:
Based on animal findings, MIPLYFFA may impair fertility and may increase post-implantation loss and reduce maternal, placental, and fetal weights.

Renal Impairment:
The recommended dosage of MIPLYFFA, in combination with miglustat, in patients with an eGFR ≥15 mL/minute to <50 mL/minute is lower than the recommended dosage (less frequent dosing) in patients with normal renal function.

MIPLYFFA capsules for oral use are available in the following strengths: 47 mg, 62 mg, 93 mg, and 124 mg.

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 cell types, including neurons. The disease is caused by mutations in the *NPC1* or *NPC2* genes, which are responsible for making the *NPC1* and *NPC2* lysosomal proteins. Both children and adults can be affected by NPC with varying clinical presentations. Those living with NPC can lose independence due to physical and cognitive limitations, with key neurological impairments presenting in speech, cognition, swallowing, ambulation, and fine motor skills. Disease diagnosis can often take years, with disease progression being irreversible and often leading to early mortality.

About Zevra Therapeutics, Inc.

Zevra Therapeutics, Inc. is a commercial-stage 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, Inc. 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.

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 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 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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i. Burton et.al., Molecular Genetics and Metabolism Volume 134, Issues 1–2, September–October 2021, Pages 182-187

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