Rhythm Pharmaceuticals Announces Clinical Development Plan of Setmelanotide for Hypothalamic Obesity in Japan

February 22, 2024

-- Supplemental cohort of 12 Japanese patients to be added to global Phase 3 hypothalamic obesity trial, with dosing expected to begin in third quarter of 2024 --

-- Significant unmet need with 5,000 to 8,000 patients with hypothalamic obesity estimated to be living in Japan --

BOSTON, Feb. 22, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a global commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with rare neuroendocrine diseases, today announced plans to add a cohort of patients with hypothalamic obesity in Japan to its ongoing global Phase 3 clinical trial of setmelanotide, with dosing expected to begin in the third quarter of 2024.

"Following constructive discussions with Japan's Pharmaceuticals and Medical Devices Agency (PMDA), we are pleased to have developed a clear and efficient plan to support the potential approval of setmelanotide for hypothalamic obesity in Japan," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "With data showing a higher per-capita incidence and prevalence of patients with hypothalamic obesity in Japan compared to the United States and Europe and no approved therapeutic options, there is a major unmet need for a therapy to treat the rapid onset of severe obesity and hyperphagia of hypothalamic obesity."

Rhythm estimates that there are approximately 5,000 to 8,000 patients in Japan with hypothalamic obesity, a rare form of obesity that occurs following damage to the hypothalamic region of the brain, which includes the melanocortin-4 receptor (MC4R) pathway and is responsible for controlling physiological functions such as hunger and weight regulation. The condition most frequently follows the growth and surgical removal or other treatment of craniopharyngioma, astrocytoma, or other rare brain tumors. These individuals often experience rapid weight gain, a reduction in energy expenditure, and an increase in hunger leading to severe obesity within six to 12 months following the hypothalamic lesions.

The Company and Japan's PMDA agreed to add a cohort of 12 Japanese patients to the ongoing trial and, pending completion of the trial, to use these data as part of the Company's registration package to seek approval from Japan's Ministry of Health, Labor and Welfare. In addition to efficacy data, Rhythm will collect and submit pharmacokinetics (PK) data from Japanese patients, expediting the typical pathway of collecting such data from an earlier-stage trial in Japanese subjects.

Rhythm also announced today that it completed enrollment in the pivotal, 120-patient cohort in its global Phase 3 trial of setmelanotide in hypothalamic obesity with patients, aged 4 years or older with hypothalamic obesity randomized 2:1 to setmelanotide therapy or placebo for a total of 60 weeks, including up to eight weeks for dose titration. As agreed to with both the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA), Rhythm's regulatory submissions would be based on data from this cohort. The additional 12-patient Japanese cohort will not affect timing for regulatory submissions in the United States or Europe. The Company remains on track to obtain top-line study results in the first half of 2025.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with rare neuroendocrine diseases. Rhythm's lead asset, IMCIVREE ® (setmelanotide), an MC4R agonist designed to treat hyperphagia and severe obesity, is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency confirmed by genetic testing, or patients with a clinical diagnosis of Bardet-Biedl syndrome (BBS). Both the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare diseases, as well as RM-718 and a preclinical suite of small molecules for the treatment of congenital hyperinsulinism. Rhythm's headquarters is in Boston, MA.

Setmelanotide Indication

In the United States, setmelanotide is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to POMC, PCSK1 or LEPR deficiency as determined by an FDA-approved test demonstrating variants in *POMC*, *PCSK1* or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) or BBS.

In the European Union, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. In Europe, setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

Limitations of Use

Setmelanotide is not indicated for the treatment of patients with the following conditions as setmelanotide would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1 or LEPR deficiency with *POMC*, *PCSK1* or *LEPR* variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Contraindication

Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

WARNINGS AND PRECAUTIONS

Skin Pigmentation and Darkening of Pre-Existing Nevi: Generalized increased skin pigmentation and darkening of pre-existing nevi have occurred because of its pharmacologic effect. Full body skin examinations prior to initiation and periodically during treatment should be conducted to monitor pre-existing and new pigmentary lesions.

Heart rate and blood pressure monitoring: In Europe, heart rate and blood pressure should be monitored as part of standard clinical practice at each medical visit (at least every 6 months) for patients treated with setmelanotide.

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Patients who have an erection lasting longer than 4 hours should seek emergency medical attention.

Depression and Suicidal Ideation: Depression and suicidal ideation have occurred. Patients should be monitored for new onset or worsening depression or suicidal thoughts or behaviors. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. If suspected, advise patients to promptly seek medical attention and discontinue setmelanotide.

Pediatric Population: The prescribing physician should periodically assess response to setmelanotide therapy. In growing children, the impact of weight loss on growth and maturation should be evaluated. In Europe, the prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: Setmelanotide is not approved for use in neonates or infants. Serious and fatal adverse reactions including “gasping syndrome” can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs.

ADVERSE REACTIONS
Most common adverse reactions (incidence ≥20%) included skin hyperpigmentation, injection site reactions, nausea, headache, diarrhea, abdominal pain, vomiting, depression, and spontaneous penile erection.

USE IN SPECIFIC POPULATIONS

Lactation: Not recommended when breastfeeding.
To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. See section 4.8 of the Summary of Product Characteristics for information on reporting suspected adverse reactions in Europe.

Please see the full Prescribing Information for additional Important Safety Information.

Forward-looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical design or progress, potential regulatory submissions, approvals and timing thereof, including our Phase 3 trial of setmelanotide for patients with hypothalamic obesity in Japan, the United States or in Europe, the potential benefits of setmelanotide for patients with hypothalamic obesity, and our business strategy and plans, including regarding commercialization of IMCIVREE. Statements using word such as “expect”, “anticipate”, “believe”, “may”, “will” and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the impact of competition, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our ability to successfully commercialize setmelanotide, our liquidity and expenses, our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel, and general economic conditions, and the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended September 30, 2023 and our other filings with the Securities and Exchange Commission. Except as required by law, we undertake no obligations to make any revisions to the forward-looking statements contained in this release or to update them to reflect events or circumstances occurring after the date of this release, whether as a result of new information, future developments or otherwise.

Corporate Contact:
David Connolly
Head of Investor Relations and Corporate Communications
Rhythm Pharmaceuticals, Inc.
857-264-4280
dconnolly@rhythmtx.com

Media Contact:

Adam Daley
Berry & Company Public Relations
212-253-8881
adaley@berrypr.com

Source: Rhythm Pharmaceuticals, Inc.