Rhythm Pharmaceuticals Announces Publication of Results from Phase 3 Study of Setmelanotide in Patients Between 2 and 5 Years Old in The Lancet Diabetes & Endocrinology

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BOSTON, Nov. 13, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a global commercial-stage biopharmaceutical company focused on transforming the lives of patients living with rare neuroendocrine diseases, today announced the publication of results from its Phase 3 VENTURE trial evaluating setmelanotide, a melanocortin-4 receptor (MC4R) agonist, in children between the ages of 2 and younger than 5 years old with Bardet Biedl syndrome (BBS) or pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency. The data are published in the peer-reviewed journal *The Lancet Diabetes & Endocrinology*.

“Severe, early-onset obesity has been shown to have a negative short-term and long-term impact on a child’s health,” said Professor Jesús Argente, M.D., Ph.D., Department of Pediatrics and Pediatric Endocrinology, Hospital Infantil Universitario Niño Jesús and Universidad Autónoma de Madrid, Madrid, Spain. “In this study, setmelanotide demonstrated clinically meaningful reductions in hunger and body weight in patients younger than 5 years of age with severe obesity. We believe these data support the use of this targeted therapy in a patient population that could benefit from intervention as early as possible.”

Rhythm enrolled 12 patients in its open-label 52-week Phase 3 VENTURE trial designed to evaluate setmelanotide in patients aged 2 to younger than 6 years with BBS or POMC, PCSK1 or LEPR deficiency. Clinically meaningful improvements were observed in both co-primary endpoints at week 52. Results of the trial demonstrated:

- 10 of 12 patients (83%)[1] achieved ≥0.2-point reduction in body mass index (BMI) Z-score;
- -18% in mean percent change in BMI from baseline;
- 91% of caregivers reported patients had reduced hunger compared with baseline, and the caregivers also reported feelings of reduced personal burden; and
- No new safety signals were observed.

Consistent with prior experience, setmelanotide was observed to have been generally well tolerated. No serious adverse events (AEs) leading to study discontinuation or death were reported. The most common treatment-emergent AEs were skin hyperpigmentation (75%), vomiting (58%), nasopharyngitis (42%), upper respiratory tract infection (33%), and injection site bruising (33%).

In July 2024, IMCIVREE (setmelanotide) received authorization as the first-ever precision medicine in the European Union for control of hunger and treatment of obesity in adults and children as young as 2 years old, living with BBS or POMC, PCSK1, or LEPR deficiency. In addition, Rhythm has completed submission of its supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) to expand the label of IMCIVREE to treat pediatric patients between the ages of 2 and younger than 6 years old in approved indications in the United States. The FDA has granted Priority Review of the sNDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of December 26, 2024.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients 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. The EC has also authorized setmelanotide for control of hunger and treatment of obesity in children as young as 2 years old, living with BBS or POMC, PCSK1, or LEPR deficiency. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare diseases, as well as investigational MC4R agonists LB54640 and 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 2 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 U.S. Prescribing Information and EU Summary of Product Characteristics 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 progress of setmelanotide or other product candidates for any specific disease indication or at any dosage, including the potential benefits of setmelanotide for pediatric patients with BBS or POMC, PCSK1, or LEPR deficiency; potential and completed regulatory submissions, approvals and timing thereof of setmelanotide and other product candidates, including the PDUFA date to expand the label of IMCIVREE; expectations surrounding potential and completed regulatory submissions and approvals, including within the United States, the EU and other regions; the publication of results from the Phase 3 VENTURE trial in a peer-reviewed journal; and the timing of any of the foregoing . Statements using words 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 Rhythm’s Quarterly Report on Form 10-Q for the three months ended September 30, 2024 and 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:
Sheryl Seapy
Real Chemistry
(949) 903-4750
sseapy@realchemistry.com

[1] One patient from the initial group of 12 did not complete follow-up appointments and discontinued early in the trial

Source: Rhythm Pharmaceuticals, Inc.