Rhythm Pharmaceuticals Announces ▼ IMCIVREE® (setmelanotide) Receives Expanded Marketing Authorization in the United Kingdom for Treatment of Obesity and Control of Hunger in Patients with Bardet Biedl Syndrome or POMC, PCSK1, or LEPR Deficiency to include Children as Young as 2 Years Old

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BOSTON, Dec. 03, 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 that the United Kingdom's Medicines & Healthcare products Regulatory Agency (MHRA) has expanded the marketing authorization for IMCIVREE® (setmelanotide) to include the treatment of obesity and control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS) or genetically confirmed loss-of-function biallelic pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or biallelic leptin receptor (LEPR) deficiency in adult and pediatric patients as young as 2 years old and older.

"This expansion is an important milestone for young patients and their families living with hyperphagia and severe obesity due to rare melanocortin-4 (MC4R) pathway diseases with underlying genetic causes," said Sadaf Farooqi, M.D., Ph.D., Professor at the Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre. "Given the serious comorbidities associated with obesity, it's critical to treat patients as early as possible to prevent negative health complications from developing or progressing. With this decision by the MHRA, patients as young as 2 years old with MC4R pathway diseases can now access a treatment option intended to address the underlying cause of their disease."

IMCIVREE initially received marketing authorization from the MHRA as an option for treating obesity and control of hunger in patients aged 6 years and older in these indications in 2022. In May 2024, the UK's National Institute for Health and Care Excellence (NICE) recommended National Health Service reimbursement for IMCIVREE in patients with genetically confirmed BBS who are 6 years of age and over, if they are between 6 and 17 years of age when treatment starts. Patients may remain on reimbursed setmelanotide as adults while they continue to benefit from therapy. With this expansion to include children as young as 2 years old, IMCIVREE is expected to be available by the end of this year through the Medicines for Children program.

"We are pleased officials with NICE and the MHRA recognize the need for new therapeutic options for patients living with rare MC4R pathway diseases like BBS and POMC, PCSK1 and LEPR deficiencies," said Yann Mazabraud, Executive Vice President, Head of International at Rhythm Pharmaceuticals. "This MHRA marketing expansion for IMCIVREE, which follows the European Commission's expansion to include children as young as 2 years old in EU countries in July 2024, is further confirmation of the medical need to treat these diseases beginning at a very young age."

A supplemental New Drug Application for IMCIVREE for patients as young as 2 years of age is currently under priority review with the U.S. Food and Drug Administration (FDA), with an assigned Prescription Drug User Fee Act (PDUFA) goal date of December 26, 2024.

Results from a Phase 3 clinical trial suggest that setmelanotide may reduce hyperphagia, weight and body mass index (BMI) in children. The most common adverse events are skin hyperpigmentation, injection site reactions, nausea and headache.

About Bardet-Biedl Syndrome and POMC, PCSK1 and LEPR Deficiencies
POMC, PCSK1 and LEPR deficiencies and BBS are rare diseases associated with impaired signaling of the MC4R pathway, a key signaling pathway in the hypothalamus region of the brain that is responsible for regulating hunger, caloric intake, and energy expenditure, which consequently affects body weight. Biallelic variants in the *POMC, PCSK1* or *LEPR* genes are known to impair MC4R pathway signaling and that can cause hyperphagia, a pathological, insatiable hunger that leads to abnormal food-seeking behaviors, and severe obesity. BBS is a rare autosomal recessive ciliopathy that presents with a variety of signs and symptoms that evolve over time including visual impairment, renal disease, polydactyly, genital abnormalities, cognitive impairment, hyperphagia and early-onset, severe obesity arising from impairment of the hypothalamic MC4R pathway.

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 2 years of age and above. 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 and the United Kingdom, 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 the European Union and the United Kingdom, 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; anticipated reimbursement and coverage of IMCIVREE in the United Kingdom; expectations surrounding potential and completed regulatory submissions and approvals, including within the United States, the EU and other regions; 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.

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