Rhythm Pharmaceuticals Announces FDA Approval of IMCIVREE® (setmelanotide) for Patients as Young as 2 Years Old

December 20, 2024

BOSTON, Dec. 20, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company focused on transforming the lives of patients living with rare neuroendocrine diseases, today announced that the U.S. Food and Drug Administration (FDA) has approved an expanded indication for IMCIVREE® (setmelanotide) to include children as young as 2 years old. IMCIVREE is indicated to reduce excess body weight and maintain weight reduction long-term in patients 2 years of age and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or genetically confirmed pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or leptin receptor (LEPR) deficiency.

BBS and POMC, PCSK1 and LEPR deficiencies are rare melanocortin-4 receptor (MC4R) pathway diseases with hallmark characteristics that include hyperphagia, or pathological, insatiable hunger and impaired satiety accompanied by persistent and abnormal food-seeking behaviors, and early-onset obesity. IMCIVREE is the first and only precision medicine to target impairment of the hypothalamic MC4R pathway, a root cause of hyperphagia and obesity due to BBS and POMC, PCSK1 and LEPR deficiencies in adults and children as young as 2 years old in the United States, as well as Europe.

“It’s important to understand that rare MC4R pathway diseases differ from general obesity as the insatiable hunger these patients experience is pathologic and a result of impairment to a pathway in the brain. With this insatiable hunger, most patients develop early-onset obesity before the age of 5,” said Ilene Fennoy, MD, MPH, pediatric endocrinologist, obesity specialist and professor of Pediatrics at Columbia University Medical Center. “Obesity in childhood, if untreated, can lead to a greater risk of severe and long-term health complications, making early intervention to treat obesity critical. With this expanded indication for IMCIVREE, patients now can receive a much needed, targeted treatment that we believe can address a root cause of their obesity at a very young age.”

Results from clinical trials demonstrate that setmelanotide delivers significant and sustained reductions in measures of weight and hunger. Results from the Phase 3 VENTURE trial were published in the peer-reviewed journal *The Lancet Diabetes & Endocrinology* in November 2024. The most common adverse events are skin hyperpigmentation, injection site reactions, diarrhea, nausea and headache.

“Today’s approval is welcome news for the BBS community and others with rare MC4R diseases who struggle with hyperphagia,” said Tim Ogden, President of the Bardet Biedl Syndrome Foundation. “Many children with BBS feel hungry or think about food regardless of how much or how recently they've eaten, leaving families to deal with children sneaking or stealing food, which makes daily life extremely stressful. Parents have enough to worry about and manage when their child has a multi-systemic syndrome like BBS and IMCIVREE can be an important tool for their obesity."

“Rhythm is focused on ensuring patients with these rare genetic diseases that are present at birth and manifest early in life have access to IMCIVREE as soon as possible,” said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm. “We remain steadfast in our commitment to continue rapidly advancing care and precision medicines that address the root cause of rare neuroendocrine diseases.”

IMCIVREE initially received approval from the FDA in November 2020 for patients 6 years old and older with POMC, PCSK1 or LEPR deficiencies and approval in June 2022 for use in patients with BBS. IMCIVREE has also received marketing authorization from the United Kingdom’s Medicines & Healthcare products Regulatory Agency (MHRA) and the European Commission (EC) for use in patients as young as 2 years of age.

BBS, which is diagnosed clinically, affects approximately 4,000 to 5,000 people in the U.S. People living with BBS may experience insatiable hunger, also known as hyperphagia, and severe obesity beginning early in life. BBS also may be associated with cognitive impairment, polydactyly, renal dysfunction, hypogonadism, and visual impairment. POMC, PCSK1 and LEPR deficiency obesities, caused by biallelic variants in the *POMC, PCSK1 or LEPR* genes, affect approximately 600 to 2,500 people in the United States.

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) to reduce excess body weight and

maintain weight reduction long term in adult and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or genetically confirmed pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or leptin receptor (LEPR) deficiency. 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 to reduce excess body weight and maintain weight reduction long term in adult and pediatric patients aged 2 years and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (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).

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 BBS or POMC, PCSK1, or LEPR deficiency, 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

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Inform patients that these events may occur and instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Depression, suicidal ideation and depressed mood have occurred. Monitor patients for new onset or worsening depression or suicidal thoughts or behaviors. Consider discontinuing IMCIVREE 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 IMCIVREE.

Skin Hyperpigmentation, Darkening of Pre-existing Nevi, and Development of New Melanocytic Nevi: Generalized or focal increases in skin pigmentation, darkening of pre-existing nevi, development of new melanocytic nevi and increase in size of existing melanocytic nevi have occurred. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new pigmented lesions.

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: IMCIVREE 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

Treatment with IMCIVREE is not recommended when breastfeeding. Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

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 progress, potential regulatory submissions, approvals and timing thereof of setmelanotide and other product candidates; the potential benefits of any of our products or product candidates for any specific disease indication, in any particular patient population, or at any dosage, including the potential benefits of setmelanotide for pediatric patients with BBS or POMC, PCSK1, or LEPR deficiency; expectations surrounding potential clinical trial results, regulatory submissions and approvals; our business strategy and plans, including regarding commercialization of setmelanotide in the United States; 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

Source: Rhythm Pharmaceuticals, Inc.