Rhythm Pharmaceuticals Receives Positive CHMP Opinion for IMCIVREE® (setmelanotide) for the Treatment of Obesity and Control of Hunger in Patients with Acquired Hypothalamic Obesity due to Hypothalamic Injury or Impairment

March 26, 2026

-- European Commission decision anticipated in second quarter of 2026 --

BOSTON, March 26, 2026 (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 European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending to expand the current marketing authorization for IMCIVREE® (setmelanotide) to include the treatment of obesity and the control of hunger in adults and children 4 years of age and above with acquired hypothalamic obesity (HO) due to hypothalamic injury or impairment.

"The positive CHMP opinion with a broad label following closely upon last week's FDA approval validates the quality of the data which supports our filings in acquired HO and further confirms our global approach to drug development," said David Meeker, M.D., Chairman, President and Chief Executive Officer of Rhythm. "Acquired HO represents a significant unmet medical need across geographies and a unique opportunity for Rhythm which we are well positioned to execute on."

"Acquired hypothalamic obesity is a devastating neuroendocrine disease characterized by reduced energy expenditure, hyperphagia (pathological insatiable hunger) and accelerated, sustained weight gain resulting from physical injury or structural abnormality of the hypothalamus. This disease condition is driven by impairment of MC4R pathway signaling and other hypothalamic functional damage, making it exceptionally difficult to manage with existing approaches," said Professor Hanneke van Santen, M.D., PhD., professor of pediatric endocrinology at the Prinses Máxima Center and Wilhelmina Children's Hospital, Utrecht, The Netherlands. "There is a clear and urgent need for a precision medicine that targets the root cause of the disease and offer patients a meaningful path forward."

The CHMP opinion will now be reviewed by the European Commission (EC), which has the authority to grant and expand marketing authorizations for medicinal products in the European Union. A final decision is anticipated in the second quarter of 2026.

About Acquired Hypothalamic Obesity
Acquired hypothalamic obesity is a rare neuro endocrine disease characterized by accelerated and sustained weight gain caused by hypothalamic injury or impairment. Hypothalamic injury or impairment may lead to decreased alpha-melanocyte-stimulating hormone (α-MSH) production and disruption of MC4R pathway signaling. The MC4R pathway is responsible for regulating energy balance and body weight. Acquired hypothalamic obesity most frequently follows the growth or treatment of craniopharyngioma, astrocytoma or other hypothalamic-pituitary tumors. Additional causes of injury or dysfunction may include traumatic brain injury, stroke, inflammation, or anatomic abnormalities. Due to impairment of the MC4R pathway, patients experience accelerated and sustained weight gain, often accompanied by hyperphagia and/or decreased energy expenditure. Rhythm estimates there are approximately 10,000 people living with acquired hypothalamic obesity in the U.S. and approximately 10,000 people living with acquired hypothalamic obesity in the EU.

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 reduction long term in adults and pediatric patients aged 4 years and older with acquired hypothalamic obesity, 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 bivamelagon 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 adults and pediatric patients aged 4 years and older with acquired hypothalamic obesity, 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 confirmed by genetic testing 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 acquired HO, BBS, or POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Important Safety Information

CONTRAINDICATIONS

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 and increased frequency of penile erections in males 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 and suicidal ideation 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 occurred in the majority of IMCIVREE-treated patients. IMCIVREE may also cause development of new melanocytic nevi or darkening of pre-existing nevi. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new pigmented lesions.

Acute Adrenal Insufficiency with Acquired HO: Patients with acquired HO and secondary adrenal insufficiency reported serious adverse reactions related to acute adrenal insufficiency in 5% of IMCIVREE-treated patients and no placebo-treated patients. In patients with secondary adrenal insufficiency, monitor for clinical signs of acute adrenal insufficiency.

Sodium Imbalance in Patients with Acquired HO and Central Diabetes Insipidus: Patients with acquired HO and concomitant central diabetes insipidus (DI)/arginine vasopressin (AVP) deficiency reported hyponatremia in 6% of IMCIVREE-treated patients and 2% of placebo-treated patients and hypernatremia in 5% of IMCIVREE-treated patients and 4% of placebo-treated patients. Monitor serum sodium levels with changes in fluid intake and hydration status. Adjust the doses of concomitant therapies for DI/AVP deficiency as needed.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥20% in at least 1 indication) 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 http://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 safety, efficacy, potential benefits of, and clinical design or progress of any of our products or product candidates at any dosage or in any indication; the approval and use of IMCIVREE in patients with acquired hypothalamic obesity and its availability for patients; the commercial growth of IMCIVREE; our expectations surrounding potential regulatory submissions, progress, or approvals and timing thereof for any of our product candidates, including a potential marketing authorization in the European Union as well as the Company's engagement with Japan's Pharmaceuticals and Medical Devices Agency and plans to seek authorization for setmelanotide to treat acquired hypothalamic obesity in Japan; the timing of review and final decision by the EC on expanding marketing authorization for IMCIVREE in the EU; the estimated market size and addressable population for our drug products, including IMCIVREE for the treatment of hypothalamic obesity in the United States, the European Union and Japan; the future announcement of data from our ongoing clinical trials, including the Japanese cohort of our Phase 3 trial evaluating setmelanotide for patients with acquired hypothalamic obesity, the substudy evaluating setmelanotide for patients with congenital hypothalamic obesity; Part C of the Phase 1 trial evaluating RM-718, and the open-label Phase 2 trial evaluating setmelanotide in patients with Prader-Willi syndrome; the ongoing enrollment in and potential progress or outcomes of our clinical trials; the presentation of the full data from the TRANSCEND study at an upcoming medical meeting; and the content, date and 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, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing our international operations and the costs of any related compliance programs, 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, including those discussed under the caption "Risk Factors" in Rhythm's Annual Report on Form 10-K for the year ended December 31, 2025 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 press release or to update them to reflect events or circumstances occurring after the date of this press 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.
dconnolly@rhythmtx.com

Media Contact:
Layne Cosgrove
Real Chemistry
llitsinger@realchemistry.com

Source: Rhythm Pharmaceuticals, Inc.