Rhythm Pharmaceuticals Announces IMCIVREE® (setmelanotide) Receives Expanded Marketing Authorization in the United Kingdom for Treatment of Obesity and Control of Hunger in Patients with Acquired Hypothalamic Obesity due to Hypothalamic Injury or Impairment

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-- MHRA grants authorization for patients 4 years of age and above with acquired hypothalamic obesity due to hypothalamic injury or impairment --

BOSTON, Aug. 11, 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 United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) has expanded the marketing authorization for IMCIVREE® (setmelanotide) to include the treatment of obesity and control of hunger in adults and children 4 years of age and older with acquired hypothalamic obesity (HO) due to hypothalamic injury or impairment. The MHRA this week also granted IMCIVREE orphan drug designation for acquired HO.

"This authorization marks an important milestone for patients in the UK living with acquired HO," said David Meeker, M.D., Chairman, President and Chief Executive Officer of Rhythm Pharmaceuticals. "Patients with acquired HO often experience persistent hunger and rapid, severe weight gain that can affect nearly every aspect of their daily life. With the MHRA's expanded authorization of IMCIVREE, healthcare providers now have an approved treatment option for eligible patients that addresses the underlying biology of this disease."

IMCIVREE initially received marketing authorization in the UK in 2021 for the treatment of obesity and control of hunger in patients with POMC, PCSK1 or LEPR deficiency and in 2022 for patients with Bardet-Biedl syndrome (BBS). In 2024, the MHRA expanded the authorization to include children as young as 2 years old.

"Acquired hypothalamic obesity is a complex condition that can have profound effects on the quality of life and long-term health of children and adults with brain tumours affecting the hypothalamus," said Prof. Sadaf Farooqi, M.D., Ph.D, University of Cambridge. "The TRANSCEND study showed substantial reductions in BMI in adults and children, demonstrating the effectiveness of MC4R pathway-targeted therapy in people with this condition. These results provide strong evidence for a targeted treatment approach in a condition for which there were previously no approved therapies in the UK."

The MHRA approval is based on results from the Phase 2 trial and the Phase 3 TRANSCEND trial of setmelanotide in acquired HO. The global, 120-patient trial met its primary endpoint, with a statistically significant -19.8% placebo-adjusted reduction in body mass index (BMI). For the primary endpoint of mean BMI change from baseline, study participants on setmelanotide therapy (n=81) achieved a -16.5% reduction compared with a +3.3% increase among patients on placebo (n=39) at 52 weeks ($p<0.0001$). Adult patients (age 18 and older; n=49) achieved a -19.2% placebo-adjusted BMI reduction at 52 weeks, and pediatric patients (younger than age 18; n=71) achieved a -20.2% placebo-adjusted BMI reduction at 52 weeks. Patients receiving setmelanotide also experienced reductions in hunger. Setmelanotide was generally well tolerated in the TRANSCEND study. The most common treatment-emergent adverse events (affecting >20% of participants) were nausea, vomiting, diarrhea, injection site reaction, skin hyperpigmentation and headache.

Results from the Phase 3 TRANSCEND trial were recently published in *The New England Journal of Medicine*. An accompanying editorial authored by Professor Sadaf Farooqi highlighted the significance of these findings for patients living with acquired HO and the potential of targeted therapies to address the underlying biology of the disease.

The Company plans to work closely with the United Kingdom’s National Health Service (**NHS**) to finalize guidance for coverage of IMCIVREE for acquired HO.

Please refer to the full Summary of Product Characteristics for a complete list of indications, contraindications, warnings and precautions.

About Acquired Hypothalamic Obesity

Acquired hypothalamic obesity is a rare neuroendocrine 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 Europe.

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 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 and Healthcare Products Regulatory Agency (MHRA) have authorized setmelanotide for the treatment of obesity and control of hunger in patients 4 years of age and above with acquired hypothalamic obesity due to hypothalamic injury or impairment; and 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, and for the treatment of obesity and control of hunger in adults and children 4 years of age and above with acquired hypothalamic obesity (aHO) due to hypothalamic injury or impairment. In the European Union and the United Kingdom, setmelanotide should be prescribed and supervised by a physician experienced in the diagnosis and management of rare forms of obesity with genetic or hypothalamic origin.

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.

Reporting of side effects.

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also contact Rhythm Pharmaceuticals at +1 (833) 789-6337. You can also report side effects directly via the Yellow Card Scheme please do so via: https://yellowcard.mhra.gov.uk/ or report directly to the FDA contact 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.

By reporting side effects, you can help provide more information on the safety of this medicine.

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, including, setmelanotide, bivamelagon, and RM-718; the use of setmelanotide in patients with acquired HO and the success of our commercial launch; our expectations surrounding potential regulatory submissions, progress, or approvals and timing thereof for any of our product candidates, including marketing authorization and launch in United Kingdom and the timing thereof; the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products, including setmelanotide for the treatment of acquired HO; 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, 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 Quarterly Report on Form 10-Q for the three months ended June 30, 2026, 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.

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