



Rhythm Pharmaceuticals Announces Commercial Launch of IMCIVREE® (setmelanotide) in Japan for Patients with Acquired Hypothalamic Obesity

October 13, 2026

-- Launch follows MHLW approval of IMCIVREE for acquired hypothalamic obesity and inclusion on Japan's National Health Insurance drug price list --

-- IMCIVREE is the first approved therapy in Japan for patients living with acquired hypothalamic obesity --

BOSTON, Oct. 13, 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 the commercial launch of IMCIVREE® (setmelanotide) in Japan to treat patients living with acquired hypothalamic obesity (HO), following its inclusion on Japan's National Health Insurance (NHI) drug price list. IMCIVREE is the first approved therapy in Japan for acquired HO.

"This launch marks an important advancement for people living with acquired HO in Japan where there were no approved therapies for this disease until now," said Yann Mazabraud, Executive Vice President and Head of International at Rhythm. "We have been building our team in Japan in preparation for this launch and are excited about the opportunity to positively impact the lives of Japanese patients. This is a significant milestone in our global efforts to bring innovative therapies to patients with rare neuroendocrine diseases around the world."

The launch follows approval by Japan's Ministry of Health, Labour and Welfare (MHLW) of IMCIVREE for acquired hypothalamic obesity in August of this year. The approval was supported by data from the pivotal Phase 3 TRANSCEND trial, which enrolled 142 patients with acquired HO, including 12 patients from a Japanese cohort and 10 supplemental patients enrolled in addition to the primary 120-patient pivotal cohort. The global study met its primary endpoint, demonstrating a statistically significant 18.8% placebo-adjusted reduction in body mass index (BMI).

As previously announced, setmelanotide received orphan drug designation from the MHLW for the treatment of acquired hypothalamic obesity. Rhythm estimates that approximately 5,000 to 8,000 people are living with acquired HO in Japan.

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 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 $\geq 20\%$ 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, including, setmelanotide, bivalmelagon, and RM-718; the use of setmelanotide in patients with acquired HO and the success of our commercialization of IMCIVREE for acquired HO; our expectations surrounding potential regulatory submissions, progress, or approvals and timing thereof for any of our product candidates, including launch in Japan; 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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