Rhythm Pharmaceuticals Announces New Data Presentations at the European Society for Paediatric Endocrinology Meeting

September 10, 2026

-- Real-world data showed reductions in BMI with up to 18 months of setmelanotide therapy in 30 paediatric patients with acquired hypothalamic obesity (HO) in France –

-- Phase 3 analyses demonstrated improvements across multiple cardiometabolic risk indices with setmelanotide in acquired HO --

BOSTON, Sept. 10, 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 Rhythm and its collaborators will present three posters and three oral presentations relating to the company's work in rare melanocortin-4 receptor (MC4R) pathway diseases at the 64th Annual European Society for Paediatric Endocrinology (ESPE) Meeting taking place September 8-10 in Marseille, France.

"Patients with acquired hypothalamic obesity often experience severe obesity, persistent hyperphagia and metabolic complications that can significantly affect their health and daily lives," said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm Pharmaceuticals. "Real-world data from France show that setmelanotide is associated with sustained improvements in BMI and hunger (hyperphagia) for up to 18 months. Together with data from our Phase 3 TRANSCEND trial demonstrating improvements across multiple cardiometabolic risk measures, these findings provide a more comprehensive picture of the treatment's impact in acquired hypothalamic obesity."

Paediatric Patients with Acquired Hypothalamic Obesity Treated with Setmelanotide: Real-World BMI and Hunger Data for up to 18 Months in France

This real-world analysis, presented as a poster presentation, evaluated paediatric patients with acquired hypothalamic obesity (HO) treated with setmelanotide through France's early-access program for up to eighteen months. A total of 30 patients between the ages of 6 and younger than 18 with acquired HO had started setmelanotide therapy, as of March 31, 2026. The results showed that patients with acquired HO on setmelanotide achieved reductions in BMI and decreases in hunger scores. Key findings include:

- -11.5% reduction in mean BMI from baseline ($p<0.0001$) in patients who reached 6 months (n=17);
- -13.4% reduction in mean BMI from baseline ($p<0.001$) in patients who reached 9 months (n=14);
- -10.5% reduction in mean BMI from baseline ($p<0.01$) in patients who reached 12 months (n=13)
- -9.0% reduction in BMI from baseline ($p<0.13$) in patients who reached 18 months (n=5)
- More than 88% of patients achieved a ≥0.2-point reduction in BMI z-score after 6, 9, or 12, and 18 months of treatment, with 100% of patients achieving ≥0.2-point reduction in BMI z-score at 12 months (n=13) and 18 months (n=5);
- Patient-reported hunger decreased after 6, 12, and 18 months of treatment in patients aged ≥12 to <18 years.
- No new safety concerns were observed and reported adverse events were consistent with Phase 3 trial data.

Impact of Setmelanotide on Metabolic Index Scores in Paediatric Participants with Acquired Hypothalamic Obesity – A Phase 3 Trial Post-Hoc Analysis

This post-hoc analysis, presented as an oral presentation, assessed the impact of setmelanotide on composite metabolic index scores in paediatric patients with acquired HO in the Phase 3 trial. Key findings include:

- Metabolic syndrome z-BMI score mean change was -0.8 vs -0.2 for the placebo group (p=0.006) (n=35 vs n=19).
- The mean change in Lipid Accumulation Product (LAP) (n=41 vs n=22) from baseline was -25.6 compared with +3.6 for the placebo group (p<0.0001).
- The mean change in Triglyceride-Glucose Waist Circumference Index (TyG-WC) (n=38 vs n=22) was -116.8 vs +34.0 for the placebo group (p<0.0001).
- The mean change in Visceral Adiposity Index (VAI) (n=40 vs n=22) was -1.3 vs -0.4 for the placebo group (p=0.004).
- The mean change in the Fatty Liver Index (FLI) (n=39 vs n=22) was -20.6 vs +6.1 for the placebo group (p<0.0001).

The findings indicate that setmelanotide may be associated with improvements in composite metabolic index scores in addition to

reductions in body weight and hunger, supporting further understanding of setmelanotide's potential effects for patients with acquired HO.

In addition, the following oral and poster presentations will be presented at ESPE:

- Weight outcomes at 5–6 years of setmelanotide in paediatric patients with POMC or LEPR deficiency or Bardet–Biedl syndrome and obesity;
- Post hoc analysis to determine the impact of setmelanotide on metabolic syndrome severity and risk score in patients with acquired hypothalamic obesity from the Phase 3 TRANSCEND trial;
- The association of clinical features of Bardet–Biedl syndrome in a large population of patients with obesity and a positive genetic test for biallelic BBS variants; and
- Clinical features associated with pathogenic or likely pathogenic biallelic Bardet–Biedl syndrome gene variants in a large population of patients with obesity.

The presentations from ESPE 2026 will be available following the conference at: https://hcp.rhythmtx.com/publications-presentations/

Satellite Symposium
Rhythm also sponsored an expert-led satellite symposium, "Advancing breakthrough therapy for patients living with rare hypothalamic melanocortin-4 receptor (MC4R) pathway diseases," at ESPE 2026. The program focused on examining how disruption of the MC4R pathway drives hyperphagia and obesity, with presentations on Phase 3 TRANSCEND data and real-world evidence in acquired HO and Bardet-Biedl syndrome.

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 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 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 ≥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, bivamelagon, and RM-718; the use of setmelanotide in patients with acquired HO, including paediatric patients, 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, the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products, including setmelanotide for the treatment of acquired HO; our participation in upcoming events and presentations, including at ESPE, and the date, time and content thereof; 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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