Rhythm Pharmaceuticals Announces New Data Presentations at the 2026 European Congress of Endocrinology

May 12, 2026

– Real world data showed clinically meaningful BMI reductions with setmelanotide in 62 adults with 12-month data living with acquired hypothalamic obesity (HO) in France –

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

– New research highlights the burden and under recognition of hyperphagia –

BOSTON, May 12, 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 Rhythm and its collaborators will present six posters, including four featuring new data, relating to the company's work with setmelanotide at The European Congress of Endocrinology (ECE), taking place May 9-12, 2026 in Prague.

"Obesity due to rare neuroendocrine diseases is often accompanied by hyperphagia and severe metabolic complications that significantly affect patients' health and daily lives," said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm Pharmaceuticals. "Real-world data generated from the pre-marketing, early-access program in France show that setmelanotide is associated with clinically meaningful improvements not only in body weight, but also improvements across multiple cardiometabolic risk measures and disease-defining features, providing a more comprehensive picture of the treatment impact in these diseases."

Real-World BMI Outcomes in Adult Patients with Acquired Hypothalamic Obesity Treated With Setmelanotide for up to 12 Months in France

This real-world analysis evaluated adults with acquired hypothalamic obesity (HO) treated with setmelanotide through France's early-access program for up to twelve months. A total of 62 patients with acquired HO had started setmelanotide therapy, as of November 30, 2025. The results showed that patients with acquired HO on setmelanotide achieved significant reductions in BMI and meaningful decreases in hunger scores. Key findings include:

- -13.0% reduction in mean BMI from baseline ($p<0.0001$) in patients who reached 6 months (n=39);
- -19.6% reduction in mean BMI from baseline ($p<0.0001$) in patients who reached 9 months (n=26);
- -16.9% reduction in mean BMI from baseline ($p<0.0001$) in patients who reached 12 months (n=25)
- The majority of patients had a BMI reduction of ≥10% after 6, 9, or 12 months of treatment;
- Patients achieved improvements in obesity classes with 18.0%, 34.6%, and 28.0% of patients no longer living with obesity after 6, 9, and 12 months, respectively;
- Patients aged ≥12 years reported improvements in all four hunger questions after 6, 9, and 12 months of treatment; and
- No new safety concerns were observed and reported adverse events were consistent with Phase 3 trial data.

Hyperphagia Severity in Adult Patients with Bardet-Biedl Syndrome – A Mixed-Methods Cross-Sectional Study in the United Kingdom

This study evaluated hyperphagia severity in adults with Bardet-Biedl syndrome (BBS) and obesity using questionnaires and expert-led interviews. Key findings include:

- A total of 39 adults completed the questionnaire and 13 completed the semi-structured, expert-led interviews;
- Questionnaires alone classified only 7.7% of patients as having severe hyperphagia, whereas semi-structured, expert-led interviews classified 69.2% of participants as having severe hyperphagia; and
- 92.3% of participants (12/13) classified a higher severity level by interview compared with only 1 participant showing the same severity classification across both methods.

This study suggests a high prevalence of severe hyperphagia in adult patients with BBS and obesity in the UK and indicates substantial underreporting with self-reported questionnaires.

Impact of Setmelanotide on Metabolic Index Scores in Phase 3 Trial Participants with Acquired Hypothalamic Obesity

A post hoc analysis of the Phase 3 TRANSCEND trial assessed the impact of setmelanotide on multiple validated cardiometabolic risk indices at Week 52. Setmelanotide treatment in patients with acquired HO led to significant improvements in multiple metabolic index scores versus placebo. Key findings include:

- Metabolic syndrome z-score mean change was -0.9 vs -0.2 for the placebo group (p<0.0001) (n=53 vs n=31)
- The mean change in Lipid Accumulation Product (LAP) (n=68 vs n=36) from baseline was -36.4 compared to -2.6 for the placebo group (p<0.0001);
- The mean change in Triglyceride-Glucose Waist Circumference Index (TyG-WC) (n=63 vs n=35) was -138.3 vs +21.2 for the placebo group (p<0.0001);
- The mean change in Visceral Adiposity Index (VAI) (n=67 vs n=35) was -1.5 vs -0.4 for the placebo group (p=0.0009); and
- The mean change in the Fatty Liver Index (FLI) (n=65 vs n=35) was -24.2 vs +4.4 for the placebo group (p<0.0001).

The findings highlight the broad metabolic benefits and strong clinically meaningful efficacy of setmelanotide in this population, supporting its potential as a therapeutic option for patients with acquired HO.

Recognising the Burden of Acquired Hypothalamic Obesity in Craniopharyngioma: Cross-Country Insights from Lived Experiences to Support Integrated Care Across All Life Stages

This study aimed to highlight the persistent and under-recognized health burden of acquired HO across life stages, drawing on the experiences of individuals with childhood-onset craniopharyngioma (CO-CP) from the Netherlands, Germany, and the UK. Findings include:

- Key disease symptom burden for craniopharyngioma (CP) included pituitary hormone dysfunction (100%), thirst and fluid imbalance (87.9%), and weight gain (78.8%);
- Fear of Addisonian crises (90.9%), social stigma (87.9%), and challenges at work/school (87.9%) were reported as the most frequent quality of life challenges associated with CP;
- Across all three countries, many of the reported disease symptoms were associated with acquired HO, such as hyperphagia, fatigue and reduced stamina, and weight gain; and
- The transition from pediatric to adult care was reported as abrupt, inconsistent and fragmented with significant needs and gaps in adult follow-up.
- Patients with craniopharyngioma require diverse, evolving long-term support to address complex medical needs, with greater emphasis on managing acquired HO, as many reported symptoms are linked to this condition.

Additional Congress Presentations
Two encore posters will also be presented at ECE:

- Efficacy and Safety of Setmelanotide in Acquired Hypothalamic Obesity: Results from a Double-Blind, Multicenter, Placebo-Controlled, Randomized Phase 3 Trial; and
- Genotype-Phenotype Correlation of Ophthalmic, Renal/Genitourinary, Neurological and Neurodevelopmental Manifestations in Published Cases of Bardet-Biedl Syndrome.

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

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. The European Commission (EC) has authorized setmelanotide for the treatment of obesity and control of hunger in patients 4 years of age and above with acquired hypothalamic obesity. 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.

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

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 our clinical data from clinical trials, including post-hoc analyses thereof, and real world data related to patients treated with setmelanotide, 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; , our anticipated presentations of data at the European Congress of Endocrinology; including 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, uncertainties and 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 March 31, 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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