Rhythm Pharmaceuticals Announces New Data Presentations in Acquired Hypothalamic Obesity at Pediatric Endocrine Society

May 4, 2026

-- Pediatric patients (n=10) with acquired hypothalamic obesity achieved sustained reductions in BMI and BMI-Z at 2.5 years of setmelanotide therapy --

-- Weight category improvements observed in pediatric patients with acquired hypothalamic obesity treated with setmelanotide --

BOSTON, May 04, 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 presentation of new data to be delivered by Rhythm and its partners at The Pediatric Endocrine Society (PES) Annual Meeting, taking place April 30-May 3, 2026, in San Francisco.

“Acquired hypothalamic obesity is a complex disease that requires long-term management, particularly in pediatric patients,” said Jennifer Miller, M.D., Professor of Pediatrics, Pediatric Endocrinology, University of Florida College of Medicine. “The data presented provide important longer-term insights into treatment response for pediatric patients treated with setmelanotide, including reductions across multiple weight-related measures.”

Long-Term Efficacy with Setmelanotide in Pediatric Patients with Acquired Hypothalamic Obesity

Ashley Shoemaker, M.D., MSCI, Associate Professor of Pediatrics, Pediatric Endocrinology at Vanderbilt Health, presented a poster on Friday, May 1 with data on the continued efficacy and safety after 2.5 years of setmelanotide treatment in pediatric patients following their participation in the 16-week Phase 2 trial. Highlights from the presentation include:

- Pediatric patients with acquired hypothalamic obesity who received setmelanotide for up to 2.5 years achieved sustained reductions across multiple age-adjusted weight-related measures.
- Among pediatric participants who completed 2.5 years of treatment (n=10) as of Nov. 10, 2025, mean changes from baseline included:
  - -16.4% change in BMI
  - -1.6 change in BMI Z-score
  - -34.2 percentage-point change in percent of the BMI 95th percentile (%BMI95)
- Adverse events observed were consistent with the previously reported safety profile of setmelanotide, with skin hyperpigmentation, nausea, vomiting, headache and injection site reaction being the most common.

Weight Category Improvement Following Setmelanotide in Pediatric Patients with Acquired Hypothalamic Obesity

Jennifer Miller, M.D., Professor of Pediatrics, Pediatric Endocrinology, University of Florida College of Medicine, presented data from the Phase 3 TRANSCEND trial in an oral presentation on Saturday, May 2 on the changes in weight category in the pediatric subpopulation of participants after 1 year of setmelanotide treatment. Highlights from the presentation include:

- At baseline, 59.7% of pediatric participants (40/67) had class II or III obesity;
- After 1 year of treatment, 71.1% of pediatric patients treated with setmelanotide (n=32) improved by ≥1 weight category, and 44.4% (n=20) improved by ≥2 weight categories, compared with 13.6% (n=3) improving one weight category and 0% improving two categories for placebo patients;
- Following 1 year of treatment, 44.4% of patients (n=20) were classified as healthy weight (n=10) or overweight (n=10), compared with 18.2% of placebo-treated patients (n=4) classified as overweight and none achieving healthy weight;
- Adverse events observed were consistent with the previously reported safety profile of setmelanotide.

These presentations from PES 2026 will be available 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. 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 our clinical data from clinical trials evaluating setmelanotide for the treatment of acquired hypothalamic obesity, including long-term extension data from those trials; 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 clinical data at the Pediatric Endocrine Society Annual 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, 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 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 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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