

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K
CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 11, 2025

RHYTHM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-38223
(Commission
File Number)

46-2159271
(IRS Employer
Identification Number)

222 Berkeley Street
12th Floor
Boston, MA 02116
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: **(857) 264-4280**

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value per share	RYTM	The Nasdaq Stock Market LLC (Nasdaq Global Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01. Regulation FD Disclosure.

On December 11, 2025, Rhythm Pharmaceuticals, Inc. (“Rhythm”) issued a press release and published a presentation announcing preliminary results from its exploratory Phase 2 trial of setmelanotide in patients with Prader-Willi syndrome (PWS), which are summarized under Item 8.01 below. The presentation is available in the “Events and Presentations” portion of the Company’s website at ir.rhythmtx.com. A copy of the press release and presentation are furnished as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2 attached hereto) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the “Securities Act”), or the Exchange Act, except as expressly provided by specific reference in such a filing.

Item 8.01. Other Events.

On December 11, 2025, Rhythm announced preliminary results from its exploratory Phase 2 trial of setmelanotide in patients with Prader-Willi syndrome (PWS), which are summarized below.

Rhythm enrolled 18 patients with PWS aged 6-65 years old with a BMI ≥ 30 kg/m² for patients ≥ 18 years of age or BMI ≥ 95 th percentile for age and sex for patients younger than 18. The 52-week trial remains ongoing.

Setmelanotide therapy demonstrated potential therapeutic benefit with BMI and hyperphagia reductions in patients with PWS at Month 3 (n=8) and Month 6 (n=5); Highlights from preliminary results, as of a cut-off date of Nov. 14, include:

- Six (6) of 8 patients who reached Month 3 of setmelanotide therapy achieved BMI reductions from baseline;
- Three (3) of 5 patients who reached Month 6 of setmelanotide therapy achieved reductions in BMI, with two seeing deeper reductions versus Month 3 and one unchanged;
- Six (6) of 7 evaluable patients who reached Month 3 of setmelanotide therapy achieved meaningful reduction in Hyperphagia Questionnaire for Clinical Trials (HQ-CT) scores; one patient’s baseline and Month 3 HQ-CT score was 0, therefore not evaluable;
- Seventeen (17) of the 18 patients enrolled remain on active setmelanotide therapy; and
- Safety and tolerability results have been consistent with setmelanotide’s well-established clinical profile.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

The following Exhibits 99.1 and 99.2 shall be deemed to be furnished and not filed.

Exhibit No.	Description
99.1	Press release dated December 11, 2025
99.2	Presentation dated December 11, 2025
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

RHYTHM PHARMACEUTICALS, INC.

Date: December 11, 2025

By: /s/ Hunter Smith
Hunter Smith
Chief Financial Officer



Rhythm Pharmaceuticals Announces Preliminary Data from Exploratory Phase 2 Trial that showed Setmelanotide Demonstrated Positive Efficacy Signal in Prader-Willi Syndrome

-- BMI and hyperphagia reductions have been observed in patients with PWS treated with setmelanotide at Month 3 (n=8) and Month 6 (n=5); 17 of 18 enrolled patients remain on therapy --

-- Promising results supportive of Phase 3, registrational trial of setmelanotide in PWS --

-- Company initiated Phase 1, Part D study to evaluate weekly MC4R agonist RM-718 in patients with PWS --

-- Company to hold conference call on Thursday, December 11 at 8:00 a.m. --

BOSTON, December 11, 2025 – 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 positive preliminary results from its exploratory Phase 2 trial of setmelanotide in patients with Prader-Willi syndrome (PWS).

The Company also announced plans to advance setmelanotide into a Phase 3 registrational trial in PWS, pending successful completion of this Phase 2 trial. Rhythm also announced that it has initiated a Part D arm in the Phase 1 trial of MC4R agonist RM-718 that will enroll up to 20 patients with PWS. Rhythm anticipates screening the first patient for this 26-week open-label trial of RM-718 in December 2025.

“There remains a profound unmet need in the PWS patient population,” said Jennifer Miller, M.D., University of Florida Division of Endocrinology, Department of Pediatrics in the College of Medicine, the principal investigator for this Phase 2 trial. “Hyperphagia and severe obesity associated with PWS present serious challenges for patients and often lead to significant health complications over time. These interim data offer meaningful insight into the potential for a future treatment option that could help address the unique and critical needs of patients living with PWS.”

Rhythm enrolled 18 patients with PWS aged 6-65 years old with a BMI ≥ 30 kg/m² for patients ≥ 18 years of age or BMI ≥ 95 th percentile for age and sex for patients younger than 18. The 52-week trial remains ongoing.

Setmelanotide therapy demonstrated potential therapeutic benefit with BMI and hyperphagia reductions in patients with PWS at Month 3 (n=8) and Month 6 (n=5); Highlights from preliminary results, as of a cut-off date of Nov. 14, include:

- Six (6) of 8 patients who reached Month 3 of setmelanotide therapy achieved BMI reductions from baseline;
- Three (3) of 5 patients who reached Month 6 of setmelanotide therapy achieved reductions in BMI, with two seeing deeper reductions versus Month 3 and one unchanged;
- Six (6) of 7 evaluable patients who reached Month 3 of setmelanotide therapy achieved meaningful reduction in Hyperphagia Questionnaire for Clinical Trials¹ (HQ-CT) scores; one patient's baseline and Month 3 HQ-CT score was 0, therefore not evaluable;
- Seventeen (17) of the 18 patients enrolled remain on active setmelanotide therapy; and
- Safety and tolerability results have been consistent with setmelanotide's well-established clinical profile.

"We are encouraged by these preliminary results, which give us confidence to advance setmelanotide into a registrational Phase 3 trial for PWS," said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm. "We look forward to additional data in the first half of 2026 and remain committed to exploring the potential of MC4R agonism for this patient population, for whom there are very few treatment options available. In parallel, we look forward to evaluating our weekly MC4R agonist RM-718 in PWS, and we expect the first patient with PWS to enter screening for this study in December."

Conference Call Information

Rhythm Pharmaceuticals will host a live conference call and webcast at 8:00 a.m. ET on Thursday, December 11 to discuss this update. Participants may register for the conference call [here](#). It is recommended that participants join the call ten minutes prior to the scheduled start.

A webcast of the call will also be available under "Events and Presentations" in the Investor Relations section of the Rhythm Pharmaceuticals website

¹ The Hyperphagia Questionnaire for Clinical Trials (HQ-CT) is a 9-item, observer-reported outcome measure that assesses changes in hyperphagic behaviors in individuals with PWS. Each item is scored from 0 to 4, for a total possible score of 36.

at <https://ir.rhythmtx.com/>. The archived webcast will be available on Rhythm Pharmaceuticals' website approximately two hours after the conference call and will be available for 30 days following the call.

About the Phase 2 PWS Trial

This trial is a single-site, open-label Phase 2 study evaluating setmelanotide for the treatment of PWS. Originally designed as a 26-week trial, the duration was extended to 52 weeks to allow early participants to remain on therapy.

Eighteen patients with PWS and obesity, aged 6 to 65 years, were enrolled. Participants were dose-escalated to 5 mg/day of setmelanotide, as tolerated. The primary endpoints are safety and tolerability, with key secondary endpoints assessing weight, hyperphagia, behavior, and pharmacokinetics. Safety and tolerability findings to date have been consistent with setmelanotide's established profile.

About Prader-Willi Syndrome

PWS is a rare genetic disorder that results in a number of physical, mental and behavioral problems. A key feature of PWS is a constant sense of hunger that usually begins at about 2 years of age. PWS is estimated to affect approximately 400,000 people worldwide and approximately 20,000 people in the United States. There are currently limited therapeutic options that effectively reduce the extreme hyperphagia and address low resting energy expenditure associated with PWS.

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 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 adult and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS), POMC, PCSK1 or LEPR deficiency as determined by an FDA-approved test 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 Europe, 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 POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Contraindication

Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

WARNINGS AND PRECAUTIONS

Skin Hyperpigmentation, Darkening of Pre-existing Nevi, and Development of New Melanocytic Nevi: Generalized increased skin pigmentation and darkening of pre-existing nevi have occurred because of its pharmacologic effect. Full body skin examinations prior to initiation and periodically during treatment should be conducted to monitor pre-existing and new pigmentary lesions.

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females 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, suicidal ideation and depressed mood 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.

Pediatric Population: The prescribing physician should periodically assess response to setmelanotide therapy. In growing children, the impact of weight loss on growth and maturation should be evaluated. In Europe, the prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: IMCIVREE is not approved for use in neonates or infants. Serious and fatal adverse reactions including "gaspings syndrome" can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs.

ADVERSE REACTIONS

Most common adverse reactions (incidence $\geq 20\%$) 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 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 U.S. Prescribing Information and EU Summary of Product Characteristics 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 potential, safety, efficacy of setmelanotide, RM-718 and other product candidates; clinical design, enrollment, or progress, and preliminary, interim and final data readouts; potential

regulatory submissions, approvals and timing thereof of setmelanotide, RM-718 and other product candidates; the potential benefits of any of the Company's products or product candidates for any specific disease indication or at any dosage, including the potential benefits of setmelanotide or RM-718 for patients with PWS, BBS or POMC, PCSK1, or LEPR deficiency; expectations surrounding pending and potential regulatory submissions and approvals, including within the United States, the EU and other regions; business strategy and plans, including regarding commercialization of setmelanotide in the United States, the EU and other regions; our participation in upcoming events and presentations; 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, 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 discussed under the caption "Risk Factors" in Rhythm's Quarterly Report on Form 10-Q for the three months ended September 30, 2025 and 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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Rhythm Pharmaceuticals

Positive Preliminary Results from Phase 2 Trial Evaluating
Setmelanotide in Patients with Prader-Willi Syndrome

December 11, 2025



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Forward-looking Statements

This presentation and the accompanying oral presentation contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy of setmelanotide, RM-718 and other product candidates; clinical design, enrollment, or progress, and preliminary, interim and final data readouts; potential regulatory submissions, approvals and timing thereof of setmelanotide, RM-718 and other product candidates; the potential benefits of any of the Company's products or product candidates for any specific disease indication or at any dosage, including the potential benefits of setmelanotide or RM-718 for patients with PWS, BBS or POMC, PCSK1, or LEPR deficiency; expectations surrounding pending and potential regulatory submissions and approvals, including within the United States, the EU and other regions; business strategy and plans, including regarding commercialization of setmelanotide in the United States, the EU and other regions; our participation in upcoming events and presentations; 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, 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, 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 September 30, 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.

Industry and Other Data

Unless otherwise indicated, information contained in this presentation concerning our industry and the markets in which Rhythm operates, including its general expectations, market position and market opportunity, is based on its management's estimates and research, as well as industry and general publications and research, surveys and studies conducted by third parties. While we believe the information from these third-party publications, research, surveys and studies is reliable, it does not guarantee the accuracy or completeness of such information, and Rhythm has not independently verified this information. Management's estimates are derived from publicly available information, their knowledge of the company's industry and their assumptions based on such information and knowledge, which they believe to be reasonable. This data involves a number of assumptions and limitations which are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in our periodic reports filed with the Securities and Exchange Commission under the captions "Cautionary Note Regarding Forward Looking Statements," "Summary Risk Factors" and "Risk Factors." These and other factors could cause Rhythm's future performance and market expectations to differ materially from its assumptions and estimates.

On Today's Call



David Meeker, MD
Chairman, President & Chief
Executive Officer,
Rhythm Pharmaceuticals



Jennifer Miller, MD
Professor of Pediatric
Endocrinology, University of
Florida

David Meeker, MD

Chairman, President & Chief Executive Officer

Promising Phase 2 Preliminary Results in Patients with Prader-Willi Syndrome

- Potential therapeutic benefit with BMI, hyperphagia reductions observed in patients with Prader-Willi syndrome (PWS) treated with setmelanotide at Month 3 (n=8) and Month 6 (n=5)
- Promising preliminary results supportive of Phase 3, registrational trial of setmelanotide in PWS
- Initiated Part D in Phase 1 study to evaluate RM-718 in patients with Prader-Willi syndrome

Significant Unmet Need in Prader-Willi Syndrome

PWS is a **complex, multi-system** disorder

Obesity and hyperphagia may begin in early childhood; if not managed by stringent food restrictions and environmental controls, often **results in life-threatening obesity**

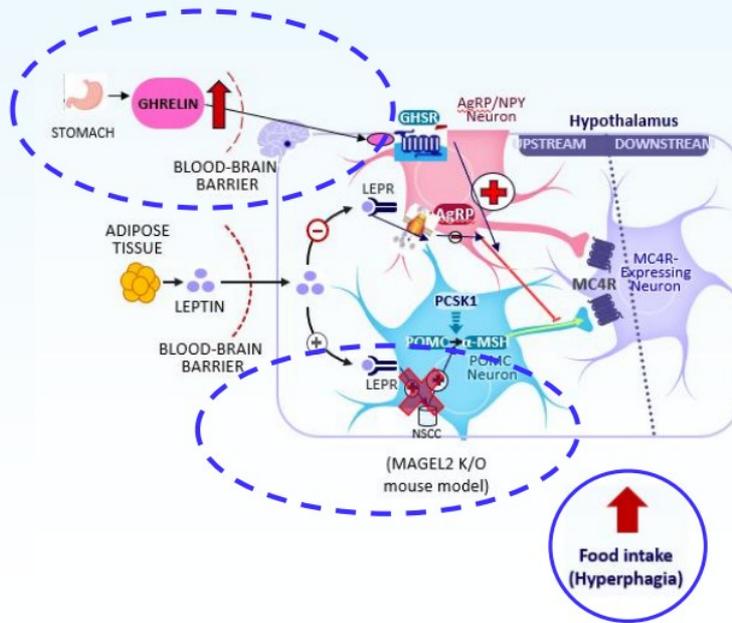
Currently **limited therapeutic options** that effectively reduce the **extreme hyperphagia** and address **low resting energy expenditure**

~20,000* patients
estimated
U.S. prevalence

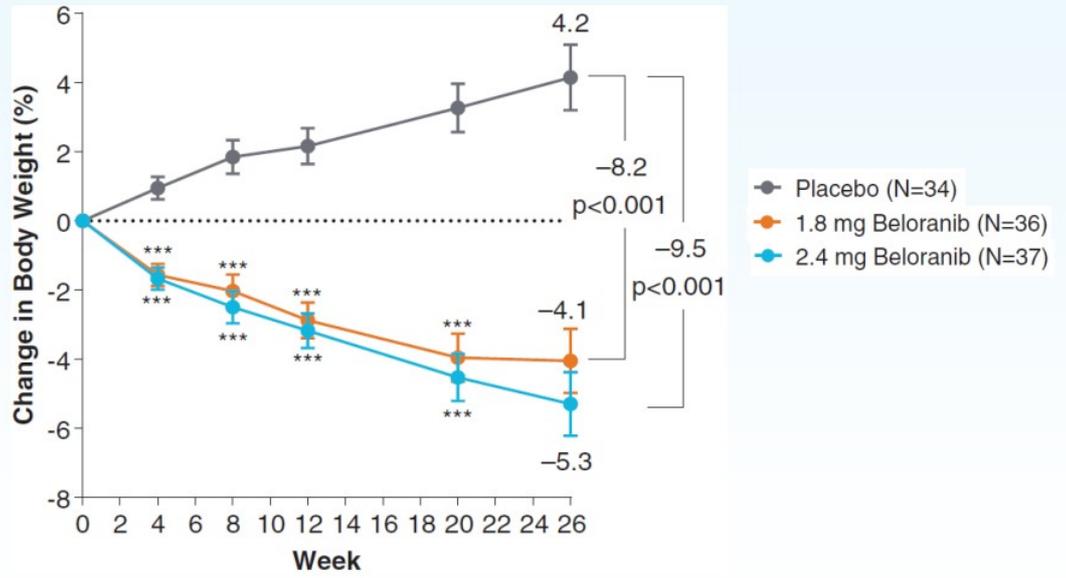
~400,000*
Estimated world-wide
prevalence

*Driscoll DJ, Miller JL, Cassidy SB. Prader-Willi Syndrome. In: Adam MP, Bick S, Mirzaa GM, et al, eds. *GeneReviews*®. 1998:1-41. Updated December 5, 2024. Accessed December 10, 2025. <https://www.ncbi.nlm.nih.gov/books/NBK1330/>

PWS: Complex Pathophysiology; MC4R Pathway Plays a Central Role



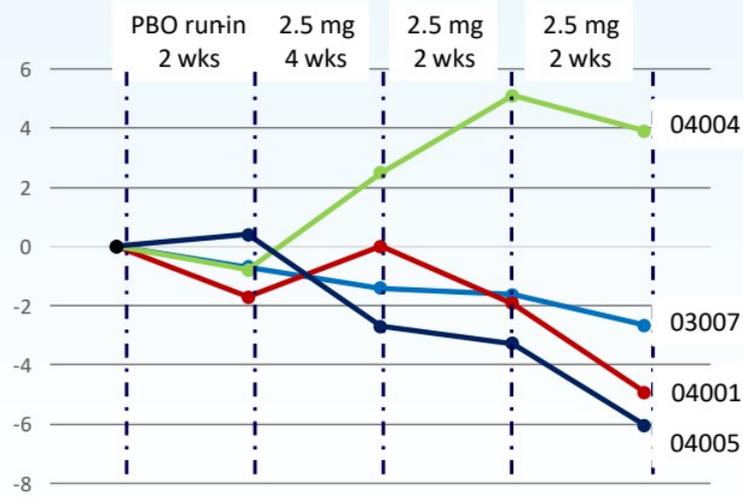
Historical Context: Beloranib Trial Results in PWS with Mean % Change in Body Weight from Baseline to Week 26



Diabetes Obes Metab. 2017;19:1751-1761.

Prior Setmelanotide Trial in PWS in 2016 had Maximum Dose of 2.5 mg for 8 Weeks in 4 Patients

Individual patients demonstrated promising weight loss after 8 weeks



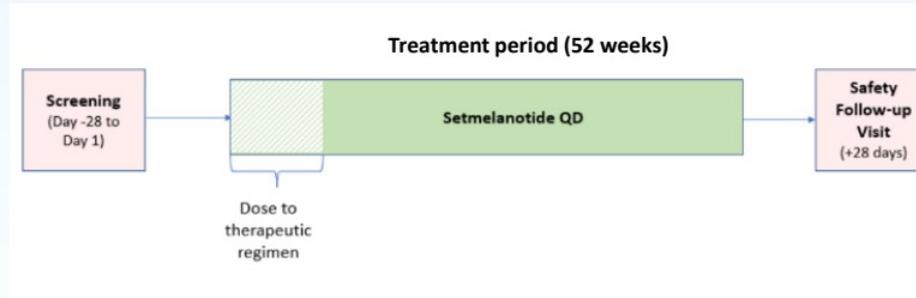
Exploratory Phase 2, Open-label Trial of Setmelanotide in PWS

18 patients with PWS and obesity aged 6 to 65 years old enrolled

Daily dose of setmelanotide escalated up to **5 mg/day** as tolerated for **52 weeks**

Primary endpoints: safety and tolerability

Key secondaries: assessments on **BMI, hyperphagia, body composition** and pharmacokinetics



Baseline Demographics

Parameter	Statistic	Overall (N=18)
Age, years	Mean (SD) (range)	17.1 (5.6) (6 – 23)
	<12 years old, n (%)	3 (16.7)
	≥12 years and <18, n (%)	4 (22.2)
	≥18 years old, n (%)	11 (61.1)
Sex, n (%)	Female / Male	8/10 (44.4/55.6)
Race, n (%)	White	15 (83.3)
	Multiple	2 (11.1)
	Asian	1 (5.6)
BMI, kg/m ²	Mean (SD)	39.1 (9.5)
	Range	24.2 – 67.0
BMI, kg/m ² (n=8*)	Mean (SD)	43.7 (10.3)
	Range	32.6 – 67.0

*BMI for the 8 patients with ≥3 months' treatment

N=18
Patients enrolled

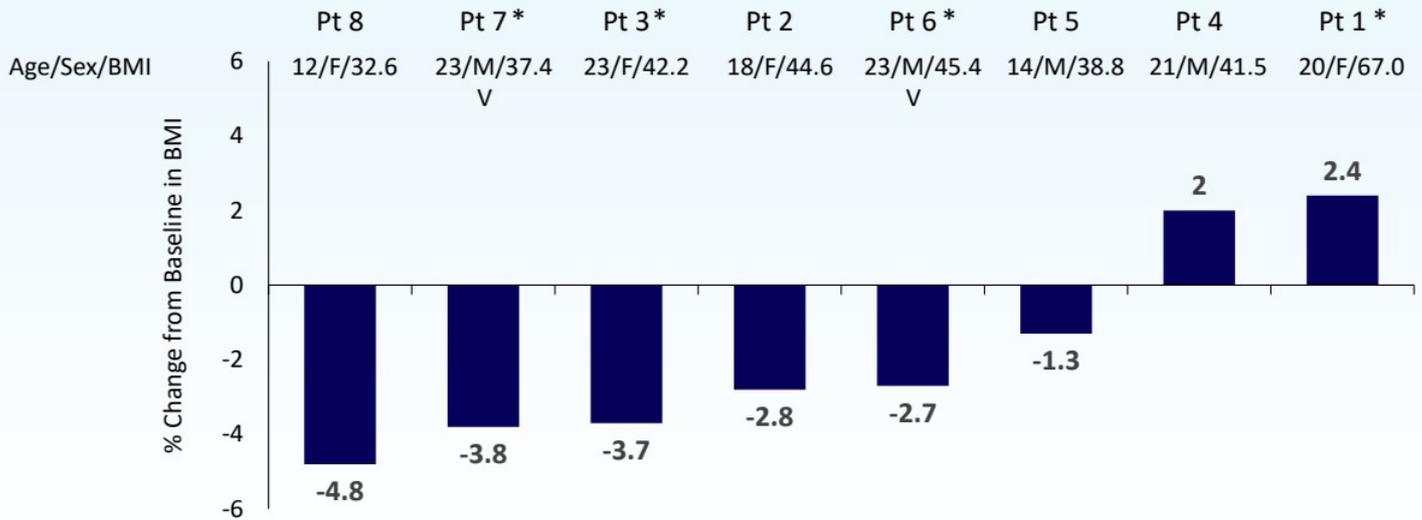
n=8
patients reached
Month 3¹

n=5
patients reached
Month 6¹

17
patients remain
on active therapy

1. Data cut-off date is Nov. 14, 2025

Setmelanotide Achieved BMI Reductions from Baseline in 6 of 8 Patients with PWS at Month 3



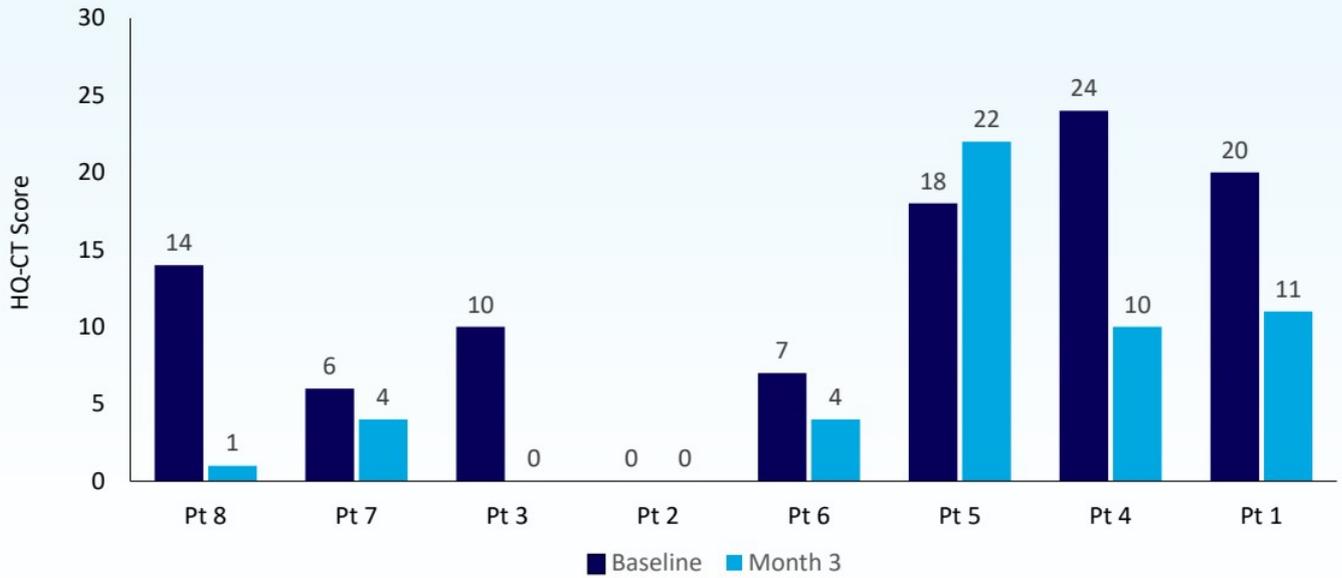
Notes:

V=Patients 7 and 6 are on Vykat™ XR (diazoxide choline); *Patients 7, 3, 6, and 1 have type 2 diabetes.

Patient 3: Worsened diabetes control after 13 weeks, started on insulin. Patient 4: stopped dosing then restarted at a low dose.

Patient 1: improved adherence with basal insulin at enrollment

HQ-CT¹ Scores Showed Meaningful Hyperphagia Reductions from Baseline Observed in 6 of 7 Evaluable Patients at Month 3



1. The Hyperphagia Questionnaire for Clinical Trials (HQ-CT) is a 9-item, observer-reported outcome measure that assesses changes in hyperphagic behaviors in individuals with PWS. Each item is scored from 0 to 4, for a total possible score of 36.

Setmelanotide Achieved BMI Reductions from Baseline in Patients with PWS After 3 and 6 Months of Treatment

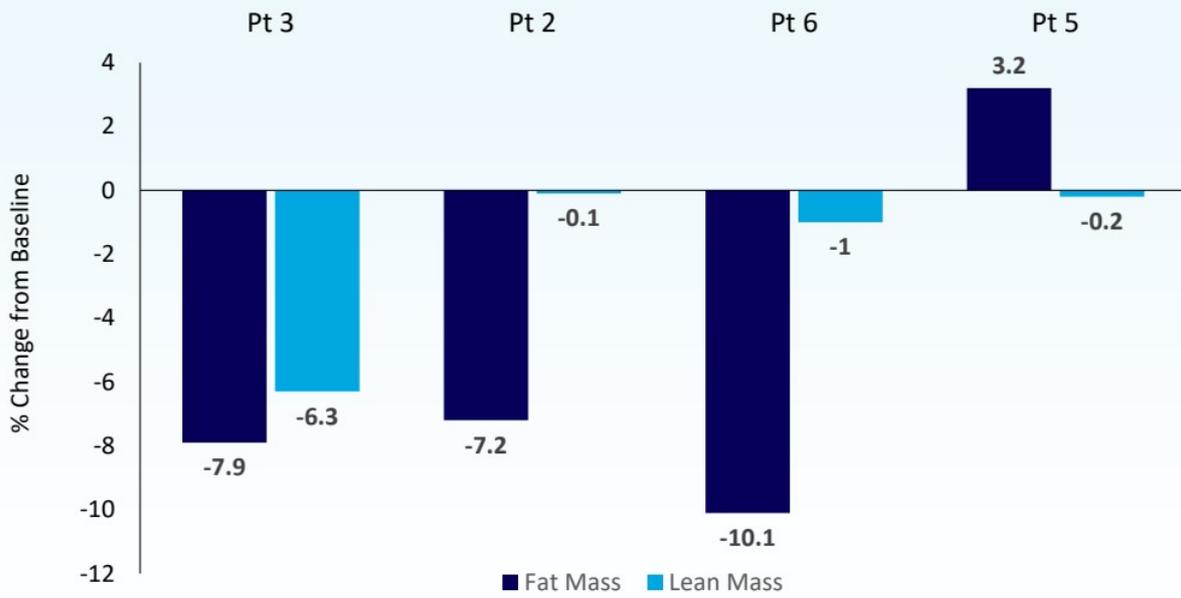


Notes:

V=Patients 7 and 6 are on Vykat™ XR (diazoxide choline); *Patients 7, 3, 6, and 1 have type 2 diabetes.

Patient 3: Worsened diabetes control after 13 weeks, started on insulin. Patient 5: non compliant after initial response; Patient 4: discontinued prior to visit 6. Patient 1: poorly controlled diabetes, lipohypertrophy, severe lower extremity lymph edema

Positive Body Composition Changes from Baseline to Month 6



Note: There are no DEXA data for Patient 1 (exceeded table's weight limits)

Setmelanotide Achieved BMI Reductions from Baseline in Patients with PWS After 3 and 6 Months of Treatment



Notes:

V=Patients 7 and 6 are on Vykat™ XR (diazoxide choline); *Patients 7, 3, 6, and 1 have type 2 diabetes.

Patient 3: Worsened diabetes control after 13 weeks, started on insulin. Patient 5: non compliant after initial response; Patient 4: discontinued prior to visit 6. Patient 1: poorly controlled diabetes, lipohypertrophy, severe lower extremity lymph edema

Adverse Events for All Patients (N=18)

Adverse Events	Overall n (%) (n=18)
Skin hyperpigmentation	5 (27.8)
Injection site reaction	4 (22.2)
Fatigue	1 (5.6)
Injection site irritation	1 (5.6)
Peripheral swelling	1 (5.6)
Nausea	1 (5.6)
Vomiting	1 (5.6)
Localized infection	1 (5.6)
Diabetes mellitus inadequate control	1 (5.6)
Lymphedema	1 (5.6)

- There were no deaths, serious AEs, or AEs that led to drug withdrawal

Discussion with Dr. Jennifer Miller

Next Steps

Setmelanotide PWS Updates

- Complete six-month data readout in H1 2026
- Submit for presentation at a medical conference in 2026
- Begin planning for Phase 3 registrational trial

Phase 1, Part D initiated to evaluate RM-718 in PWS

- Up to 20 patients; 28-day screening period followed by 26 weeks open-label therapy
- Weekly dose titration: 10, 20, 30, 40 mg; may increase to 50 mg with PI and sponsor approval
- 1st patient screening anticipated in December 2025

Questions?