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 6, 2023**

RHYTHM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38223**	**46-2159271**
(State or other jurisdiction of incorporation)	(Commission File Number)	(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 8.01 Other Events.

Phase 3 Pediatrics Trial

On December 6, 2023, Rhythm Pharmaceuticals, Inc. (the "Company") presented new data from its 52-week, Phase 3 pediatrics trial in patients between 2 and younger than 6 years old. The trial is a multi-center, one-year, open-label trial in pediatric patients with obesity due to biallelic proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency or a clinical diagnosis of Bardet-Biedl syndrome (BBS) with genetic confirmation. The primary efficacy endpoint is a responder analysis, based on the proportion of patients who experience a decrease from baseline in BMI-Z score of ≥0.2.

Highlights from the data include:

- 83.3% of all patients (10 of 12) achieved ≥ 0.2 reduction in BMI-Z score from baseline to week 52;
- 18.4 percent mean reduction from baseline in BMI at week 52 (N=12);
- 3.04 mean reduction from baseline in BMI-Z score at week 52 (N=12);
- 11 patients completed the trial, and all remain on therapy, as of Dec. 5, 2023; one patient discontinued and was lost to follow-up; and
- The safety profile is consistent with past trials evaluating setmelanotide.

The Company also announced it has submitted a Type II variation application to the European Medicines Agency seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in pediatric patients between 2 and younger than 6 years old with BBS or POMC, PCSK1 or LEPR deficiency in the European Union. The Company anticipates submitting a supplementary New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) in the first half of 2024 seeking a similar label expansion.

Phase 2 DAYBREAK Trial

Also on December 6, 2023, the Company announced data from the open-label part of its exploratory Phase 2 DAYBREAK trial. The Company presented data from the full analysis set for DAYBREAK, which includes 164 patients. A total of 112 patients completed the 16-week Stage 1 of the Phase 2 trial, with 52 patients who discontinued.

The primary endpoint of the trial is the proportion of patients by genotype who achieve a BMI reduction of ≥5% from baseline in response to setmelanotide at the end of Stage 1. The rates of response from Stage 1 of the trial were:

- 30% of patients (12 of 40) with variants in the *SEMA3* gene cohort;
- 35.6% of patients (16 of 45) with variants in the *PLXN*s gene cohort;
- 56.3% of patients (9 of 16) with variants in the *PHIP* gene cohort;
- 40% of patients (2 of 5) with variants in the *TBX3* gene cohort;
- 30% of patients (3 of 10) with variants in the *MAGEL2* gene cohort; and
- 25% of patients (5 of 20) with variants in the *SIM1* gene cohort.

For those who completed Stage 1, the rates of response of patients who achieved a BMI reduction of greater than 5% from a post-hoc analysis were:

- 44.4% of patients (12 of 27) with variants in the *PLXN*s gene cohort;
- 61.5% of patients (16 of 26) with variants in the *SEMA3* gene cohort than 5%; and
- 69.2% of patients (9 of 13) with variants in the *PHIP* gene cohort.

A total of 49 patients who completed Stage 1 with a response to setmelanotide were randomized into Stage 2 of the trial. Stage 2 is a 24-week, double-blind, placebo-controlled withdrawal study. These patients were stratified into genetically defined cohorts and randomized 2:1 to receive setmelanotide or placebo.

The Company anticipates announcing DAYBREAK Stage 2 data in the second half of 2024.

RM-718

Also on December 6, 2023, the Company announced that it completed submission of a new investigational drug application for RM-718, a new, weekly, MC4R-specific agonist, to the FDA. The Company anticipates beginning Phase 1 in-human trials in the first half of 2024, including a multiple-ascending dose study in patients with hypothalamic obesity.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Current Report on Form 8-K that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical progress of setmelanotide, including the anticipated timing for initiation of clinical trials and release of clinical trial data and the Company's expectations surrounding potential regulatory submissions. Statements using word such as "expect", "anticipate", "believe", "may", "will", "aim" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, risks relating to the Company's liquidity and expenses, the Company's ability to enroll patients in clinical trials, the design and outcome of clinical trials, the ability to achieve necessary regulatory approvals, risks associated with data analysis and reporting, failure to identify and develop additional product candidates, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing the Company's international operations and the costs of any related compliance programs, the impact of competition, risks relating to product liability lawsuits, inability to maintain collaborations, or the failure of these collaborations, the Company's reliance on third parties, risks relating to intellectual property, the Company's ability to hire and retain necessary personnel, the impact of the COVID-19 pandemic and general economic conditions on the Company's business and operations, including its preclinical studies, clinical trials and commercialization prospects, failure to realize the anticipated benefits of the Company's acquisition of Xinvento B.V. or significant integration difficulties related to the acquisition, and the other important factors discussed under the caption "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 and its other filings with the Securities and Exchange Commission. Except as required by law, the Company undertakes 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.

SIGNATURES

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

RHYTHM PHARMACEUTICALS, INC.

Date: December 6, 2023

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