Rhythm Pharmaceuticals

First Quarter 2026
Financial Results and Business Update

May 5, 2026

On Today's Call

- David Connolly, Vice President of Investor Relations and Corporate Communications
- David Meeker, MD, Chair, President and Chief Executive Officer
- Jennifer Lee, Executive Vice President, Head of North America
- Yann Mazabraud, Executive Vice President, Head of International
- Hunter Smith, Chief Financial Officer

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 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 hypothalamic obesity (HO) 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, including marketing approval in Japan and the timing thereof; the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products, including setmelanotide for the treatment of acquired HO; the future announcement of data from our ongoing clinical trials, including the substudy evaluating setmelanotide for patients with congenital hypothalamic obesity, Part C of the Phase 1 trial evaluating RM-718, and the open-label Phase 2 trial evaluating setmelanotide, in patients with PWS, the ongoing enrollment in our clinical trials; existing or future collaboration agreements; the Company's business strategy and plans; our anticipated financial performance and financial position for any period of time, including our estimated Non-GAAP Operating Expenses for the year ending December 31, 2026; and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations for at least 24 months; 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 quarter 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 press release or to update them to reflect events or circumstances occurring after the date of this press release, whether as a result of new information, future developments or otherwise.

Non-GAAP Financial Measures

This presentation and the accompanying oral presentation include Non-GAAP Operating Expenses, a supplemental measure of our performance that is not required by, or presented in accordance with, U.S. GAAP and should not be considered as an alternative to operating expenses or any other performance measure derived in accordance with GAAP. We define Non-GAAP Operating Expenses as GAAP operating expenses excluding stock-based compensation and fixed consideration related to in-licensing. We caution investors that amounts presented in accordance with our definition of Non-GAAP Operating Expenses may not be comparable to similar measures disclosed by our competitors because not all companies and analysts calculate this non-GAAP financial measure in the same manner. We have not provided a quantitative reconciliation of forecasted Non-GAAP Operating Expenses to forecasted GAAP operating expenses because we are unable, without making unreasonable efforts, to calculate the reconciling item, stock-based compensation expenses, with confidence. This item, which could materially affect the computation of forward-looking GAAP operating expenses, is inherently uncertain and depends on various factors, some of which are outside of our control.

David Meeker, MD

Chair, President and CEO

Q1 2026: Transformational Quarter for Rhythm

Business Highlights

- **Strong start to US launch of IMCIVREE®** (setmelanotide) for acquired hypothalamic obesity (HO) with **>150 start forms*** received following FDA approval
- **European Commission granted marketing authorization for IMCIVREE** for the treatment of acquired HO; launches expected in 2027
- **Japan's PMDA** accepted, **validated IMCIVREE new drug application for acquired HO**; anticipated decision in the second half of 2026 and, if positive, expected commercial launch by the end of 2026
- Solid **Q1 2026 with $60.1M** in global net sales of IMCIVREE

* As of May 1, 2026

Significant Global Market Opportunity in Acquired HO

~10,000

estimated U.S. prevalence[1]

~10,000

estimated European prevalence[2]

5,000 – 8,000

estimated Japanese prevalence[3]

~500

Estimated incidence in each U.S., Europe and Japan[1, 2, 3]

1. U.S. estimates based on reported incidence of hypothalamic obesity following craniopharyngioma and long-term survival rates, (Zacharia, et al., *Neuro-Oncology* 14(8):1070–1078, 2012. doi:10.1093/neuonc/nos142; and Muller, et al., *Neuro-Oncology* 17(7), 1029–1038, 2015 doi:10.1093/neuonc/nov044.); 2. European estimates limited to the EU4 (Germany, France, Spain, Italy), UK and the Netherlands and prevalence of 0.1-0.3 in 10,000 patients; 3. Rhythm estimates the prevalence of acquired hypothalamic obesity in Japan to be approximately 5,000 to 8,000 based on our review of tumor registries and claims data; Prevalence is 2-3 times higher than in the USA & Europe due to a higher reported frequency of craniopharyngioma.

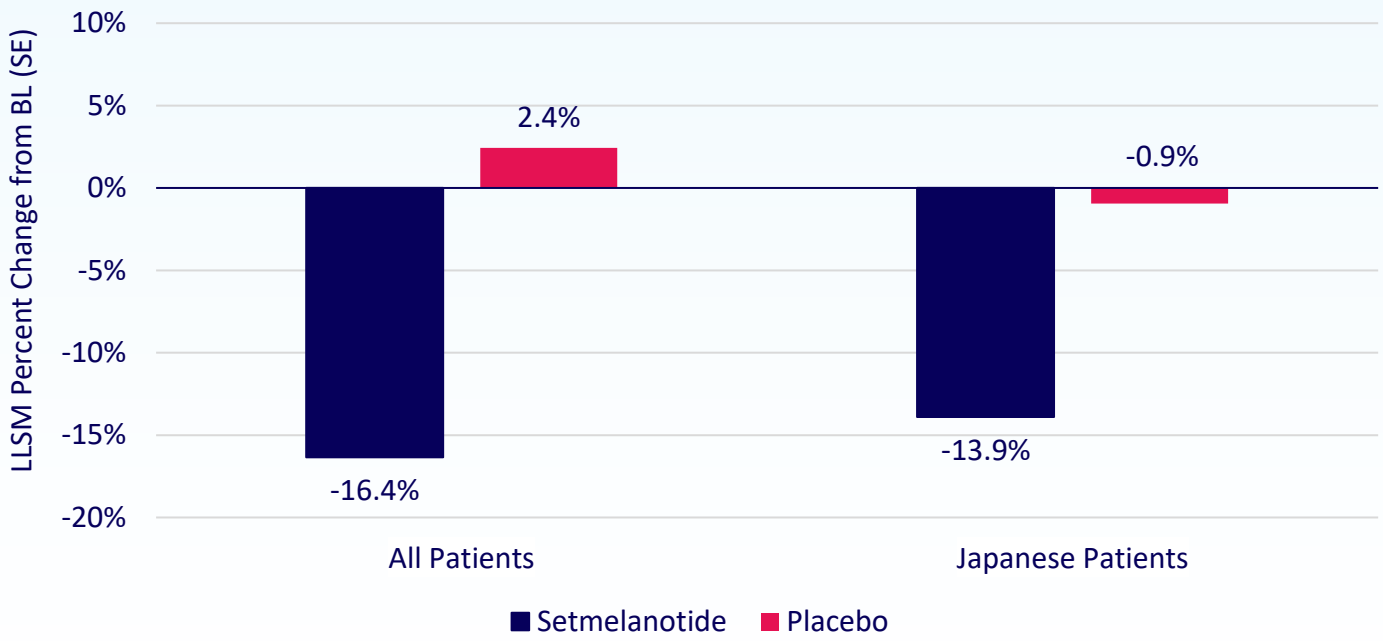
Phase 3 TRANSCEND Results: Data from 12-patient Japanese Cohort Consistent with Full Data Set

-18.8%*

p <0.0001
(n=142: 94 setmelanotide, 48 placebo)

-13.0%*

p = 0.0388
(n=12: 8 setmelanotide, 4 placebo)



*LSM Difference (Setmelanotide-Placebo); primary endpoint based on pre-specified statistical analysis plan

Anticipated Upcoming Milestones

Hypothalamic Obesity

- **Mid 2026:** Disclose data in the **Ph1/2, Part C trial** evaluating **RM-718** in **acquired hypothalamic obesity**
- **H2 2026:** Complete enrollment in **substudy** evaluating **setmelanotide** in **congenital hypothalamic obesity**
- **YE 2026:** Initiate **pivotal Ph3 trial** evaluating **oral bivamelagon** in **acquired hypothalamic obesity**

Prader-Willi Syndrome

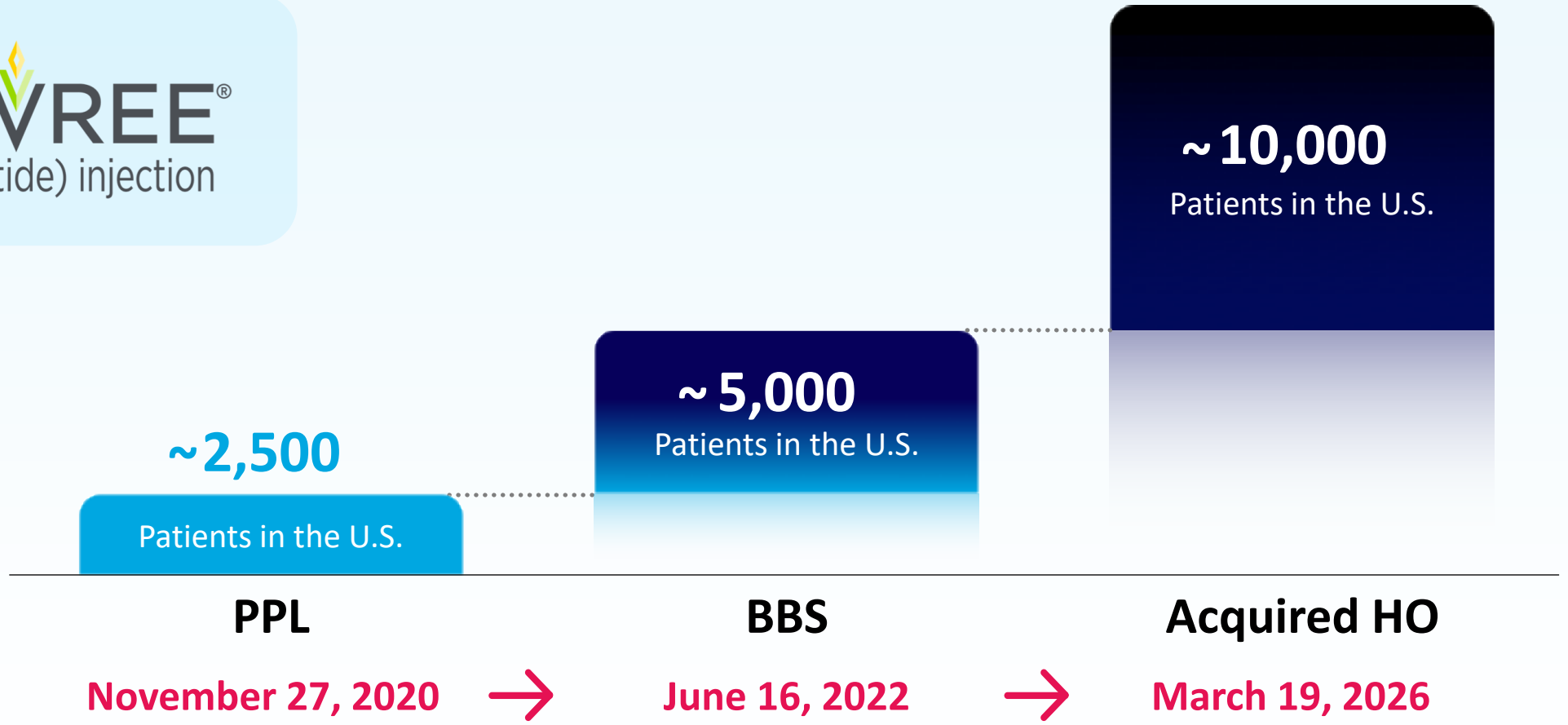
- **Q2 2026:** Disclose six-month results from exploratory **Ph2 trial** evaluating **setmelanotide** in **Prader-Willi syndrome**
- **H2 2026:** Complete enrollment in the **Ph1/2, Part D trial** evaluating **RM-718** in **Prader-Willi syndrome**

Jennifer Lee

EVP, Head of North America

Label Expansion Extends the Reach of IMCIVREE in the U.S.

IMCIVREE® (setmelanotide) injection



NOTE: Estimated prevalence of U.S. patients based on company estimates; does not include ex-U.S. prevalence estimates

Rhythm® PHARMACEUTICALS

U.S. Launch of IMCIVREE for Acquired HO off to a Strong Start

Patients

>150

Patient start forms

Prescribers

~110

Unique prescribers

~80%

New IMCIVREE prescribers

Payers

Early approvals secured

Expect 3 - 9 months for policies to become established

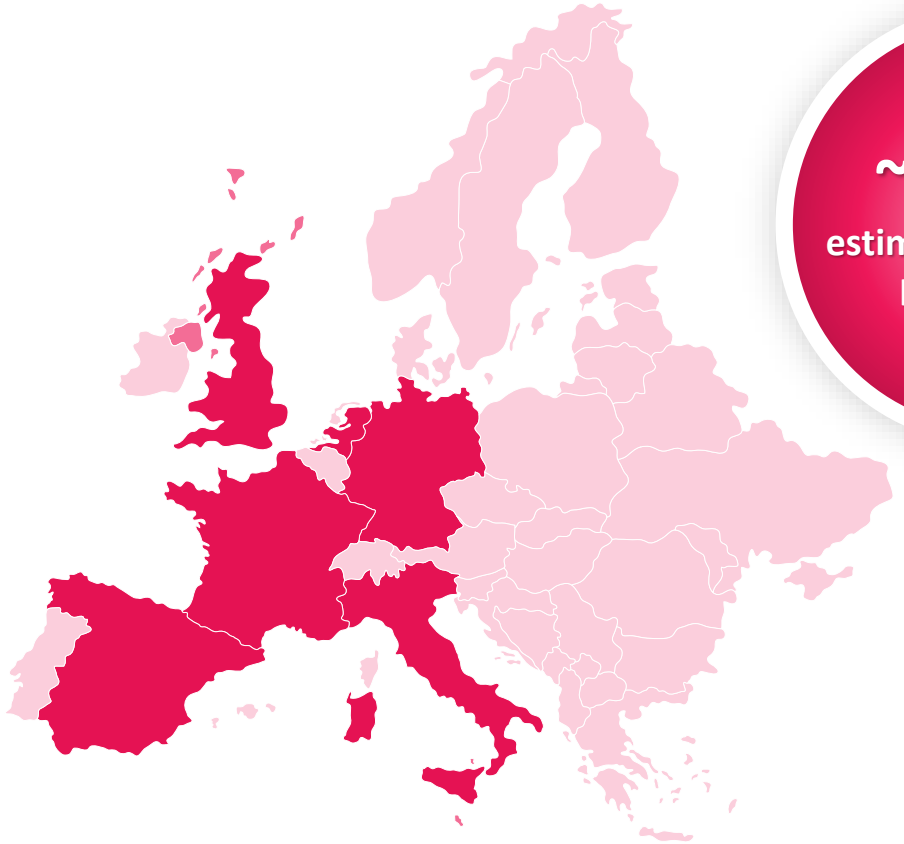
Note: As of May 1, 2026

Yann Mazabraud

EVP, Head of International

IMCIVREE Granted Marketing Authorization by European Commission for the Treatment of Acquired Hypothalamic Obesity

Country-level launches expected to begin in 2027



~10,000
estimated European prevalence[1]

1. European estimates limited to the EU4 (Germany, France, Spain, Italy), UK and the Netherlands and prevalence of 0.1-0.3 in 10,000 patients

Japanese Regulatory Review Underway; Potential Approval and Launch for Acquired HO Anticipated by End of 2026

5,000 – 8,000
estimated Japanese prevalence[1]

PMDA accepted, validated new drug application

Regulatory decision and potential launch by YE 2026

Focus of Japanese Team

- Disease awareness
- Patient identification
- Preparing for pricing negotiations

1. Rhythm estimates the prevalence of acquired hypothalamic obesity in Japan to be approximately 5,000 to 8,000 based on Rhythm review of tumor registries and claims data

IMCIVREE available in >25 countries outside the United States

Ongoing BBS, POMC/LEPR sales and paid early-access acquired HO programs in France and Italy

Q1 2026

Continued growth in patients on reimbursed therapy

Hunter Smith

Chief Financial Officer

Q1 2026: Continued Growth in IMCIVREE Global Sales

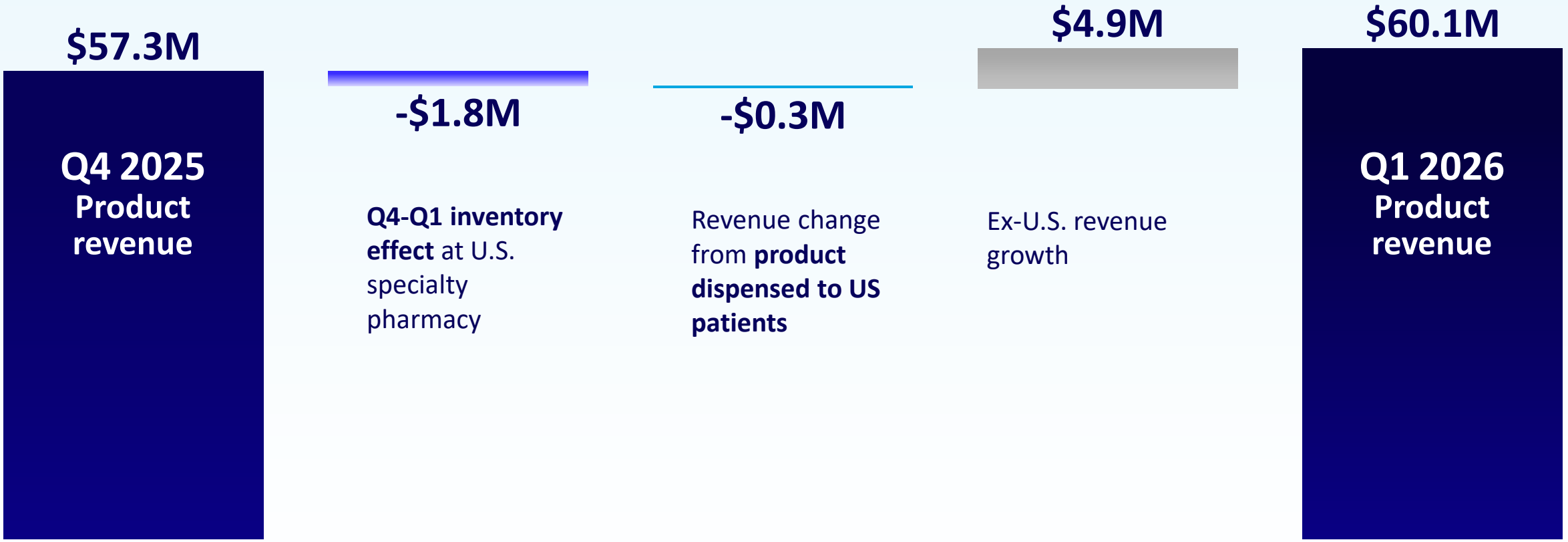
$60.1M
Total product revenue

5% **QoQ** increase from Q4 2025

61% of **Q1 2026** revenue **from U.S.**

~8%
increase in number of patients globally on **reimbursed therapy**

Q4 ‘25 to Q1 ‘26: Consistent Growth in Global Patient Demand Continues



Q1 2026 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended March 31, 2026	Three months ended March 31, 2025
Product revenue, net	$60.1M	$37.7M
R&D expenses	$41.7M	$37.0M
SG&A expenses	$63.6M	$39.1M
Net Loss attributable to common stockholders	$(56.7)M	$(50.8)M
Weighted average common shares outstanding	67,974,193	63,059,165
Net Loss per share attributable to common stockholders – basic and diluted	$(0.83)	($0.81)
Cash, cash equivalents and short-term investments position (period end)	$340.6M	$314.5M

RYTM expects cash to be sufficient
to fund planned operations for **at least 24 months**

Q1 2026 Financial Highlights

Q1’ 2026 OpEx

$105.3M

GAAP OpEx, which includes **$23.1M** in stock-based compensation

$82.2M*

Non-GAAP OpEx

2026 OpEx Guidance

$385M to $415M

anticipated **non-GAAP Operating Expenses*** for 2026 includes:

R&D: $197M to $213M

SG&A: $188M to $202M

* Non-GAAP Operating Expenses is a non-GAAP financial measure. We define Non-GAAP Operating Expenses as GAAP operating expenses excluding stock-based compensation and fixed consideration related to in-licensing. For more information, see slide 3 – Non-GAAP Financial Measures;

Concluding Comments

MC4R Agonism Development Across Three Pillars

Genetic MC4R Pathway Diseases

- Promising signals in POMC Hets and SRC1
- Additional DAYBREAK genes

Hypothalamic Obesity

- U.S. launch
- Ex-US expansion
- Ongoing Ph2 trial with RM-718
- Initiate Ph3 trial with bivamelagon by YE 2026

Prader-Willi Syndrome

- Ongoing Ph2 trial with setmelanotide
- Ongoing Ph1/2 trial with RM-718

Next-generation MC4R agonists

Questions