

Rhythm Pharmaceuticals

First Quarter 2025 Financial Results
and Business Update

May 7, 2025

Rhythm[®]
PHARMACEUTICALS

On Today's Call

- David Connolly, Executive Director 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 potential use of setmelanotide in patients with acquired hypothalamic obesity; our expectations surrounding potential regulatory submissions, progress, or approvals and timing thereof for any of our product candidates; the announcement of data from our clinical trials, including our Phase 3 trial evaluating setmelanotide for patients with acquired hypothalamic obesity, the substudy evaluating setmelanotide for patients with congenital hypothalamic obesity, the Phase 3 EMANATE trial evaluating setmelanotide in genetically caused MC4R pathway diseases, and the Phase 2 trial evaluating the oral MC4R agonist bivamelagon in acquired hypothalamic obesity; Part C of the Phase 1 trial evaluating RM-718; the open-label Phase 2 trial evaluating setmelanotide in patients with Prader-Willi syndrome; 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 estimated Non-GAAP Operating Expenses for the quarter ending March 31, 2025; and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations; and the timing of any of the foregoing. Statements using words 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, our 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 our 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, our reliance on third parties, risks relating to intellectual property, our ability to hire and retain necessary personnel, general economic conditions, risks related to internal control over financial reporting, and the other important factors discussed under the caption "Risk Factors" in our Form 10-Q for the quarter ended March 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 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

Executing on Long-term Growth Strategy

- Strong results from Ph3 trial of setmelanotide in acquired hypothalamic obesity (HO); On track to complete U.S. and EU regulatory submissions in Q3 2025
- Solid patient demand growth for IMCIVREE® (setmelanotide) in Q1 2025
- Data readout for Ph2 trial of oral bivamelagon in acquired HO on track for Q3 2025
- Well capitalized with expected cash runway into 2027

Severe, Life-long Burden for Patients with Acquired HO

Frequent visits with multiple specialists, a complex regimen of medications, and hospitalization

“Treatment of patients with tumor/treatment-related hypothalamic obesity in the first two years following surgical treatment or radiotherapy”

Müller et al., 2025

scientific reports

3.7

average hospitalizations during the two years following index;

23%

included ICU admission in the first year

12

average number of general practitioner visits and

20

specialist visits, during the two years following index

5.5

average active prescriptions per quarter

22.1

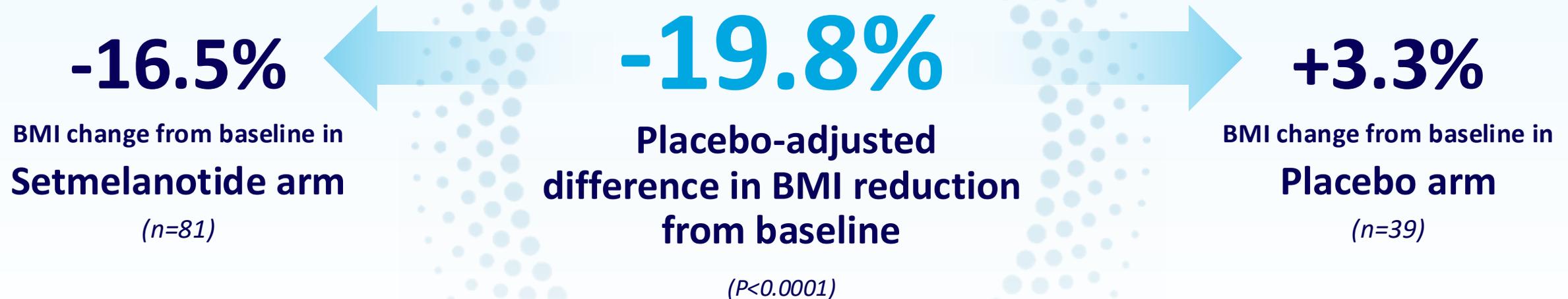
average number of unique medications over 2 years

89%

were receiving ≥ 3 therapies for neuroendocrine dysfunction

Setmelanotide Achieved Statistically Significant and Highly Clinically Meaningful Reduction in BMI in Phase 3 Acquired HO Trial

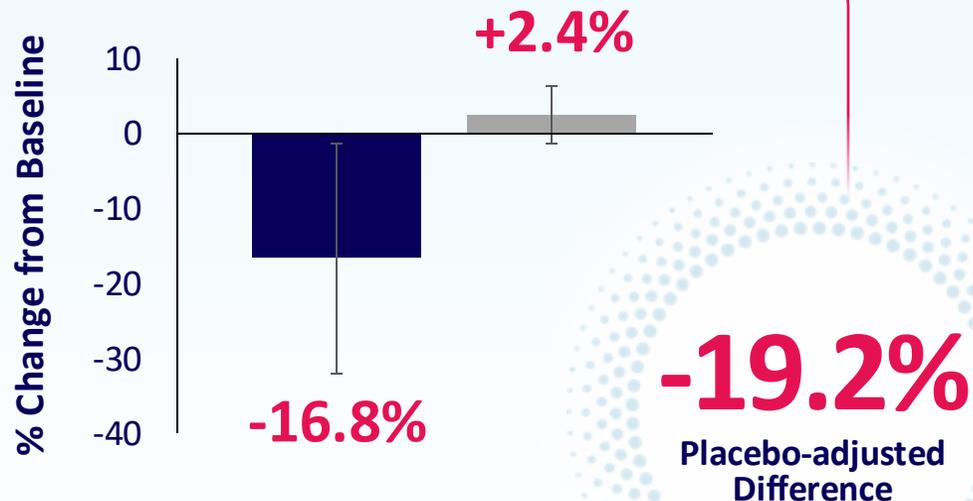
Primary analysis cohort (N=120)



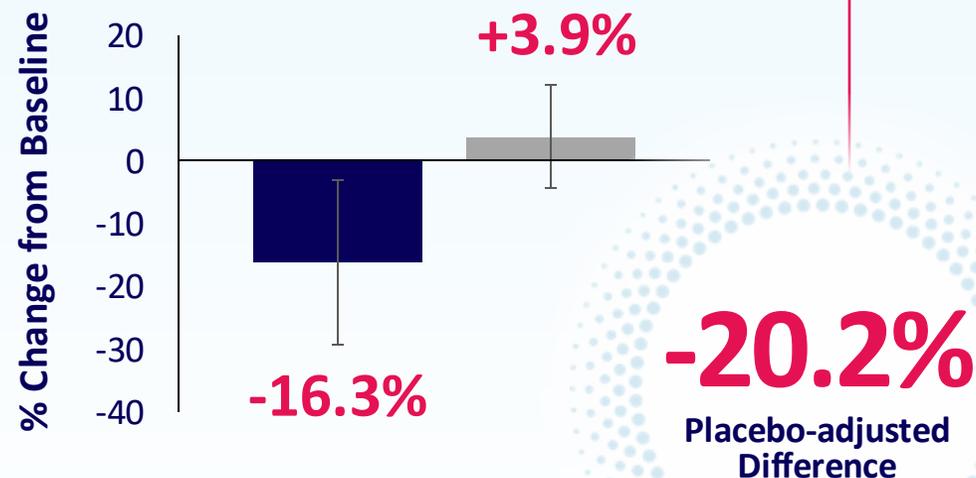
NOTE: Shown are the least square (LS) means for setmelanotide and placebo groups and the LS mean difference in mean percentage change from baseline in BMI at Week 52, obtained from an analysis of covariance (ANCOVA) model. Rubin's Rule was used to provide the overall estimates of differences in LS means and p-value.

Significant Reductions in BMI Observed in both Adults and Children in Phase 3 Trial Evaluating Setmelanotide in Acquired HO

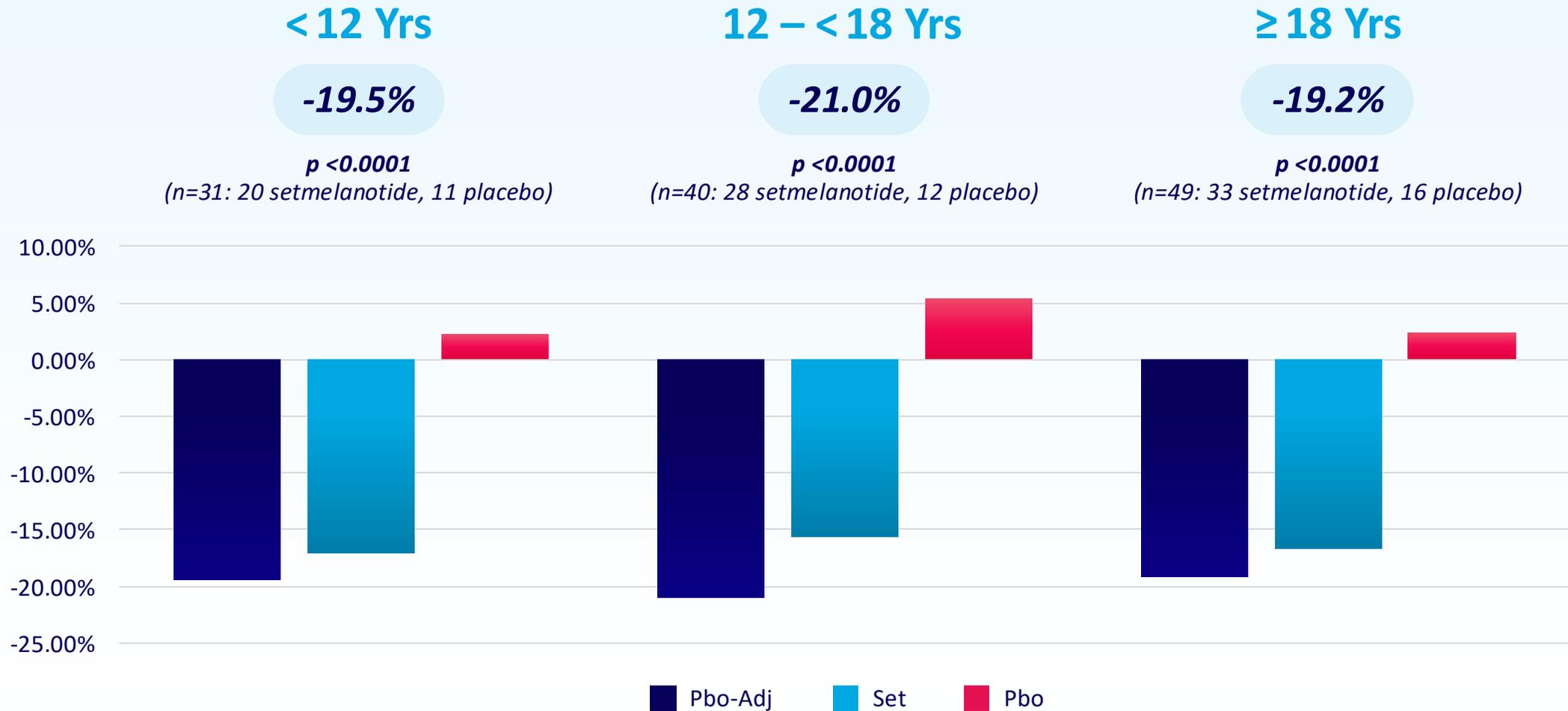
≥18 Years Old (n=49)



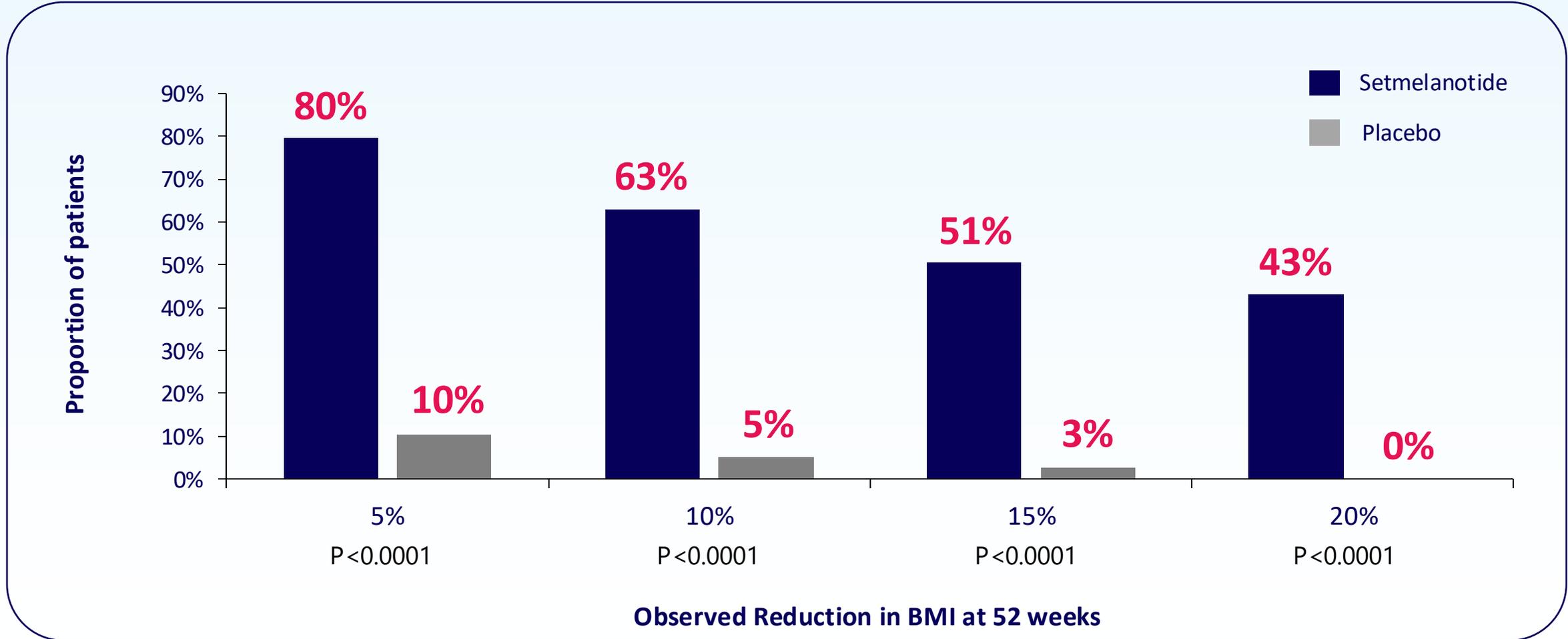
<18 Years Old (n=71)



Mean BMI Reduction Consistent Across Stratified Age Groups in Phase 3 Trial Evaluating Setmelanotide in Acquired HO



Consistent Response to Setmelanotide Therapy Observed across Majority of Patients in Phase 3 Trial in Acquired HO



Vast Majority of Patients with Acquired HO Completed Phase 3 Trial and Transitioned to Extension Study

143 Total Enrolled

120 from pivotal cohort

11 supplemental patients

12 from Japanese cohort

120 Remain on Active Therapy

108 in open label extension (OLE)

12 in ongoing Japanese cohort

Hypothalamic Obesity: A Potentially Transformative Opportunity



5,000 – 10,000

estimated U.S. prevalence¹



3,500 – 10,000

estimated European prevalence²



5,000 – 8,000

estimated Japanese prevalence³

✓ Unmet medical need is high

✓ Patients are identified

✓ Patients engaged with system

~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.

Jennifer Lee

EVP, Head of North America

Consistent Demand and Steady Growth in U.S. BBS Prescriptions

Consistent demand for new prescriptions QoQ

Growth in patients on **reimbursed therapy**

Typical new-year increase in patients on Bridge **resolved by end of Q1**

Disease Education

Clinical Suspicion

Diagnosis

Decision to Treat

Rx IMCIVREE

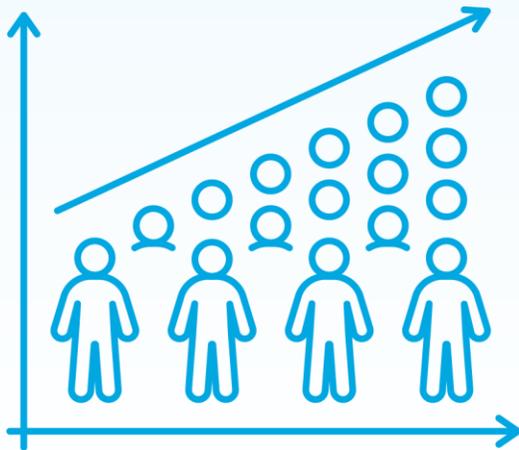
Access

IMCIVREE[®]
(setmelanotide) injection

Maintenance

Growth in both First-time and Repeat IMCIVREE Prescribers in Q1

Consistent growth in prescriber base



13%

**growth in number
of prescribers**
from Q4'24 to Q1'25

32%

**of first-time prescribers
turn into repeat prescribers**
(since launch)

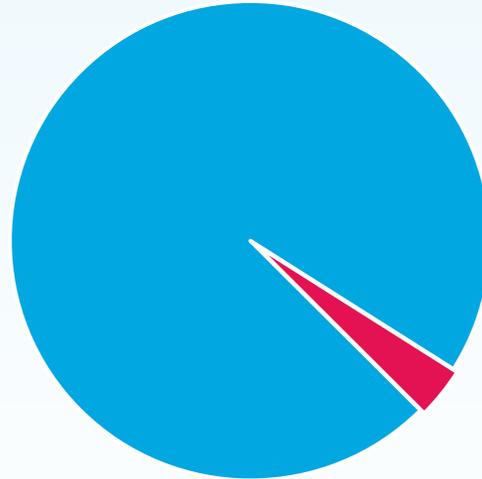
Continued Improvement in Medicaid Access and Reimbursement

>95%**

of covered lives split between states with:

- an IMCIVREE policy in place; or
- or a positive coverage decision in the absence of an IMCIVREE policy**

Medicaid Covered Lives
~85 million*



<5%**

of covered lives in states with:

- no IMCIVREE prescription received;
- or IMCIVREE prescription being processed;
- or no access by policy**

Payor mix remains consistent as ~90% of reimbursed BBS prescriptions since launch fall under commercial and Medicaid plans**

* According to Medicaid, there were approximately 85 million individuals enrolled in Medicaid in all fifty states, Puerto Rico and the District of Columbia, as of December 2022; ** As of Dec. 31, 2023

Endocrinologists Detail Significant Unmet Need in HO

~80%

of patients with acquired HO will remain under endocrinologists' care in perpetuity*

Weight gain, lack of energy, and hyperphagia all ranked as having a **significant impact** on patients' day to day lives

Vast majority of endos are **not satisfied with current therapeutic options** to address overall HO symptoms

All endos outlined they would **prescribe setmelanotide** when showed a blinded target product profile

“

“We need a treatment that is going to be more effective, well tolerated, safe to continue long term because this problem is not going to go away. These patients are going to be on this treatment for their lifetime. Once you withdraw the treatment, they will regain the weight and more.”

– **Endocrinologist**

* Source: Internal market research.

The Majority of Patients and Caregivers Describe Hyperphagia, Weight Gain, and Fatigue as Most Impactful Symptoms on their Daily Lives

“

I was just feeling like a different person after the tumor and the hunger rules your life.”

PATIENT

Hyperphagia



“

To not be able to lose a pound no matter what you do, is very frustrating.”

PATIENT

Weight Gain



“

He can't really get through an entire day without a nap...It's a big issue throughout the day.”

CAREGIVER OF PEDIATRIC PATIENT

Fatigue/Decreased Energy



* Source: Internal market research.

Yann Mazabraud

EVP, Head of International

Strong International Growth Driven by BBS, PPL and now HO

>15

COUNTRIES

Countries with reimbursed access or named patient sales for patients with BBS and POMC or LEPR deficiency obesity

6

COUNTRIES

with reimbursed -early access programs or named patient sales for patients with HO

10 Presentations (including 5 orals) and 2 Expert-led Symposia Planned for Key Medical Conferences in May



Four new data presentations:

- ‘Real-world setmelanotide weight outcomes in French patients with acquired or congenital hypothalamic obesity’ (oral)
- ‘Patient and caregiver experiences with setmelanotide treatment in Bardet-Biedl syndrome – real-world evidence and a patient support program’ (poster)
- ‘Setmelanotide Treatment in Individuals With Obesity and *PHIP* Variants: Results From the DAYBREAK Trial’ (rapid oral)
- ‘Age of onset of hyperphagia and/or obesity as key predictors of a positive genetic test for POMC, PCSK1 or LEPR deficiency or BBS’ (rapid oral)

Two symposia on rare MC4R pathway diseases led by multiple European experts

Confirming reduction in hyperphagia

Hunter Smith

Chief Financial Officer

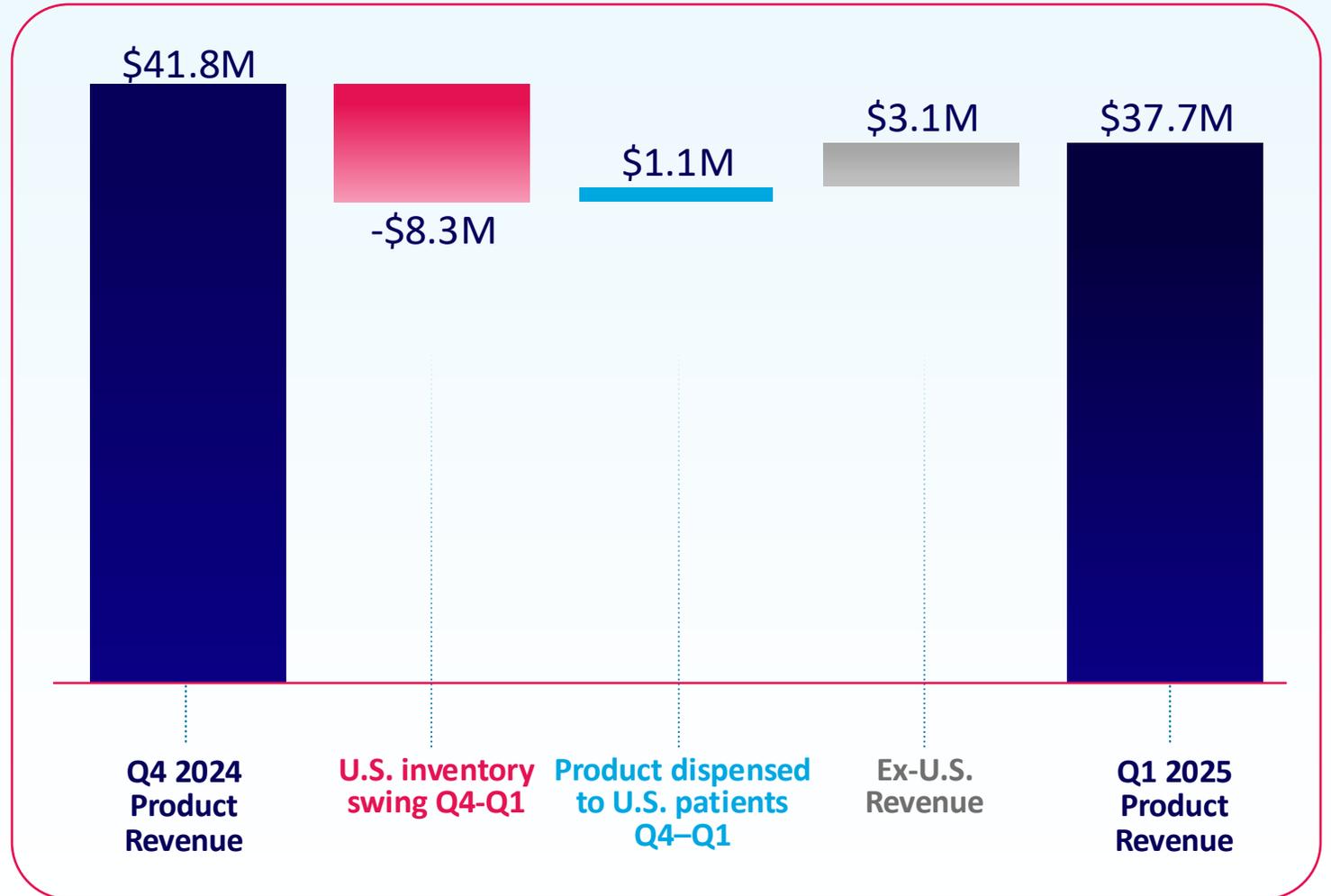
Q1 '25: Patient Demand Continued to Grow in U.S. and ex-U.S.

Patients on reimbursed therapy grew by ~14% globally quarter-over-quarter

Typical Q4-Q1 inventory swing affected U.S. overall revenue

U.S. demand growth driven by increased number of patients on reimbursed therapy

Ex-U.S. growth driven by Germany, France and Italy



1Q 2025 Financial Snapshot

(\$ in millions, except per share data and shares outstanding)	Three months ended March 31, 2025	Three months ended March 31, 2024
Product revenue, net	\$37.7M	\$26.0M
R&D expenses	\$37.0M	\$128.7M
SG&A expenses	\$39.1M	\$34.4M
Net Loss attributable to common stockholders	\$(50.8)M	\$(141.4)M
Common shares outstanding	63,059,165	60,143,558
Net Loss per share attributable to common stockholders – basic and diluted	(\$0.81)	(\$2.35)
Cash, cash equivalents and short-term investments position (period end)	\$314.5M	\$201.2M

Q1 2025 Financial Highlights

\$314.5M

cash, cash equivalents
and short-term
investments as of
March 31, 2025

65%

of Q1 2025 revenue
from U.S. sales of
IMCIVREE, compared
to 74% in Q4 2024

Q1 2025 OpEx
includes

\$12.9M

in stock-based
compensation
expense

1Q 2025
GAAP EPS of
\$(0.81)

**RYTM expects cash to be sufficient
to fund planned operations into 2027**

2025 OpEx Guidance

\$285M to \$315M

anticipated **non-GAAP Operating Expenses*** for 2025 includes:

SG&A: \$135M to 145M

R&D: \$150M to \$170M

\$40M LGC in-license milestone payable by July 4, 2025
accounted for in 2024

* 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

Questions