

Rhythm Pharmaceuticals

Third Quarter 2025 Financial Results
and Business Update

November 4, 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, bivalmelagon, 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 including in relation to the PDUFA goal date for the sNDA for setmelanotide in acquired hypothalamic obesity; our business strategy and plans, including regarding commercialization of setmelanotide and our other product candidates and the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products; 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, our Phase 2 and the anticipated Phase 3 trial evaluating the oral MC4R agonist bivalmelagon in acquired hypothalamic obesity, Part C of the Phase 1 trial evaluating RM-718, and 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; our anticipated financial performance and financial position for any period of time, including estimated Non-GAAP Operating Expenses for 2025; 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”, “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 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 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

Well Positioned to Deliver Long-term, Sustained Growth

Q3'25 Highlights

- Steady growth in global IMCIVREE[®] (setmelanotide) sales in Q3 2025 primarily driven by Bardet-Biedl syndrome
- sNDA for setmelanotide in acquired hypothalamic obesity (HO) accepted by FDA for Priority Review with PDUFA goal date of December 20, 2025
- On track to report preliminary results from setmelanotide Phase 2 trial in Prader-Willi syndrome in Q4 2025
- Well-capitalized to advance clinical trials of weekly MC4R agonist, RM-718, and oral MC4R agonist, bivamelagon, in acquired HO

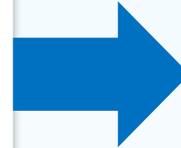
German Investigator-led Observational Study Showed Setmelanotide associated with Improvement in Measures of MASLD, Kidney Function in Patients with BBS

26 patients with BBS completed six months on setmelanotide therapy.



100%

of patients (N=26) with both BBS and metabolic dysfunction-associated steatotic liver disease (MASLD)



>80%

of patients exhibited either resolution of MASLD or stabilization at grade S1*



Adapted from Hühne, T., et al. (2025). *Impact of the melanocortin-4 receptor agonist setmelanotide on MASLD and kidney function in Bardet-Biedl syndrome*. The Journal of Clinical Endocrinology & Metabolism. <https://doi.org/10.1210/clinem/dgaf483>; * MASLD improvement was correlated with only liver size, not BMI reduction; This study was funded by the German Federal Ministry of Research and Education and by Rhythm Pharmaceuticals.

Rhythm is Ready for a Successful U.S. Launch in Hypothalamic Obesity

PDUFA goal date of December 20, 2025



**Significant
unmet need**



**Setmelanotide's
demonstrated
efficacy**



**Transformative
opportunity**

~10,000
estimated U.S. prevalence¹

Multiple Anticipated Milestones

Dec. 20, 2025

PDUFA goal date for setmelanotide **in conditions associated with acquired hypothalamic obesity**

Q4 2025

Disclose preliminary results from exploratory **Ph2 Prader-Willi trial** evaluating setmelanotide

Q1 2026

Complete enrollment in **Part C of Ph1 trial evaluating RM-718** in acquired hypothalamic obesity

Q1 2026

Topline data from **12-patient Japanese cohort** of **Ph3 acquired hypothalamic obesity trial** evaluating setmelanotide

Q1 2026

Topline data from **Ph3 EMANATE trial** evaluating setmelanotide in four genetically-defined, rare MC4R pathway diseases

H1 2026

Complete enrollment in **Ph3 congenital hypothalamic obesity substudy** evaluating setmelanotide

2026

Initiate **pivotal Ph3 trial** evaluating **oral bivamelagon** in **acquired hypothalamic obesity**

Jennifer Lee

EVP, Head of North America

Steady Growth in BBS Commercial Performance Continued in Q3

**Increase in
patients on
IMCIVREE**

**Increased
breadth and depth
of prescribers**

**Disease
Education**

**Clinical
Suspicion**

Diagnosis

**Decision
to Treat**

**Rx
IMCIVREE**

Access

IMCIVREE[®]
(setmelanotide) injection

Maintenance

Strategic Priorities for IMCIVREE Launch in Acquired Hypothalamic Obesity, if approved

PDUFA goal date of December 20, 2025



**Differentiating
MC4R pathway
diseases**



**Expediting
patient
diagnosis**



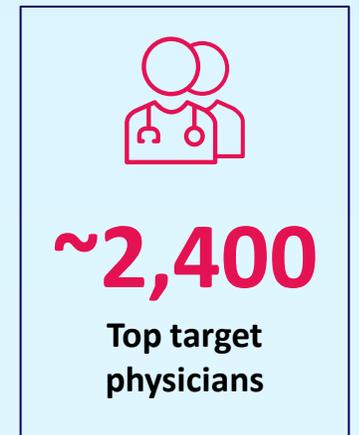
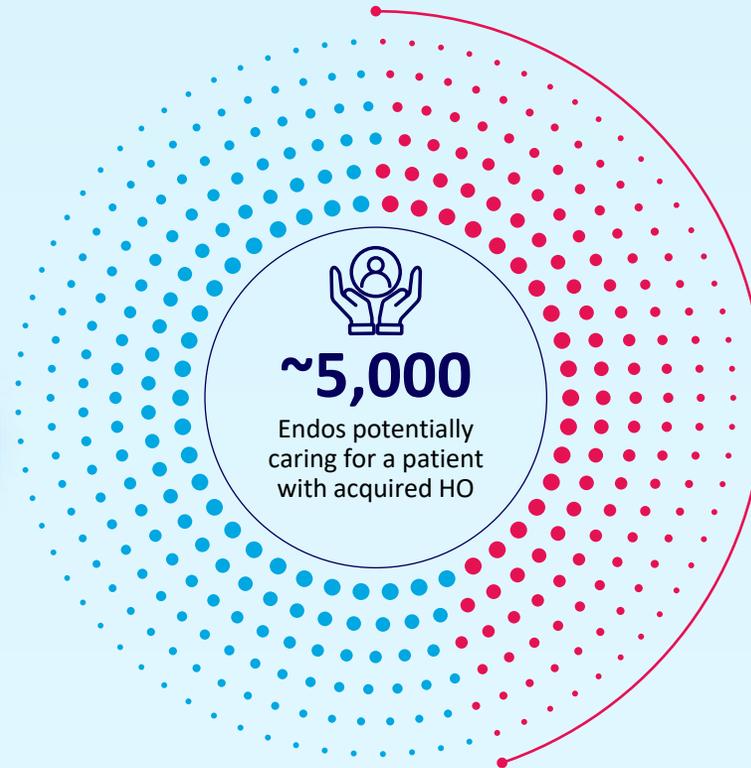
**Establishing
IMCIVREE as *the*
foundational
treatment upon
approval**



**Securing
market access**

Claims Analysis to Inform Physician Targeting

Patients with....



Patient Identification through Physician Profiling



Field teams prioritize top tier
physicians IDed through
claims analysis



Ongoing efforts profiling physicians

>2,000
potential patients

Suspected to have....
or... diagnosed with
**acquired hypothalamic
obesity**

Ready to Launch!

PDUFA goal date of December 20, 2025



Access team
engaging with payers



Territory managers
engaging with HCPs



Patient services team
engaging with
patients, families

Yann Mazabraud

EVP, Head of International

IMCIVREE available in >25 countries outside the United States



Continued execution

Ongoing BBS, POMC/LEPR sales

Final agreement on French price

**Early-access acquired HO programs in
France and Italy**

Named patient sales

Advancing Setmelanotide towards European Launches for Acquired Hypothalamic Obesity

✓ EMA Submission

○ CHMP Opinion

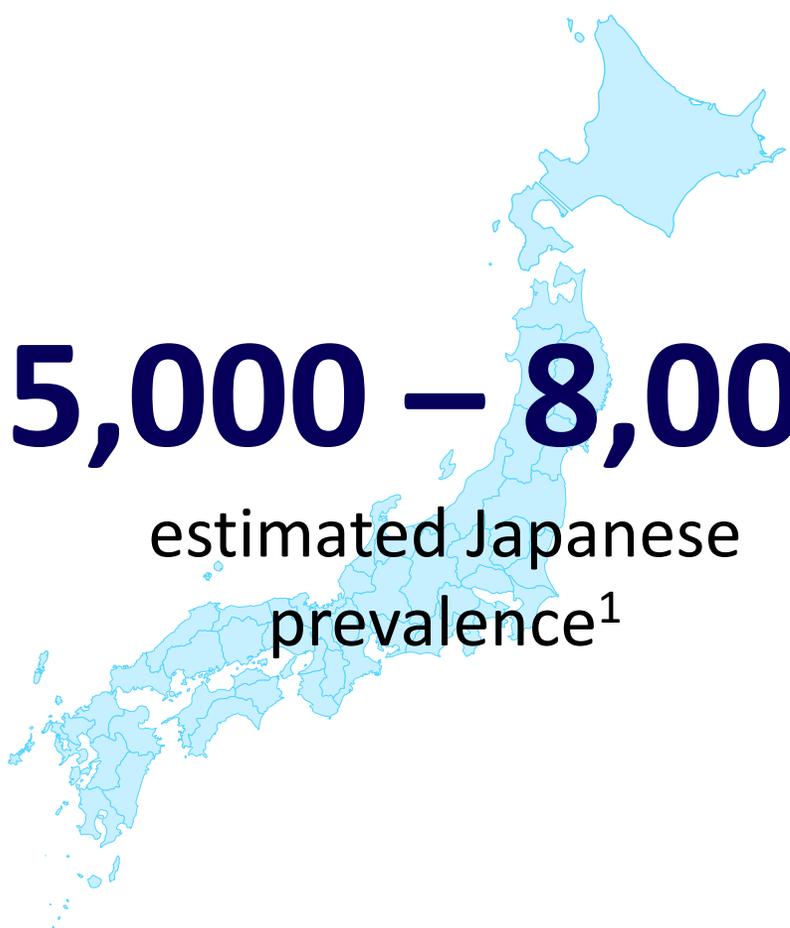
○ EMA Authorization

○ Country-by-country Negotiations



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 people

Building Team in Japan to Support Regulatory Submission, Potential Launch

A light blue map of Japan is positioned in the background of the slide. The text '5,000 – 8,000 estimated Japanese prevalence¹' is overlaid on the map.

5,000 – 8,000

estimated Japanese prevalence¹

Experienced team in place:

- Regulatory
- Quality
- CMC
- Medical affairs
- Market access
- Marketing
- General Management

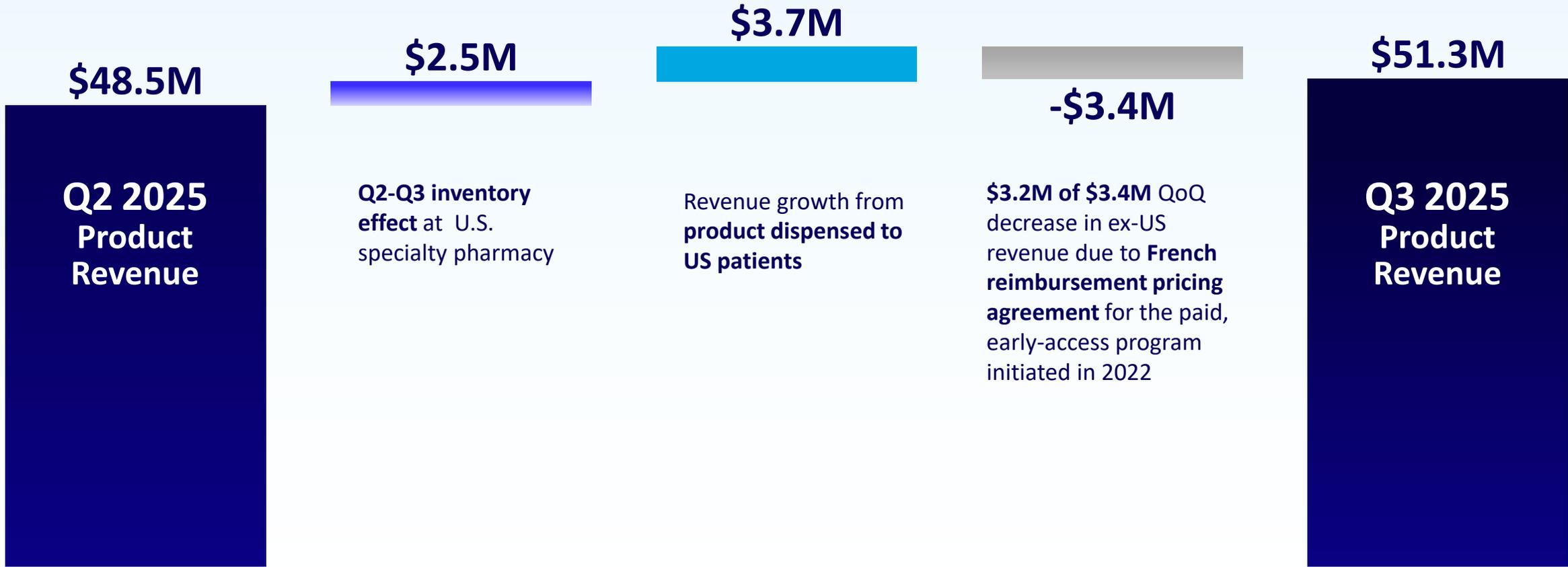
1. Rhythm estimates the prevalence of acquired hypothalamic obesity in Japan to be approximately 5,000 to 8,000 based on our review of tumor registries and claims data

Hunter Smith

Chief Financial Officer

Q2 to Q3 '25: Consistent Growth in Patient Demand Continues in U.S. and ex-U.S.

10% growth in patients on reimbursed therapy globally QoQ



Q3 2025 Financial Snapshot

(\$ in millions, except per share data and shares outstanding)	Three months ended September 30, 2025	Three months ended September 30, 2024
Product revenue, net	\$51.3M	\$33.3M
R&D expenses	\$46.0M	\$37.9M
SG&A expenses	\$52.4M	\$35.4M
Net Loss attributable to common stockholders	\$(54.3)M	\$(45.0)M
Weighted average common shares outstanding	66,261,055	61,219,918
Net Loss per share attributable to common stockholders – basic and diluted	(\$0.82)	(\$0.73)
Cash, cash equivalents and short-term investments balance (period end)	\$416.1M	\$298.4M

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

Operating Expenses in Q3 '25; Updated Full-Year Guidance

Q3 '25 OpEx

\$98.5M

Q3 2025 OpEx
includes

\$18.8M

in stock-based compensation
expense

2025 OpEx Guidance

\$295M to \$315M

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

R&D: \$150M to \$165M

\$40M LGC in-license milestone paid in
July 2025 accounted for as R&D expense in 2024

SG&A: \$145M to \$150M

* 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