

Rhythm Pharmaceuticals

Fourth Quarter, Full Year 2024 Financial Results
and Business Update

February 26, 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 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, 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 year ending December 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 Annual Report on Form 10-K for the year ended December 31, 2024 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

Focus on Long-term Value Drivers

1

Significant potential **expansion opportunity in hypothalamic obesity** (both acquired and congenital)

2

Driving life-cycle management with bivamelagon and RM-718

3

Advancing setmelanotide clinical development in Prader-Willi syndrome and genetically-defined MC4R pathway diseases

4

Continued **BBS global commercial execution**

2025: A Year of Important Milestones and Data Readouts

Acquired hypothalamic obesity

Setmelanotide

Pivotal data readout
on track for

Q2 2025

Bivamelagon

Ph2 enrollment
complete; data
anticipated in

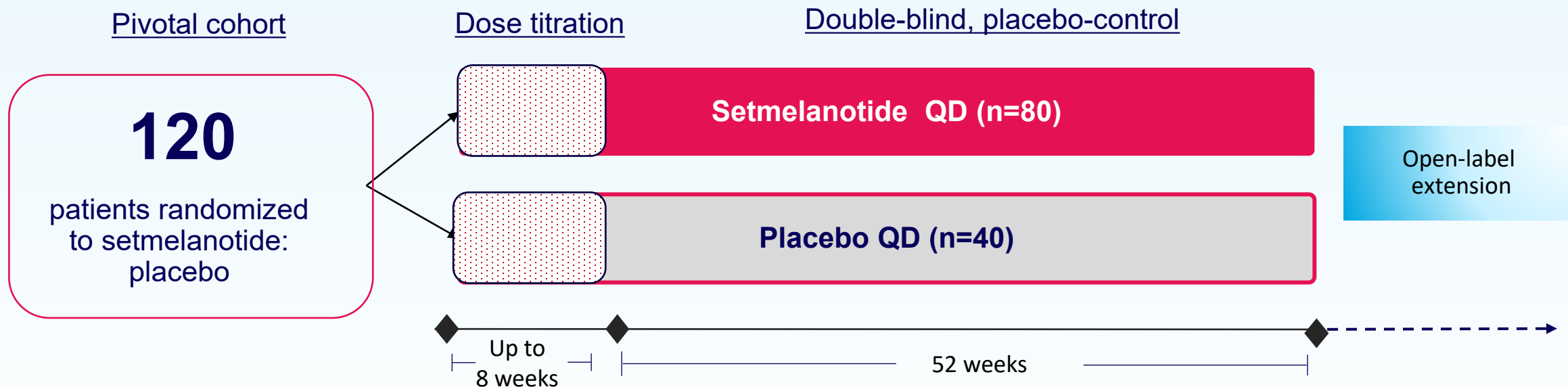
H2 2025

RM-718

HO enrollment to begin
Q1 2025; aiming
for data in

H2 2025

Phase 3 Hypothalamic Obesity Trial: Enrollment Complete, Top-line Data Expected in Q2 2025



+12 Japanese patients enrolled supplemental cohort; Data from this supplemental cohort will serve as the basis for a regulatory submission in Japan.

Hypothalamic Obesity: A Transformative Opportunity for Rhythm



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 frequency of craniopharyngioma been reported.

Multiple Anticipated Milestones

Q1 2025

Begin enrolling patients with **acquired hypothalamic obesity** in **Part C of Ph1 trial evaluating RM-718**

Q1 2025

Begin enrolling patients with **congenital hypothalamic obesity** in substudy of **Ph3 trial** evaluating setmelanotide

Q1 2025

Begin enrolling patients with **Prader-Willi syndrome** in exploratory **Ph2 trial** evaluating setmelanotide

Q2 2025

Topline data from **Ph3 acquired hypothalamic obesity trial**

H2 2025

Topline data from **Ph2 trial** evaluating **bivamelagon (LB54640)** in **acquired hypothalamic obesity**

H1 2026

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

Jennifer Lee

EVP, Head of North America

Steady Progress with Prescriptions, Prescribers and Approvals for Reimbursement

Consistent **new prescriptions**
QoQ

Continued success with **approvals for reimbursement** and **re-authorizations**

Multiple process enhancements designed to **maintain patients on therapy**

Disease Education

Clinical Suspicion

Diagnosis

Decision to Treat

Rx
IMCIVREE

Access

IMCIVREE[®]
(setmelanotide) injection

Maintenance

IMCIVREE Now Approved for Children as Young as 2 Years Old

Patient report: **Ben, now 6, LEPR biallelic patient on therapy for >2.5 years**



“It was a constant struggle because he was always crying because of the hunger, even directly after a meal or with a snack in his hand. A few doctors along the way said to wait and see what happens, but as his parent, I knew something wasn't right.”



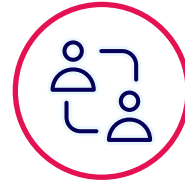
“It has changed his life; his personality is different now that he's not focused on food, and as a family, we now have more freedom because our lives do not revolve around food anymore.”

- Karen, Ben's mother

Planning for Potential Success in Acquired Hypothalamic Obesity



Ongoing market research with physicians, payers, and patients and families



Engaging actively with patient advocacy

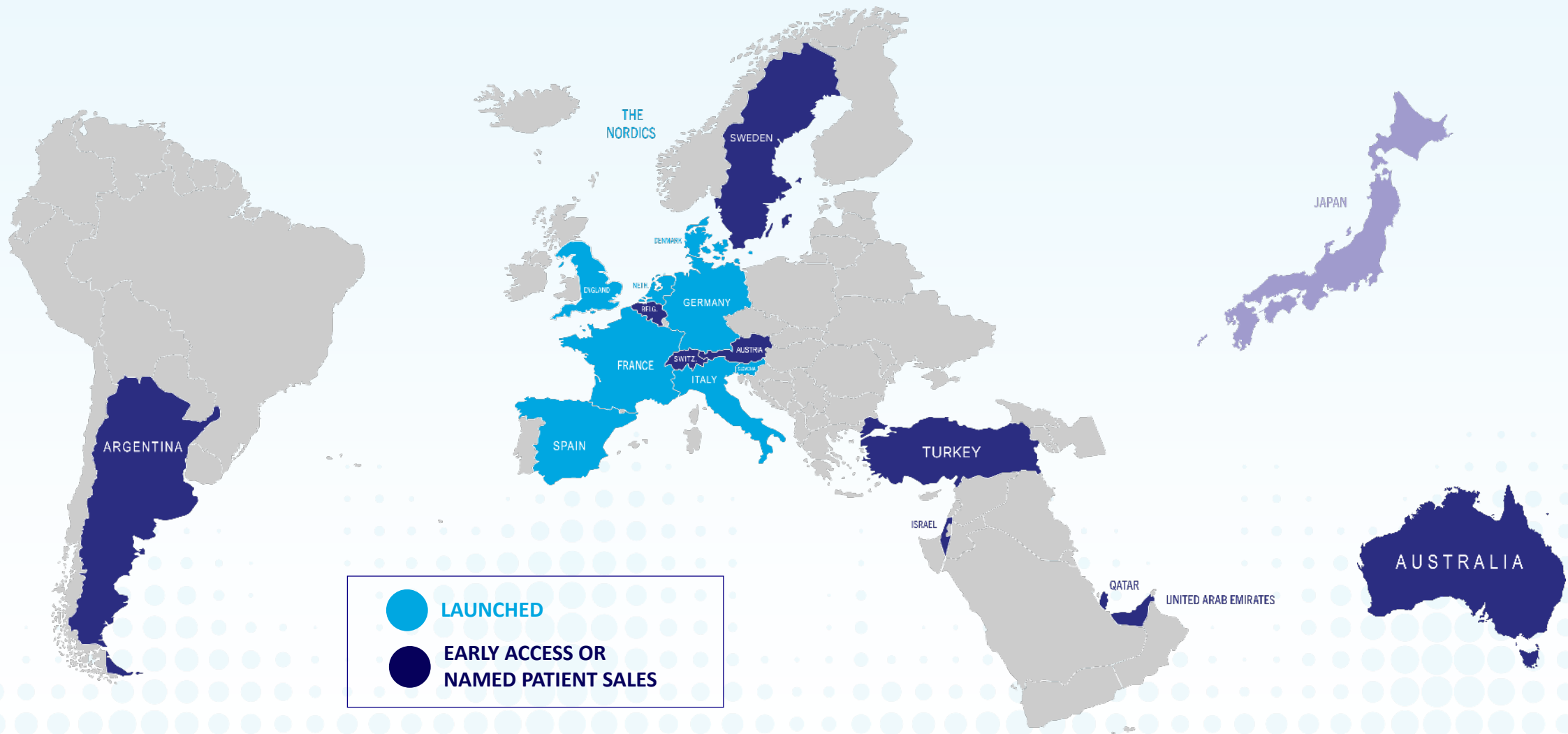


Field teams engaging with physicians

Yann Mazabraud

EVP, Head of International

IMCIVREE available in >15 countries outside the United States



Hunter Smith

Chief Financial Officer

Well Capitalized Entering 2025

\$320.6M

cash equivalents and
short-term investments
as of December 31, 2024

\$75M

of gross proceeds raised through ATM
program

\$40M raised in 4Q 2024 and
\$35M raised in January 2025

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

Q4, Full-year Financial Snapshot

(\$ in millions, except per share data and shares outstanding)	Three months ended December 31, 2024	Three months ended December 31, 2023	Year ended December 31, 2024	Year ended December 31, 2023
Product revenue, net	\$41.8M	\$24.2M	\$130.1M	\$77.4M
R&D expenses	\$41.2M	\$29.9M	\$238.0M	\$135.0M
SG&A expenses	\$38.1M	\$32.4M	\$144.3M	\$117.5M
Net Loss attributable to common stockholders	\$(44.6)M	\$(32.4)M	\$(264.6)M	\$(184.7)M
Common shares outstanding	61,596,442	59,211,199	60,995,204	57,673,128
Net Loss per share attributable to common stockholders – basic and diluted	(\$0.72)	(\$0.70)	(\$4.34)	(\$3.20)
Cash, cash equivalents and short-term investments position (period end)	\$320.6M	\$275.8M	\$320.6M	\$275.8M

4Q, Full-year 2024 Financial Highlights

\$41.8M

of Q4 2024
revenue from
IMCIVREE sales,
76% US

\$130.1M

of FY 2024
revenue from
IMCIVREE sales,
74% US

\$382.3M

2024 GAAP OpEx includes
\$39.7M in stock-based
compensation and **\$92.4M**
in LGC purchase consideration

\$250.2M*

Non-GAAP¹ OpEx

* 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;

1. Non-GAAP OpEx of \$250.2 million in 2024 excludes \$39.7 million in stock-based compensation and \$92.4 million in fixed consideration related to in-licensing of bivamelagon (LB54640) from LG Chem.

2025 OpEx Guidance

\$285M to \$315M

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

SG&A: \$135M to 145M

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

Does not include \$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 and related milestone payments. For more information, see slide 3 – Non-GAAP Financial Measures

Questions