Rhythm Pharmaceuticals

Third Quarter 2024 Financial Results and Business Update

November 5, 2024

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 contains 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, and regulatory and clinical design or progress; potential regulatory submissions, approvals and timing thereof of any of our products and product candidates, including bivamelagon (LB54640), RM-718 and setmelanotide; our Phase 3 trial of setmelanotide for patients with hypothalamic obesity in Japan, the United States or Europe and enrollment in our other ongoing clinical trials; the potential benefits of setmelanotide for patients with hypothalamic obesity and our expectations surrounding potential regulatory submissions, approvals and timing thereof; the Company's business strategy and plans, including regarding commercialization of setmelanotide; expectations surrounding sales and reimbursement of IMCIVREE, the potential expansion of IMCIVREE for use by patients as young as 2 years old and the anticipated PDUFA date, and the potential use of setmelanotide in patients with acquired hypothalamic obesity; our anticipated financial performance and financial position, including estimated Non-GAAP Operating Expenses for the year ending December 31, 2024 and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations. 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, 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, 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 presentation or to update them to reflect events or circumstances occurring after the date of this presentation, 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.

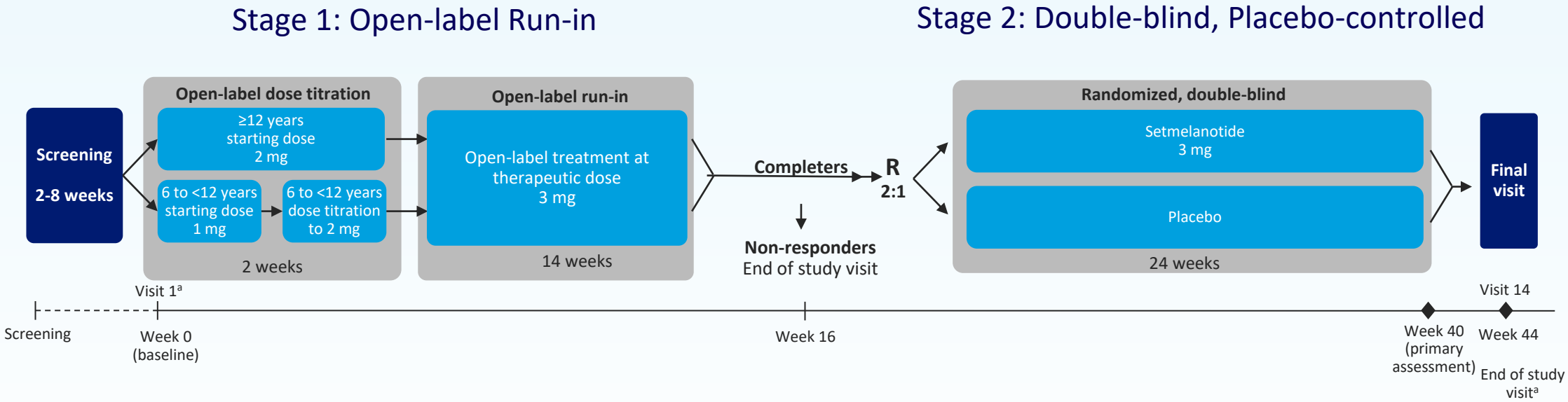
David Meeker, MD

Chair, CEO and President

2024: Continued Execution to Achieve Rhythm's Value Drivers

1. BBS global **commercial execution**
2. Acquired hypothalamic obesity offers a significant **expansion opportunity**
3. **Advancing clinical development pipeline** with new MC4R agonists, disease states

DAYBREAK 2-Stage Design: 16-Week Run-in Followed by 24-week Randomized Withdrawal and Double-blind, Placebo-controlled



Eligibility Criteria: Genetic confirmation in patients 6-65 years; Obesity: BMI ≥40 kg/m2 (adults ≥18 years) or BMI ≥97th percentile for age and sex (children <18)

Primary Endpoint: proportion of patients by genotype who achieve a BMI reduction of ≥5% from baseline in response to setmelanotide at the end of Stage 1

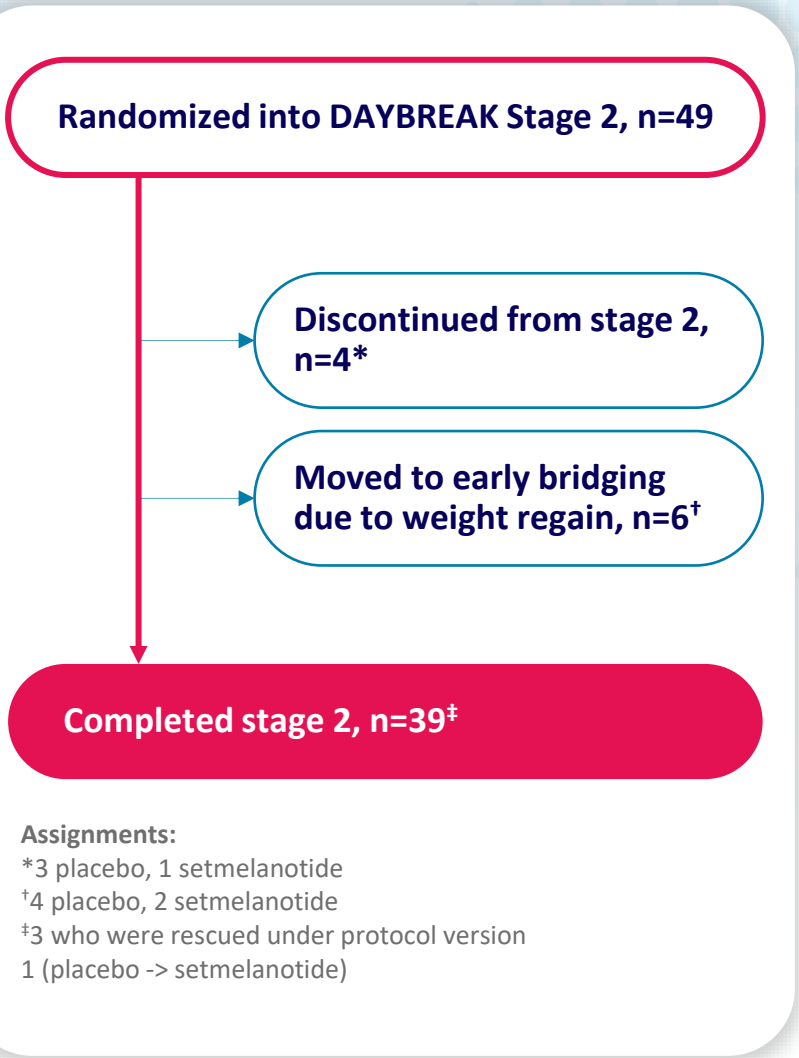
S2 Eligibility Criteria Reduction at end of S1, from baseline: Adult: Reduction of ≥3% BMI; Pediatric: reduction of ≥3% BMI OR of ≥0.05 BMI Z-score

[a]Virtual visit. R, randomization.

DAYBREAK Baseline Demographics

Sex, N=49	All	<18 yrs	≥18 yrs
Male n (%)	22 (44.9)	10 (45.5)	12 (54.5)
Female n (%)	27 (55.1)	14 (51.9)	13 (48.1)

N=49	n	Mean (SD)	Range	% of S1 starters
BMI, kg/m^2				
Adult Baseline	25	46.1 (7.2)	40.4 - 69.9	23%
Adult Stage 2 start	25	42.6 (7.0)	36.2 - 66.3	-
BMI-Z (CDC)				
Pediatric Baseline	24	2.5 (0.3)	1.83 - 2.97	44%
Pediatric Stage 2 start	24	2.25 (0.4)	1.48 - 2.92	-



Assignments:
*3 placebo, 1 setmelanotide
†4 placebo, 2 setmelanotide
‡3 who were rescued under protocol version 1 (placebo -> setmelanotide)

Data Highlights from Stage 2 of DAYBREAK Phase 2 Trial

-12.4%

Mean BMI change from baseline
(SD: 8.0%; range 1.2%-35.0%)

n=32

patients on continuous
setmelanotide therapy*

84%

or **27 of 32**

patients on

setmelanotide

vs.

29%

or **5 of 17**

patients on

placebo

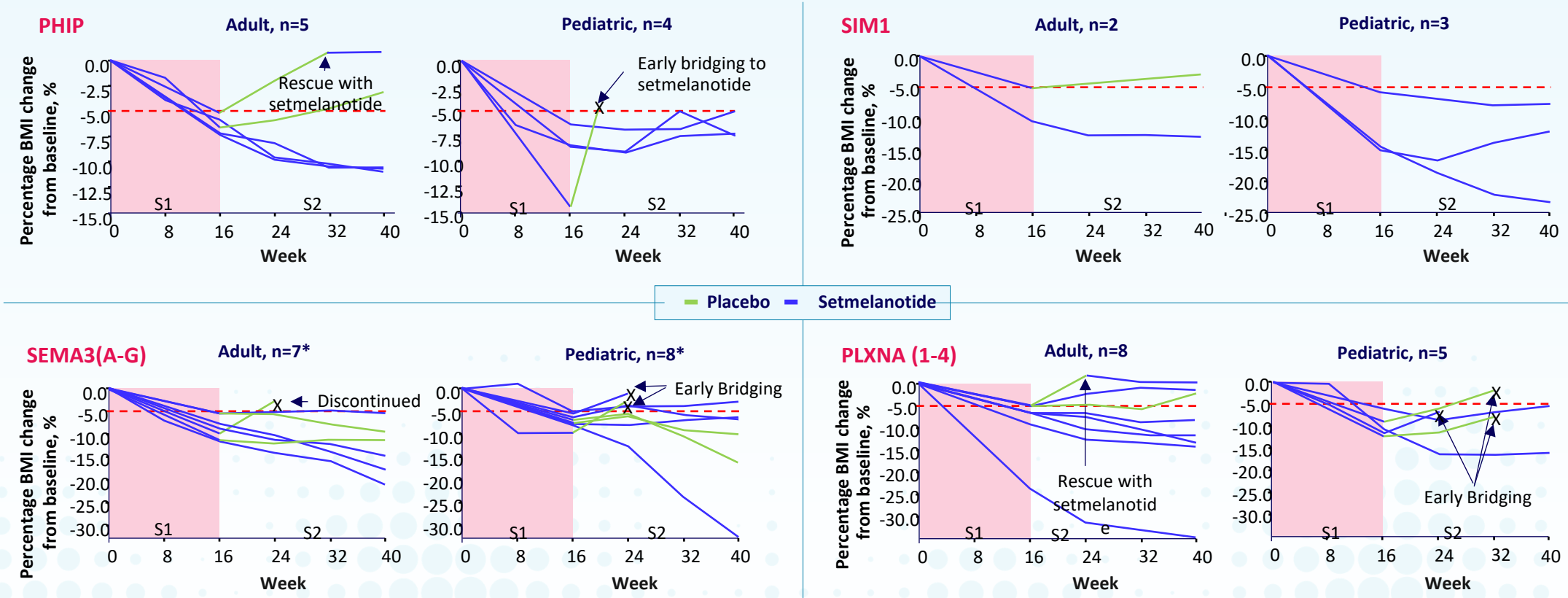
achieved or maintained
>5% BMI reduction from baseline

P=0.001

* Analyses were limited by the small number of PBO-treated pts

Variable Responses Observed in DAYBREAK Stage 2 in Different Genetic Cohorts

Several genetically defined subgroups may merit further study with next-generation MC4R agonists



*One adult and one pediatric SEMA3G patient dropped out of S2 prior to having any data and are not shown

Positive Real-world Setmelanotide Data Reported from French Early-access Program in Adult Patients with Acquired Hypothalamic Obesity

N=8*
patients

19.3 years
Mean age at resection

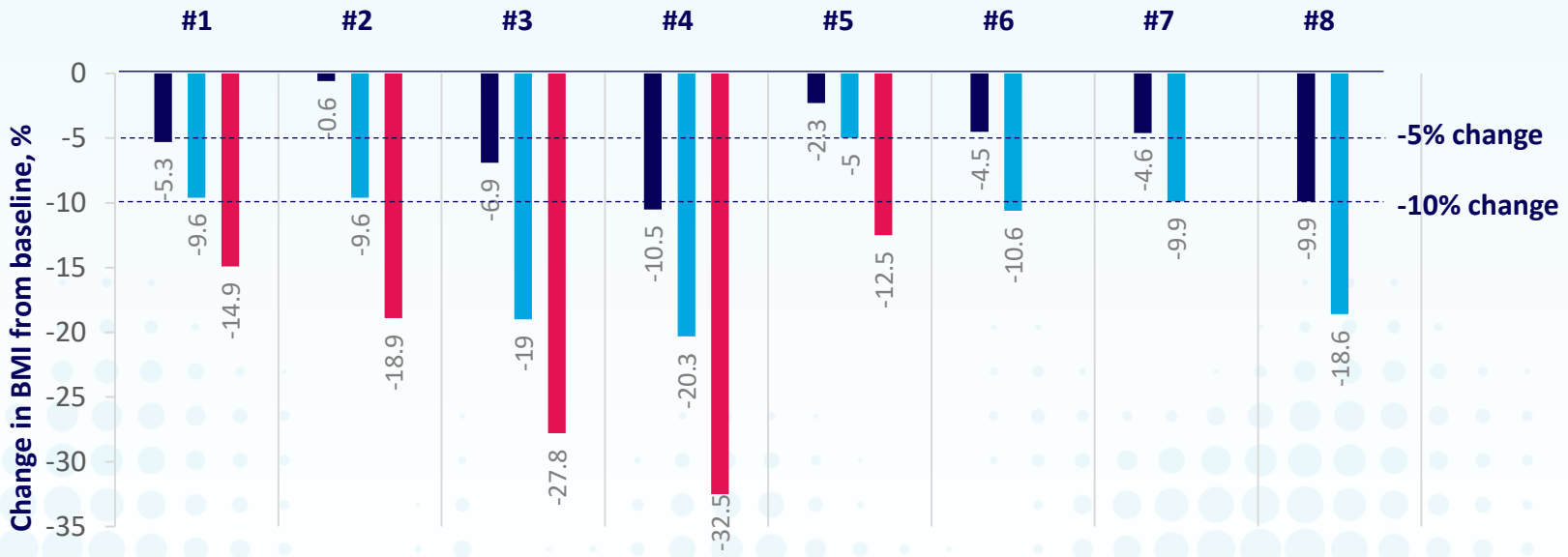
31.4 years
Mean age at initiation of setmelanotide therapy

44.1 kg/m²
Mean BMI at baseline

-5.6%
Mean BMI reduction
■ **Month 1**

-12.8%
Mean BMI reduction
■ **Month 3**

-21.3%
Mean BMI reduction
■ **Month 6**



*50% male; all aged ≥18 years, with a previous resection of craniopharyngioma (n=7) or of Rathke cleft cyst (n=1); Adapted from "3-Month Real-World Setmelanotide Hunger and Weight Outcomes in Patients with Hypothalamic Obesity" poster presented ObesityWeek®; November 3-6, 2024, in San Antonio, TX, USA.

Multiple Anticipated Milestones

Dec. 26, 2024	FDA PDUFA goal date for **IMCIVREE label expansion** to treat 2- to <6 year olds
4Q 2024	Complete enrollment in supplemental, **12-patient Japanese cohort** in Ph3 acquired hypothalamic obesity trial
4Q 2024	Complete enrollment in 2 cohorts in **Ph3 EMANATE** trial
1Q 2025	Complete enrollment in **Ph2 trial** evaluating **bivamelagon (LB54640)** in hypothalamic obesity
1Q 2025	Begin dosing patients with acquired hypothalamic obesity in **Part C** of **Ph1 trial evaluating RM-718**
1H 2025	Topline data in **Ph3 acquired hypothalamic obesity trial**

Jennifer Lee

EVP, Head of North America

3Q 2024: Steady Progress with Prescriptions, Prescribers and Approvals for Reimbursement

Consistent demand with new prescriptions QoQ

Continued **increase** in both **depth and breadth of prescribers**

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

PDUFA Date for IMCIVREE Label Expansion to 2 Year Olds: Dec. 26, 2024

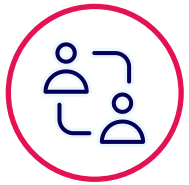
Significant unmet need for **clearly differentiated MC4R pathway diseases** with severe impact on patients and families

Treating severe obesity early can lead to **better health outcomes**, improved life expectancy

Regulatory approval for patients as young as 2yo would **reinforce IMCIVREE's unique impact**

Planning for Anticipated Success in Acquired Hypothalamic Obesity

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



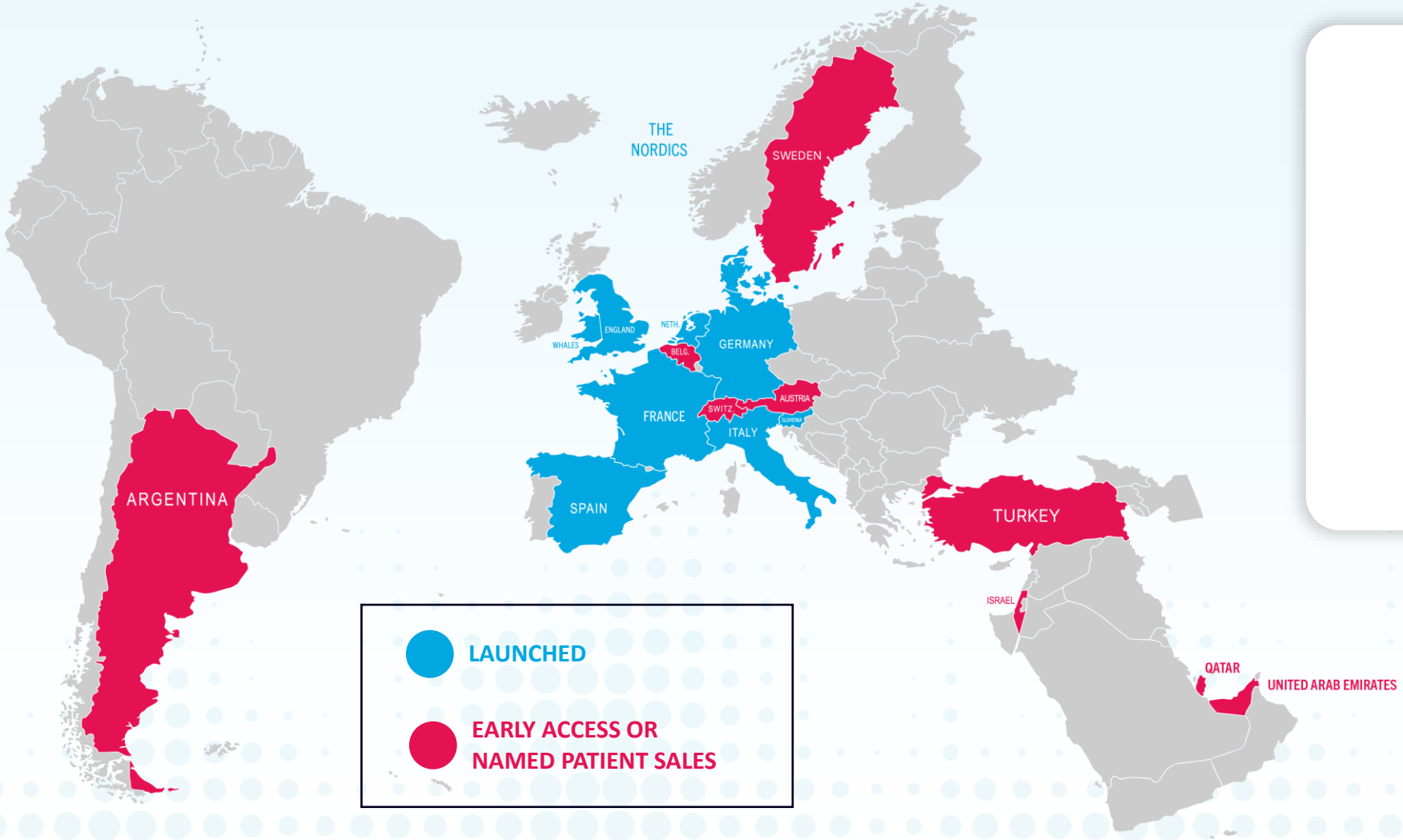
Engaging actively with patient advocacy

Preparing for team expansion in 2025

Yann Mazabraud

EVP, Head of International

Continued Progress in Securing Market Access for IMCIVREE



IMCIVREE
is available in
>15 countries
outside the
United States

Rhythm® PHARMACEUTICALS

Setmelanotide Benefiting Patients with Hypothalamic Obesity through Reimbursed Early-access Programs in France and Italy

France

- Steady uptake since first available in early 2024
- Access granted by joint federal multidisciplinary committee monthly
- Positive responses reported in adult patients at 2024 ObesityWeek® in San Antonio, TX

Italy

- Eligibility: patients between 6-24 yo with HO caused by craniopharyngioma
- Physician makes request for access directly to Italian MoH
- First patients beginning therapy

BBS Commercial Launch Underway in England and Wales in Q4 2024

England and Wales

- NICE recommended NHS reimbursement for patients younger than 18yo with BBS
- 4 NHS BBS specialized clinics:
  2 for adult patients, 2 for pediatric patients
- Patients to be trained in hospital setting with at-home nursing support

Continued Engagement with European MC4R Pathway Experts

Hunter Smith

Chief Financial Officer

3Q 2024 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended September 30, 2024	Three months ended September 30, 2023
Product revenue, net	**$33.3M**	**$22.5M**
R&D expenses	**$37.9M**	**$33.6M**
SG&A expenses	**$35.4M**	**$30.5M**
Net Loss attributable to common stockholders	**($45.0M)**	**($44.2M)**
Common shares outstanding	**61,219,918**	**57,874,960**
Net Loss per share attributable to common stockholders – basic and diluted	**$(0.73)**	**$(0.76)**
Cash, cash equivalents and short-term investments position (period end)	**$298.4M**	**$299.3M**

3Q 2024 Financial Highlights

$298.4M

cash, cash equivalents and short-term investments as of September 30, 2024

70%

of 3Q 2024 revenue from U.S. sales of IMCIVREE, compared to 74% in 2Q 2024

3Q 2024 **OpEx** includes

$11.0

in stock-based compensation expense

3Q 2024 **GAAP EPS** of

$(0.73)

2024 OpEx Guidance

$245M to $255M anticipated **non-GAAP Operating Expenses*** for 2024 includes:

SG&A: $113M

R&D: $137M**

RYTM expects cash to be sufficient to fund planned operations **into 2026**

* 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; **Does not include stock-based compensation or $92.4 million in fixed consideration related to in-licensing of bivamelagon (LB54640) from LG Chem.

Questions