Rhythm Pharmaceuticals

Second Quarter 2024 Financial Results and Business Update

August 6, 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 setmelanotide and LB54640, including our Phase 3 trial of setmelanotide for patients with hypothalamic obesity in Japan, the United States or in Europe, the potential benefits of setmelanotide for patients with hypothalamic obesity, our expectations surrounding potential regulatory submissions, approvals and timing thereof, including the IND application for RM-718, the Company's business strategy and plans, including regarding commercialization of setmelanotide, including approval and reimbursement of IMCIVREE in England, Wales and Scotland, expectations surrounding sales and reimbursement of IMCIVREE, our anticipated financial performance and financial position, including estimated Non-GAAP Operating Expenses for the year ending December 31, 2024, 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 June 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

Rhythm's Value Drivers

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

Continued Strong Execution in 2Q 2024

Commercial progress

- Steady QoQ revenue growth
- Positive decision for BBS from NICE

Hypothalamic obesity

- Ph3 topline data on track for 1H2025
- First patient in Japanese cohort in Ph3 trial dosed

Next-generation MC4R agonists

- First patient dosed in Ph2 trial of oral LB54640 in hypothalamic obesity
- RM718 Ph1 SAD, MAD cohorts advancing

Advancing IMCIVREE Label Expansion to Treat 2-6yo Patients in Europe and United States

- ✓European Commission expanded IMCIVREE marketing authorization to include children as young as 2 years old
- ✓Completed sNDA submission to FDA in 2Q 2024; anticipated PDUFA date by the end of 2024

Ph3: Clinically Meaningful Reductions in BMI, BMI-Z in 2-<6yo Patients with POMC/LEPR Deficiency or BBS

83.3% (10 of 12)

of all patients achieved ≥0.2 reduction in BMI-Z score from baseline to Week 52

-18.380%

Mean percent change from baseline in BMI at Week 52

Jennifer Lee

EVP, Head of North America

2Q 2024: Steady Progress with Prescriptions, Prescribers and Access

Consistent demand with new prescriptions QoQ

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

Continued **success with approvals for reimbursement** as well as high success rate with **re-authorizations**

Steady Progress with Second Quarter 2024 Prescriptions and Approvals for Reimbursement

~100

Prescriptions received during Q2 2024

~70

Approvals for reimbursement during Q2 2024

Focus on Patient and Physician Engagement to support the BBS Community

Rhythm InTune supporting patients to gain access, and initiate and maintain on therapy

Physician Engagement

Finding and engaging with new prescribers and collaborating with healthcare providers to advance multi-disciplinary care for BBS patients

Yann Mazabraud

EVP, Head of International

European Commission Expands Marketing Authorization for IMCIVREE to Treat Patients as Young as 2 Years Old

Authorization now includes patients as young as 2yo with BBS or POMC, PCSK1 or LEPR deficiency

"Annex 2" exemption process already started in Germany

Reimbursement dossiers submitted to French and Italian authorities

Underscores significant unmet need and severe impact of rare MC4R pathway diseases on young children

Rhythm Model Presented at ECO 2024 Demonstrates Negative Impact of Early-onset Obesity on Life Expectancy and Comorbidities

- Early-onset, severe obesity has a major negative impact on life expectancy and comorbidities
- Young children with persistent severe obesity could have half average life expectancy
- Early weight reduction leads to a significant increase in life expectancy and to a large reduction in the risk of comorbidities

Patient with BMI-Z of 2.5 at age 2, BMI-Z of 4 at age 4 - typical of rare MC4R pathway diseases		Life Expectancy (years)	Likelihood Comorbidities by Age 35 (%)					
			TIIDM	CV events	MASLD	Asthma	OSA	Cancer
No intervention		**37**	54.9	39.2	95.3	39.7	76.7	1.3
Intervention: BMI Z-score decrease at age 6	1 point	42	38.6	33.6	86.2	26.1	72.5	1.3
	1.5 pts	50	36.3	28.6	72.6	18.9	71.4	1.1
	2 pts	**64**	28.9	26	54	15	33.3	1

* 6 key morbidities: Type II DM, CV events, MASLD, Asthma, Obstructive Sleep Apnea, Cancer

The Guardian

Young children with persistent severe obesity could have half average life expectancy, study finds

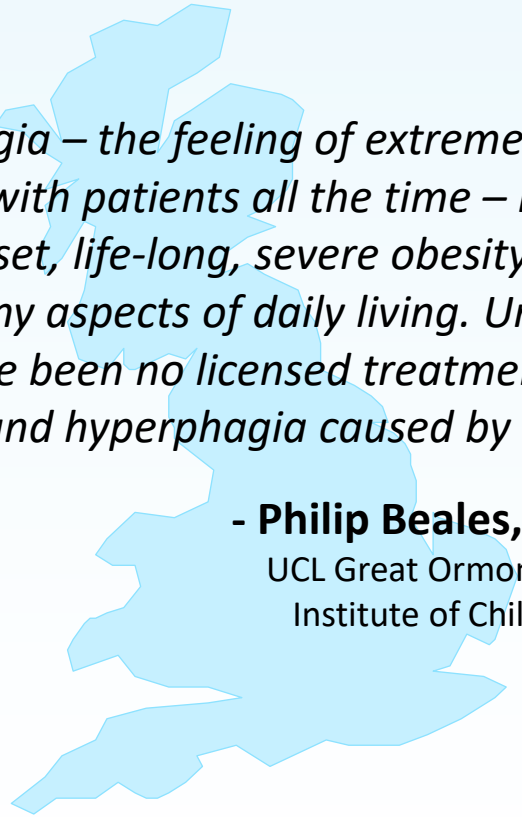
Research finds four-year-old boy who remains severely obese into adulthood has life expectancy of 39

It is clear that childhood obesity should be considered a life-threatening disease. It is vital that treatment isn't put off until the development of type 2 diabetes, high blood pressure or other 'warning signs' but starts early.

- Presenter Dr. Urs Wiedeman

NICE Recommended Reimbursement for IMCIVREE for Treatment of Obesity, Hyperphagia in Patients with BBS

IMCIVREE to be funded in England and Wales through the National Health Service in Q3 2024



"Hyperphagia – the feeling of extreme hunger that stays with patients all the time – leads to early-onset, life-long, severe obesity that affects many aspects of daily living. Until now there have been no licensed treatments for obesity and hyperphagia caused by BBS."

- Philip Beales, M.D.,
UCL Great Ormond Street
Institute of Child Health

- Funding available for patients 6-17 years of age at treatment initiation
- Northern Ireland expected to adopt NICE guidance; Scottish Medicines Consortium reimbursement decision expected in 2025
- MHRA decision on 2-6yo marketing authorization expected in Q4 2024

Continued Progress in Securing Market Access for IMCIVREE

United Kingdom
Launched in POMC/LEPR; BBS launch expected in 2H2024 with NICE reimbursement

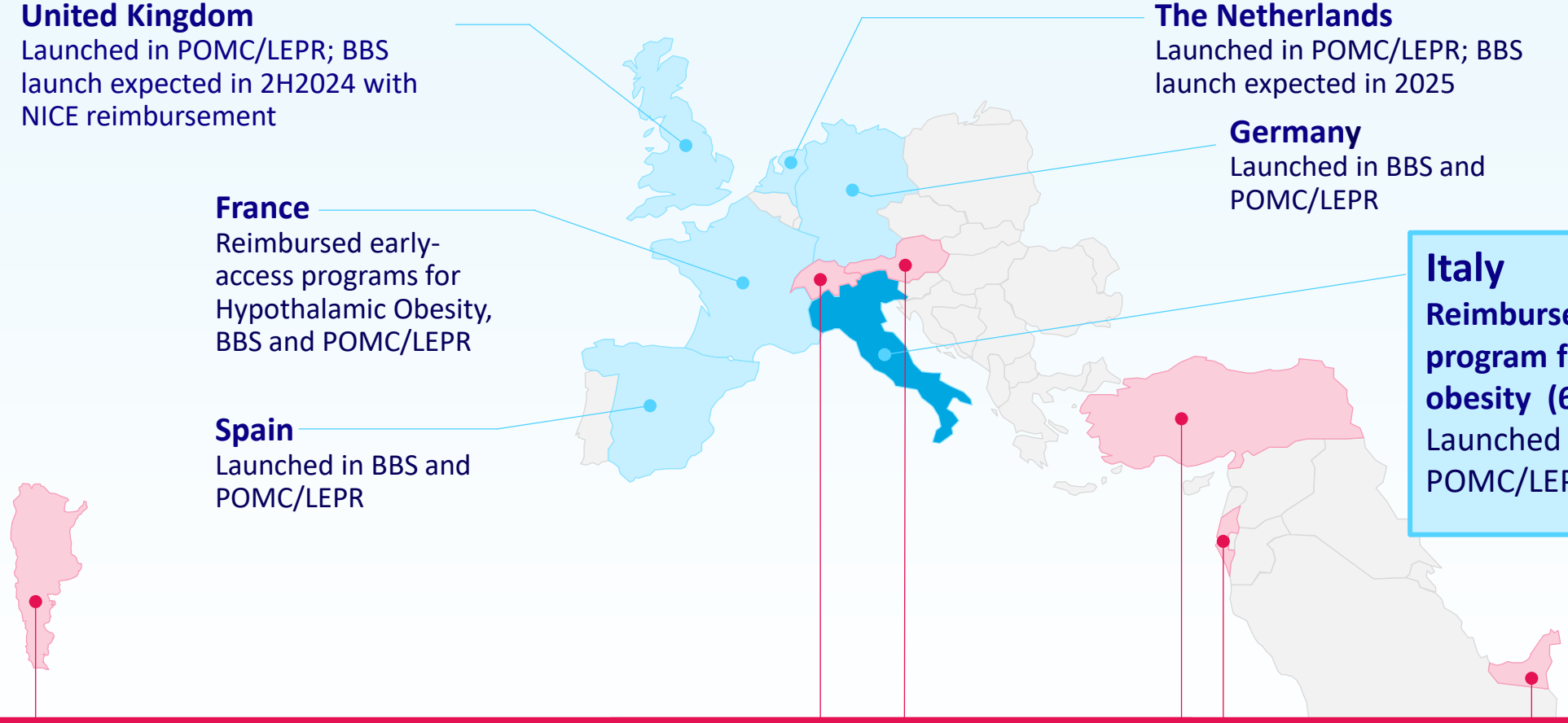
The Netherlands
Launched in POMC/LEPR; BBS launch expected in 2025

Germany
Launched in BBS and POMC/LEPR

France
Reimbursed early-access programs for Hypothalamic Obesity, BBS and POMC/LEPR

Spain
Launched in BBS and POMC/LEPR

Italy
Reimbursed early access program for hypothalamic obesity (6-24 years old)
Launched in BBS and POMC/LEPR.



EARLY ACCESS OR NAMED PATIENT SALES

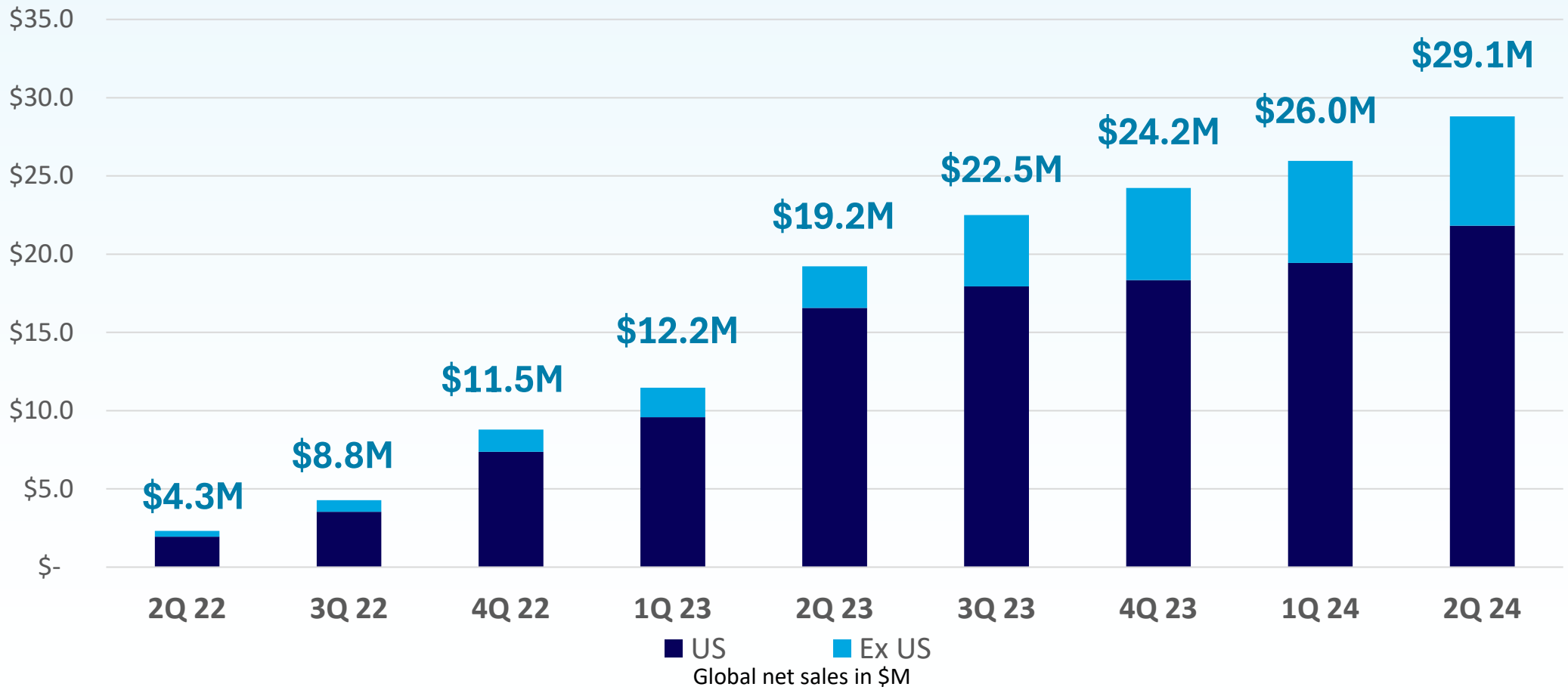
Argentina · Switzerland · Austria · Turkey · Israel · United Arab Emirates

Hunter Smith

Chief Financial Officer

Steady Growth in Net Product Revenues since BBS Launch

FDA approved IMCIVREE for BBS in June 2022



Global net sales in $M

Rhythm® PHARMACEUTICALS

2Q 2024 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended June 30, 2024	Three months ended June 30, 2023
Product revenue, net	$29.1M	$19.2M
R&D expenses	$30.2M	$33.5M
SG&A expenses	$36.4M	$30.0M
Net Loss attributable to common stockholders	($33.6M)	($46.7M)
Common shares outstanding	61,011,824	56,867,662
Net Loss per share attributable to common stockholders - basic and diluted	$(0.55)	$(0.82)
Cash, cash equivalents and short-term investments position (period end)	$319.1M	$254M

2Q 2024 Financial Highlights

$319.1M
cash, cash equivalents and short-term investments as of June 30, 2024

74%
of 2Q 2024 revenue from U.S. sales of IMCIVREE, consistent with 1Q 2024

2Q 2024
OpEx includes
$10.4M
in stock-based compensation expense

2Q 2024
GAAP EPS of
$(0.55)*
reflects convertible preferred financing

* GAAP EPS for 2Q 2024 reflects $0.13 of net favorability from a one-time non-cash gain of $8.9M, or $0.15 per share, and accrued dividends of $1.3M , or ($0.02) per share. The one-time non-cash gain is the result of a decrease in fair value of issued convertible preferred stock between deal execution date ($150M on April 1, 2024) and closing date ($141M on April 15, 2024). This is a non-cash GAAP accounting gain with no impact to preferred shares issued (i.e. 150,000 shares @ $1,000).

2024 OpEx Guidance

$250M to $270M anticipated **non-GAAP Operating Expenses*** for 2024 includes:

R&D:	**SG&A:**
$145M to $160M*	$105M to $110M

With **$150M** investment from **convertible preferred** financing received during 2Q 2024**,** 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. R&D includes $10M-$15M of LB54640 development costs; Does not include stock-based compensation or $92.4 million in fixed consideration related to in-licensing of LB-54640 from LG Chem.

Questions