Rhythm Pharmaceuticals

Second Quarter 2026
Financial Results and Business Update

August 4, 2026

On Today's Call

- David Connolly, Vice President 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 use of setmelanotide in patients with acquired hypothalamic obesity (HO) and the success of our commercial launch; our expectations surrounding potential regulatory submissions, progress, or approvals and timing thereof for any of our product candidates, including potential marketing approval and launch in Japan and launches in the European Union and the timing thereof; the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products, including setmelanotide for the treatment of acquired HO; the future announcement of data from our ongoing clinical trials, including the substudy evaluating setmelanotide for patients with congenital hypothalamic obesity, Part C and Part D of the Phase 1 trial evaluating RM-718, and the open-label Phase 2 trial evaluating setmelanotide in patients with PWS, and 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 our estimated Non-GAAP Operating Expenses for the year ending December 31, 2026; 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" 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 impact of competition, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, 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, our ability to successfully commercialize setmelanotide, our liquidity and expenses, our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel, and general economic conditions, and the other important factors, including those discussed under the caption "Risk Factors" in Rhythm's Quarterly Report on Form 10-Q for the quarter ended June 30, 2026 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

Q2 2026: Continued Execution for Rhythm

Business Highlights

- **Strong start to acquired HO launch**
- **Multiple clinically meaningful improvements** achieved with setmelanotide in **PWS**
- *New today:* Encouraging preliminary results with **RM-718** in acquired HO

Phase 3 TRANSCEND Trial Results in Acquired HO Published

The NEW ENGLAND JOURNAL of MEDICINE

Setmelanotide for the Treatment of Acquired Hypothalamic Obesity

Original article
by J.L. Miller, et al.

With an accompanying editorial

Science behind the Study

Treating Acquired Hypothalamic Obesity

-- By Sadaf Farooqi, MB, ChB, PhD

N Engl J Med 2026;395:138-50. DOI: 10.1056/NEJMoa2512275

Rhythm® PHARMACEUTICALS

Preliminary Phase 2 Data Show RM-718 Demonstrated Positive Efficacy Signal in Acquired HO

Baseline Demographics

Parameter	Statistic	Overall (N=11)
Age, years	Mean (SD) (range) ≥12 years and <18, n (%) ≥18 years old, n (%)	26.7 (13.1) (12 – 48) 4 (36.4) 7 (63.6)
Sex, n (%)	Female / Male	9/2 (81.8/18.2)
Race, n (%)	White Black or African American	10 (90.9) 1 (9.1)
BMI, kg/m^2	Mean (SD)	41.0 (7.1)

N=11
patients enrolled

n=8
remain on active therapy*

n=7
reached Week 16

n=2
discontinued due to AEs

1 withdrew from LTE

n=2
on therapy <4 weeks*

*Data cutoff of July 16, 2026: two (2) patients had not yet reached 16 weeks, and one (1) patient who completed 16 weeks then discontinued from extension due to personal reasons; AE, adverse event; BMI, body mass index; LTE, long-term extension.

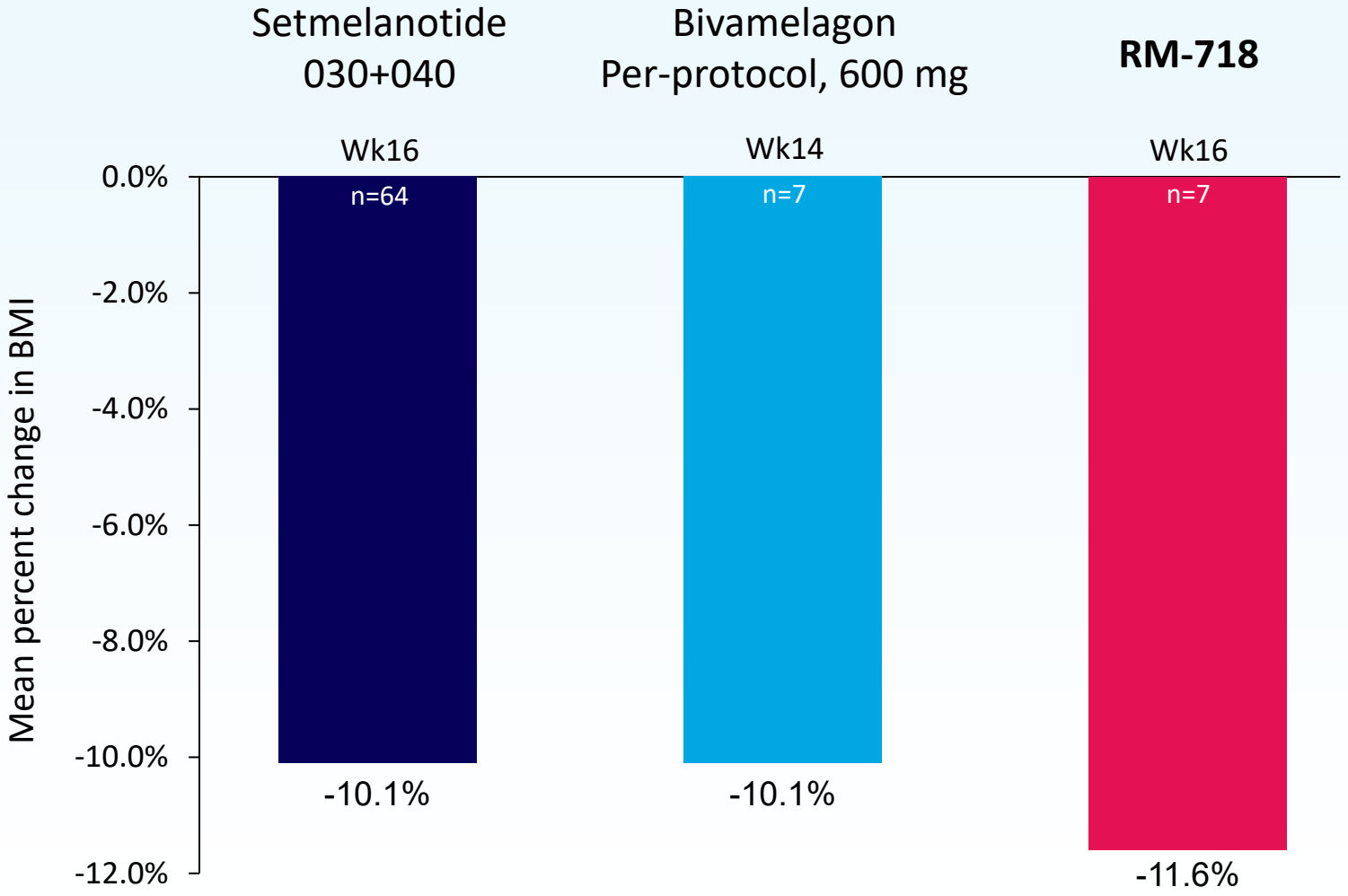
RM-718 Achieved Clinically Meaningful BMI Reduction in Patients with Acquired HO at Week 16

-11.6%

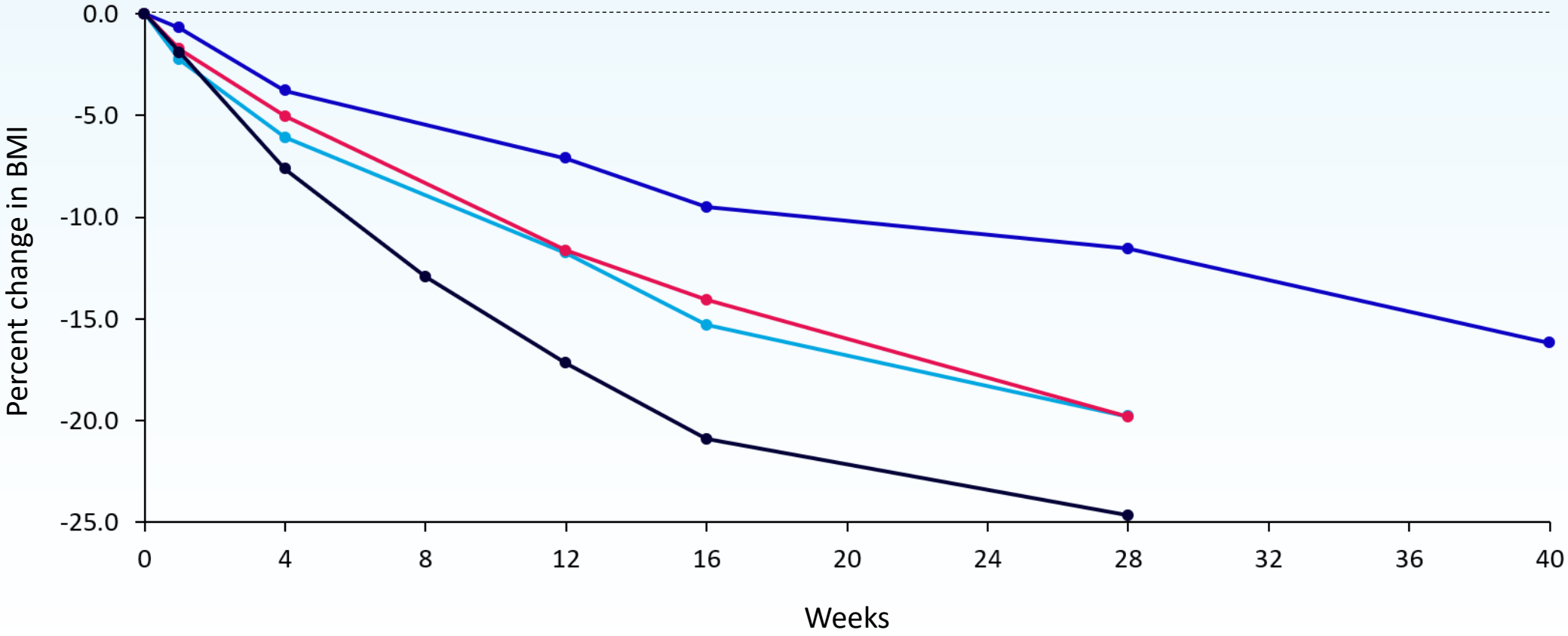
mean BMI reduction
from baseline
at **Week 16**
(n=7)

BMI, body mass index.

RM-718 Exhibited Comparable Reductions to Setmelanotide and Bivamelagon



Four Patients Achieved Deepening BMI Reductions at 28-40 Weeks on Therapy with RM-718



Rhythm® PHARMACEUTICALS

Most Common (≥2 Patients) Adverse Events for All Patients (N=11)

Adverse Events, n (%)	All Patients (N=11)
Injection site reactions	9 (81.8)
Nausea	6 (54.5)
Vomiting	3 (27.3)
Abdominal pain	2 (18.2)
Anxiety	2 (18.2)
Cough	2 (18.2)
Decreased appetite	2 (18.2)
Depression	2 (18.2)
Fatigue	2 (18.2)
Headache	2 (18.2)
Nasopharyngitis	2 (18.2)
Oropharyngeal pain	2 (18.2)

Multiple Anticipated Milestones

H2 2026	Complete enrollment in the **Ph1/2, Part D trial** evaluating **RM-718** in **Prader-Willi syndrome**
H2 2026	Complete enrollment in **substudy** evaluating **setmelanotide** in **congenital hypothalamic obesity**
YE 2026	**Launch IMCIVREE for acquired HO in Japan** pending marketing authorization from Ministry of Health, Labour and Welfare (MHLW)
YE 2026	Initiate **pivotal Ph3 trial** evaluating **oral bivamelagon** in **acquired HO**
2027	Anticipated **European launches** of **IMCIVREE** for **acquired HO**

Jennifer Lee

EVP, Head of North America

U.S. Launch of IMCIVREE for Acquired HO off to a Strong Start

Strong patient demand

Broad prescriber base

Positive early payer experience

Strong Patient Demand and Early Uptake

Start Forms

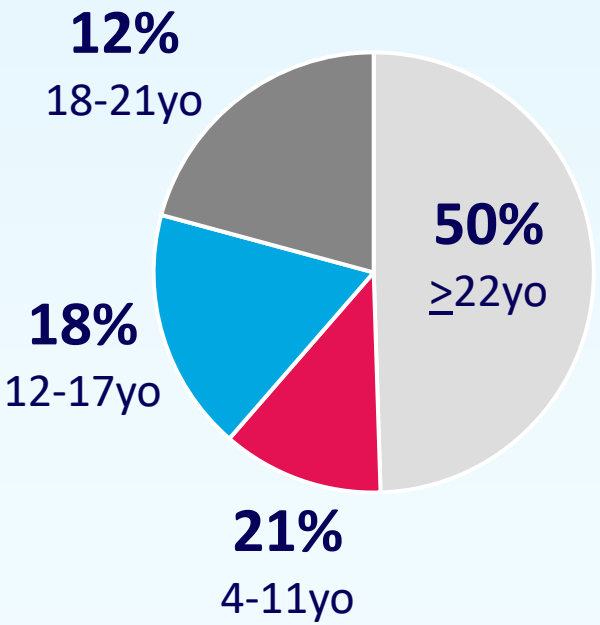
>400

Patient Start Forms

Inclusive of **66**

start forms from
clinical trial patients

Patients by age



Hypothalamic injury

~15%

within two years

~50%

>10 years

Note: Between FDA approval on March 19, 2026 and June 30, 2026.; yo = years old

Rhythm® PHARMACEUTICALS

Broad Prescriber Activation and Engagement

Prescribers

~300

Unique prescribers

~20%

Repeat aHO Prescribers

Specialty

43%

Adult Endocrinologist

37%

Pediatric Endocrinologist

Priority Accounts

~65%

Activated

~25%

of Prescriptions

Note: Between FDA approval on March 19, 2026 and June 30, 2026.

Encouraged by Early Payer Engagement

Majority of early approvals came **at prior authorization** without aHO specific policy in place

Payer **engagement continues** with majority of P&T meetings expected by year end

Payers

Positive policies secured

25%

of Medicaid covered lives

35%

of commercial covered lives

Note: Between FDA approval on March 19, 2026 and June 30, 2026.

New Diagnostic Algorithm Supports Diagnosis of BBS

AMERICAN JOURNAL OF medical genetics PART A

REVIEW ARTICLE OPEN ACCESS

Streamlining Diagnosis of Bardet–Biedl Syndrome: New Diagnostic Algorithm With Updated Criteria

Jeremy J. Pomeroy[1] | Jesse Richards[2] | Brooke R. Sweeney[3] | Seema Kumar[4] | Katie E. Queen[5] | Joshua Zarlisky[6] | Carl H. Cramer[7] | Elias I. Traboulsi[8] | Britini A. Scruggs[9] | Erica E. Davis[10,11] | Ekaterina Kefer[1] | Emma McGibbon[12] | Timothy Ogden[13] | Bendert De Graaf[14] | Tonia Hymers[15] | Elizabeth Forsythe[16,17] | Philip Beales[18]

[1]Marshfield Clinic Research Institute, Marshfield, Wisconsin, USA | [2]Department of Internal Medicine, University of Oklahoma School of Community Medicine, Tulsa, Oklahoma, USA | [3]Children's Mercy Kansas City, Center for Children's Healthy Lifestyles & Nutrition, Kansas City, Missouri, USA | [4]Division of Pediatric Endocrinology, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, USA | [5]Our Lady of the Lake Children's Health Weight and Nutrition Center, Baton Rouge, Louisiana, USA | [6]Department of Nephrology, Phoenix Children's Hospital, Phoenix, Arizona, USA | [7]Division of Pediatric Nephrology and Hypertension, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, USA | [8]Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, USA | [9]Department of Ophthalmology and Department of Pediatrics, Mayo Clinic, Rochester, Minnesota, USA | [10]Stanley Manne Children's Research Institute, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, USA | [11]Department of Pediatrics, Cell and Developmental Biology, Flenberg School of Medicine, Northwestern University, Chicago, Illinois, USA | [12]Wolfson Neurodisability Service, Great Ormand Street Hospital NHS Foundation Trust, London, UK | [13]Bardet Biedl Syndrome Foundation, Unionville, Pennsylvania, USA | [14]Bardet-Biedl Stichting, Kampen, the Netherlands | [15]Bardet-Biedl Syndrome UK, Essex, UK | [16]Clinical Genetics Department, Guys and St. Thomas' Hospitals, London, UK | [17]National Bardet-Biedl Syndrome Clinics, Great Ormond Street Hospital, London, UK | [18]Genetics and Genomic Medicine Programme, University College London Great Ormond Street Institute of Child Health, London, UK

Correspondence: Philip Beales (p.beales@ucl.ac.uk)

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Keywords: Bardet–Biedl syndrome | ciliopathies | diagnostic algorithm | diagnostic criteria | genetics | obesity

ABSTRACT

Considerable advances have been made in our understanding of Bardet–Biedl syndrome (BBS), particularly in its core clinical features and molecular genetics, warranting an update to the existing diagnostic criteria framework. Using a rigorous, evidence-based, and consensus-driven process, a multidisciplinary group of international experts and patient-led organizations developed an updated diagnostic algorithm. This algorithm provides practical, updated guidance for clinicians, including a pathway for accurately incorporating genetic findings into the diagnostic process. We recommend that a clinical diagnosis requires either 4 major criteria or 3 major and 2 minor criteria. Revised major criteria are retinal dystrophy, obesity (or overweight in individuals <2 years old), congenital anomalies of the kidney and urinary tract or chronic kidney disease, hypogonadism/genital anomalies, neurodevelopmental/neurocognitive manifestations, and postaxial polydactyly. The diagnosis can also be established with a positive genetic testing result in patients exhibiting ≥ 1 major criterion, provided that genetic findings should be interpreted in the context of the patient's clinical presentation, age, family history, and overlap with related ciliopathies. These consensus criteria offer a simple algorithm incorporating updated definitions for major and minor criteria and genetic testing to support a timely

Expert consensus, evidence-based diagnostic algorithm

Supports earlier recognition and diagnosis

Aligns around current clinical and genetic evidence

Rhythm® PHARMACEUTICALS

Field Force Expansion and Focus

42

Territory managers focused on acquired HO

+10

Territory managers focused on BBS

Yann Mazabraud

EVP, Head of International

Japanese Approval and Launch for Acquired HO Anticipated by End of 2026

5,000 – 8,000
estimated Japanese prevalence[1]

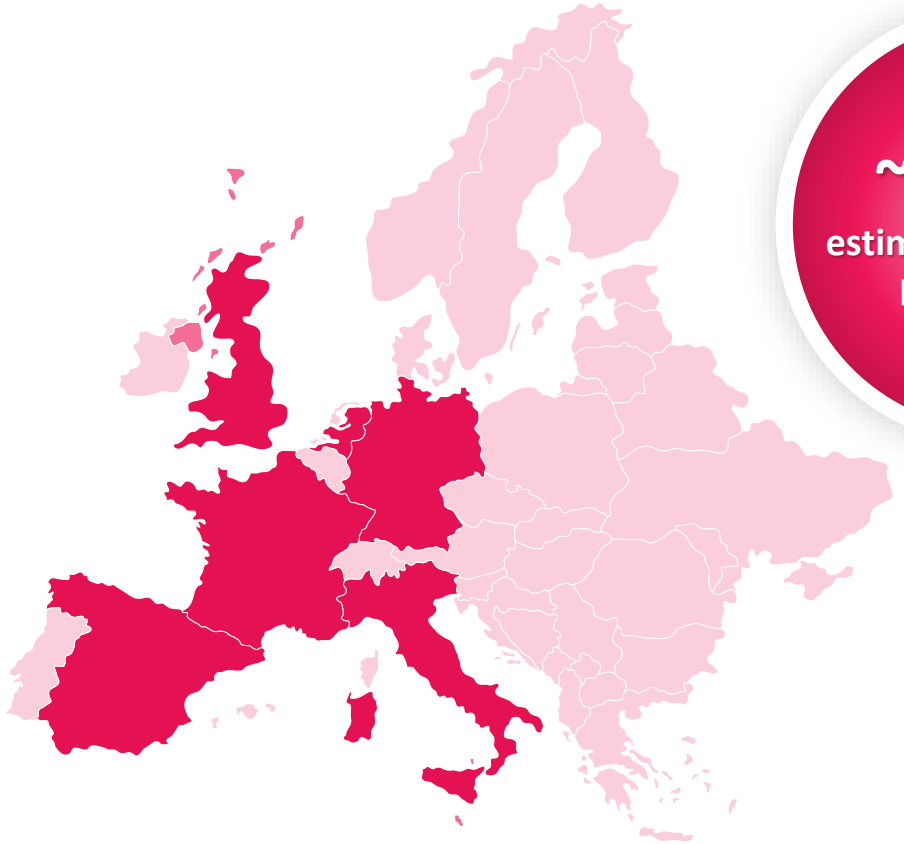
- ☐ **PMDA review of new drug application**
- ☐ **Final authorization from MHLW**
- ☐ **Price discussions with NHI**

PMDA: Pharmaceuticals and Medical Devices Agency; MHLW: Ministry of Health, Labour and Welfare; NHI: National Health Insurance

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

IMCIVREE HO Country-level Launches Expected in 2027

- **Germany** G-BA process initiated
- Reimbursement dossiers submitted:
  - France
  - UK
  - Spain
  - The Netherlands



~10,000
estimated European prevalence[1]

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 patients

Hunter Smith

Chief Financial Officer

Q2 2026: Continued Growth in IMCIVREE Global Sales

$71.3M
Net Product Revenue

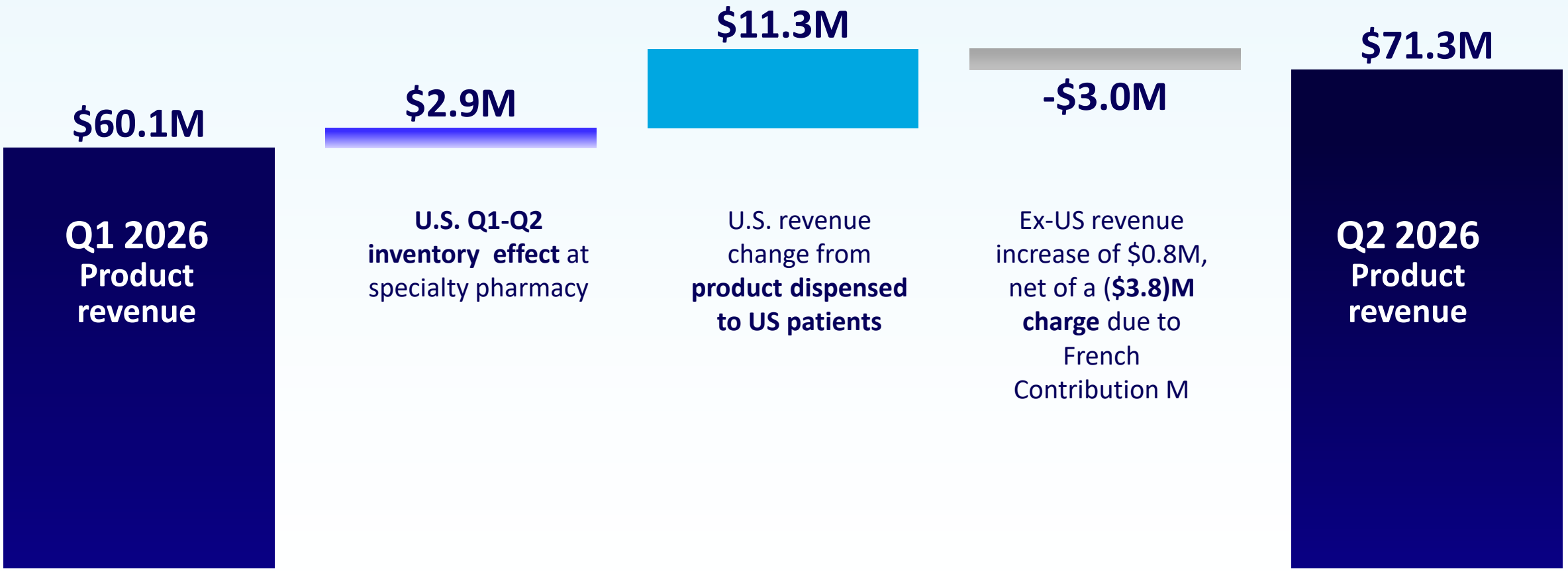
19% **QoQ** increase from Q1 2026

72% of **Q2 2026** revenue **from U.S.**

>20%
increase in number of patients globally on **reimbursed therapy**

Rhythm® PHARMACEUTICALS

Q1 ‘26 to Q2 ‘26: Consistent Growth in Global Patient Demand Continues



Q2 2026 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended June 30, 2026	Three months ended June 30, 2025
Product revenue, net	$71.3M	$48.5M
R&D expenses	$43.4M	$42.3M
SG&A expenses	$67.4M	$45.9M
Net Loss attributable to common stockholders	$(50.4)M	$(48.0)M
Weighted average common shares outstanding	68,592,661	63,684,359
Net Loss per share attributable to common stockholders – basic and diluted	$(0.73)	($0.75)
Cash, cash equivalents and short-term investments position (period end)	$330.9M	$291.0M

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

Q2 2026 Financial Highlights

Q2’ 2026 OpEx

$110.9M

Q2 2026 OpEx includes

$26.1M

in stock-based compensation expense

2026 OpEx Guidance

$363M to $397M

anticipated **non-GAAP Operating Expenses*** for 2026 includes:

R&D: $175M to $195M

SG&A: $188M to $202M

* Non-GAAP Operating Expenses is a non-GAAP financial measure. We define Non-GAAP Operating Expenses as GAAP operating expenses excluding stock-based compensation, fixed consideration related to in-licensing and potential milestone payments. For more information, see slide 3 – Non-GAAP Financial Measures.

Concluding Comments

MC4R Agonism Development Across Three Pillars

Genetic MC4R Pathway Diseases

Hypothalamic Obesity

Prader-Willi Syndrome

Next-generation MC4R agonists	
RM-718 (weekly injection)	Bivamelagon (daily oral)

IMCIVREE® (setmelanotide) injection

Global commercial foundation driven by IMCIVREE in BBS

Questions