Rhythm Pharmaceuticals

Fourth Quarter and Year End 2025
Financial Results and Business Update

February 26, 2026

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, including the March 20, 2026 PDUFA goal date for our sNDA for setmelanotide in acquired hypothalamic obesity; the commercial growth of IMCIVREE; the estimated market size and addressable population for our drug products, including setmelanotide for the treatment of hypothalamic obesity; the future announcement of data from our ongoing clinical trials, including the Japanese cohort of 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; Part C of the Phase 1 trial evaluating RM-718, and the open-label Phase 2 trial evaluating setmelanotide in patients with PWS; 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 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 Annual Report on Form 10-K for the year ended December 31, 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

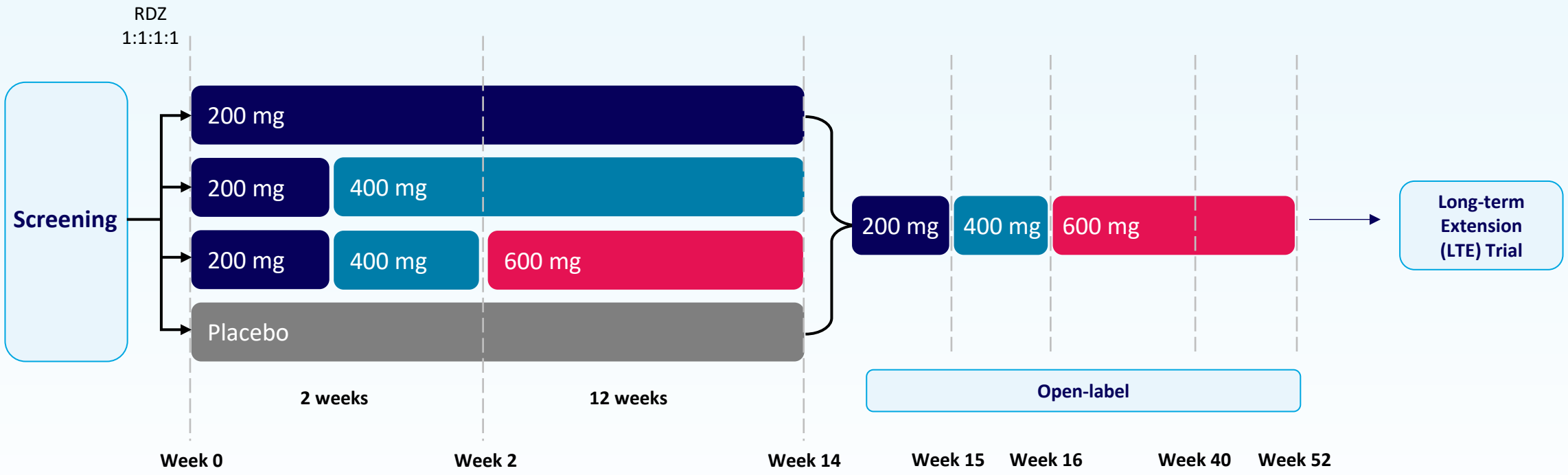
Chair, President and CEO

Well Positioned to Deliver Long-term, Sustained Growth

Business Highlights

- Steady growth in global IMCIVREE® (setmelanotide) sales in Q4 2025 primarily driven by Bardet-Biedl syndrome
- U.S. team in place and ready to launch setmelanotide for acquired HO, pending FDA approval on March 20th
- Early-access for HO in Europe reinforces confidence in global opportunity
- Positive update on Bivamelagon open-label extension data in acquired hypothalamic obesity and end-of-Phase 2 meeting with FDA

SIGNAL Trial: 14-week, Phase 2 Open-label Trial Evaluating Bivamelagon in Patients with Hypothalamic Obesity



Inclusion criteria

≥18yo BMI ≥30 kg/m²

12-<18 yo ≥95th percentile

Setmelanotide-naive

Rhythm® PHARMACEUTICALS

Vast Majority of Patients Transitioned to Open-label Extension and Have Remained on Bivamelagon Therapy

ENROLLED

(n=28)

DISCONTINUED

1 discontinuation due to SAE in Week 1

COMPLETED

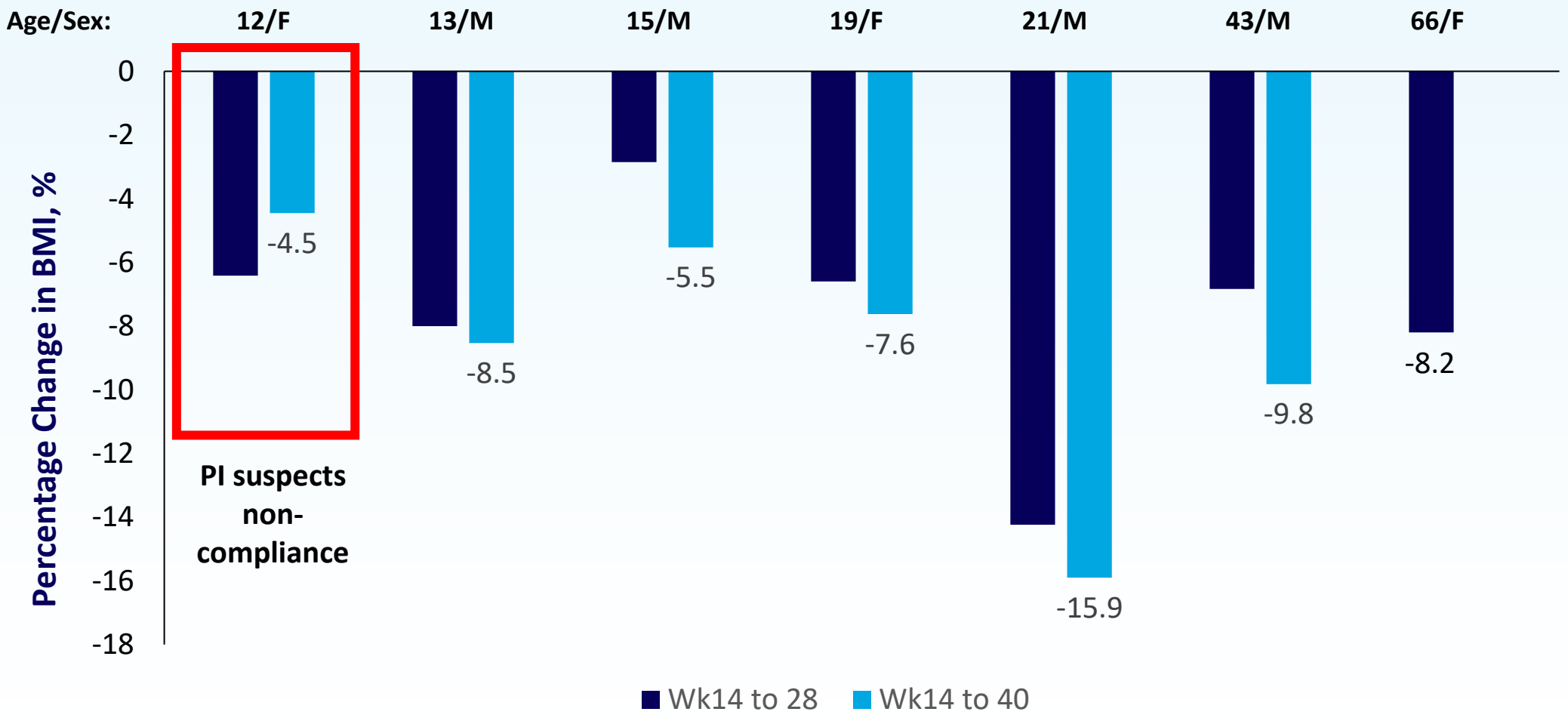
(n=27)

26 of 27 eligible participants transitioned to open-label extension (OLE) phase for up to 38 weeks

OLE participants retitrated from 200mg to maximum 600mg dose, as tolerated, to preserve blind

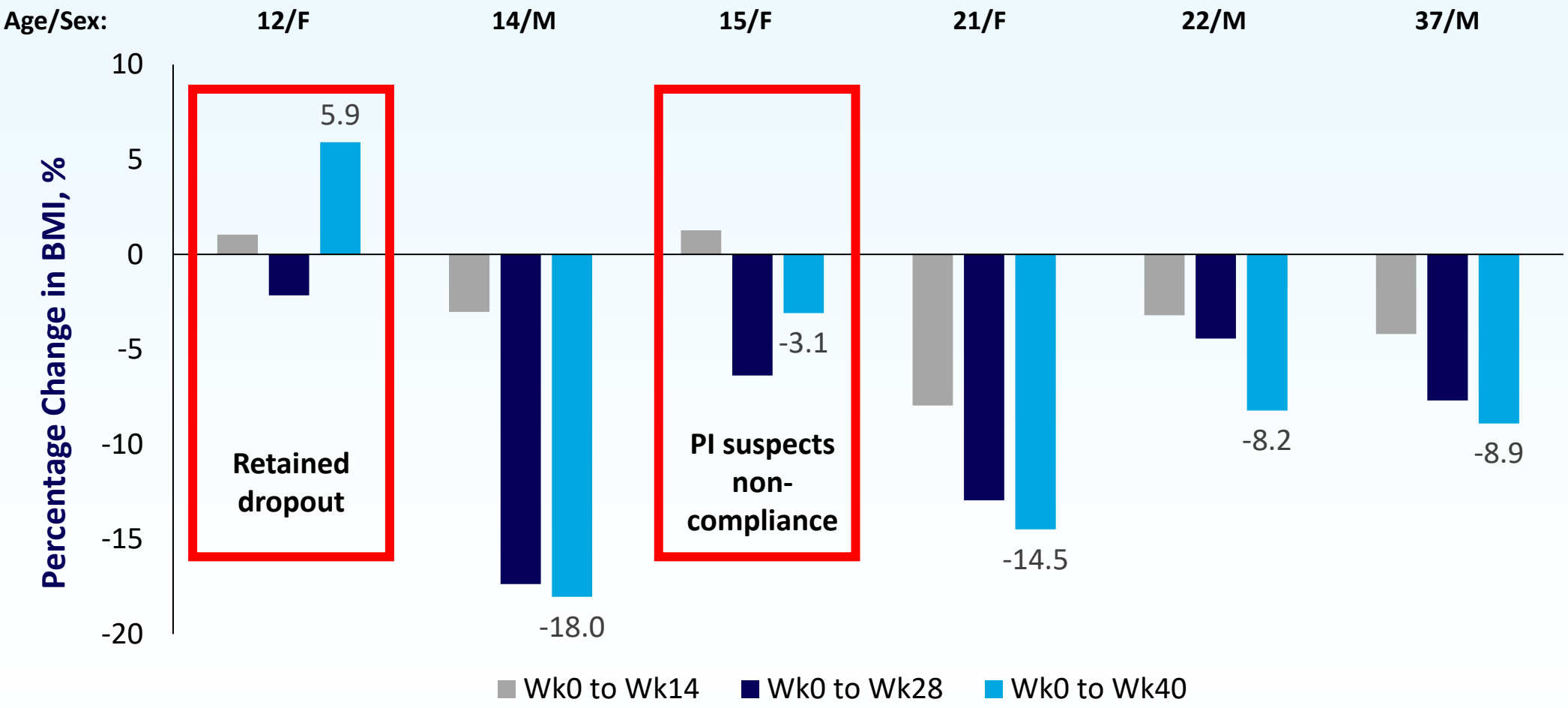
26 patients entered OLE

Placebo Patients Titrated to 600mg Achieved Meaningful Reductions in BMI at Week 28 and Deepening Responses at Week 40



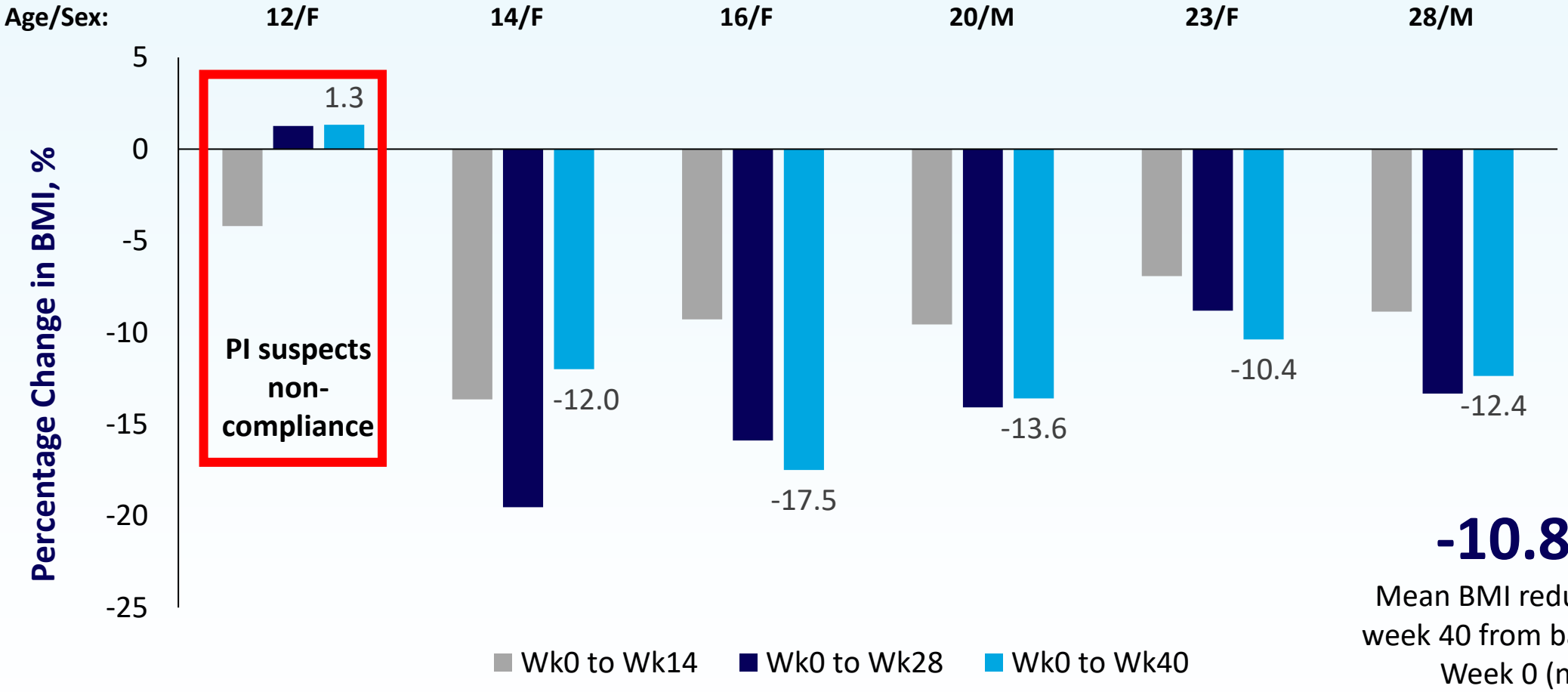
NOTE: Preliminary data; pending source verification

Patients Initially Randomized to 200mg and Titrated to 600mg Achieved Meaningful Reductions in BMI at Weeks 28 and 40



NOTE: Preliminary data; pending source verification

Patients* Titrated from 400mg to 600mg Achieved Deepened, Sustained BMI Reduction at Weeks 28 and 40

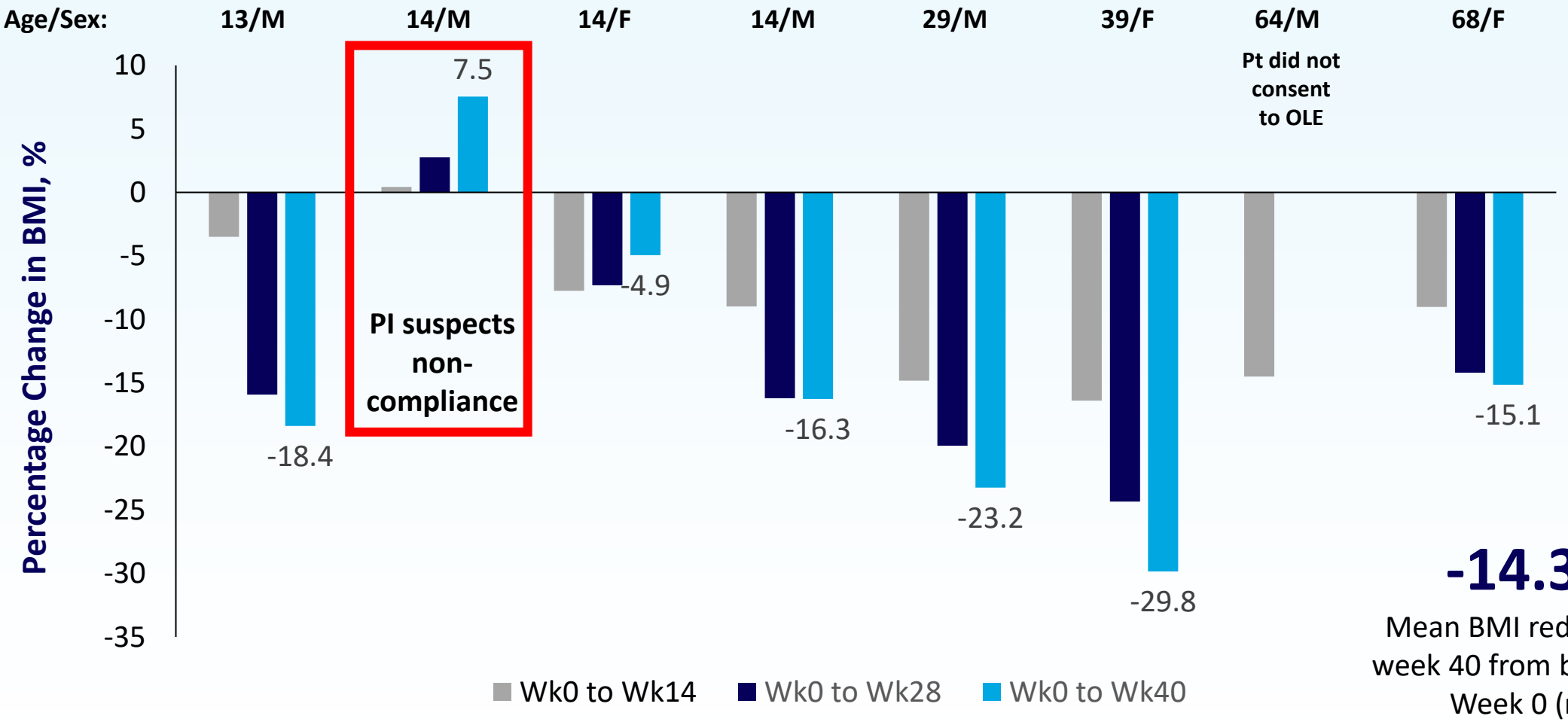


-10.8%

Mean BMI reduction at week 40 from baseline at Week 0 (n=6)

NOTE: Preliminary data; pending source verification; * One 34-yr-old male patient discontinued after Visit 1 and is not shown

Patients on 600mg Achieved Deepened and Sustained BMI Reduction at Week 40



-14.3%

Mean BMI reduction at week 40 from baseline at Week 0 (n=6)

NOTE: Preliminary data; pending source verification

Bivamelagon Long-term Extension Data Demonstrated Sustained Efficacy

- Open-label extension data show persistent, deepening BMI reductions at 6- and 9-months
- Extension safety and tolerability generally consistent with 14-week results
- End of Phase 2 meeting with FDA completed
- On track to initiate Phase 3 aHO study by the end of 2026

Multiple Anticipated Milestones

Mar. 20, 2026	**PDUFA goal date** for setmelanotide **in conditions associated with acquired hypothalamic obesity**
Q1 2026	Complete enrollment in **Part C** of **Ph1/2 trial evaluating RM-718** in acquired hypothalamic obesity
Q1 2026	Topline data from **12-patient Japanese cohort** of **Ph3 trial** evaluating setmelanotide in **acquired hypothalamic obesity**
Q1 2026	Topline data from **Ph3 EMANATE trial** evaluating setmelanotide in four genetically-defined, rare MC4R pathway diseases
H1 2026	Disclose six-month results from exploratory **Ph2 trial** evaluating setmelanotide in **Prader-Willi syndrome**
H2 2026	Complete enrollment in **Ph3 substudy** evaluating setmelanotide in **congenital hypothalamic obesity**
H2 2026	**Complete** enrollment in **Part D** of **Ph1/2 trial evaluating RM-718** in **PWS**
YE 2026	Initiate **pivotal Ph3 trial** evaluating **oral bivamelagon** in **acquired hypothalamic obesity**

Jennifer Lee

EVP, Head of North America

Anticipated US Launch of IMCIVREE in Acquired Hypothalamic Obesity

PDUFA goal date of March 20, 2026

Significant unmet need without an approved therapy

Estimated US Prevalence of ~10,000 patients[1]

Team in place and ready to launch

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.);

Rhythm® PHARMACEUTICALS

Pituitary Centers Use Multiple Care Models for HO

Tumor treatment	**Neurosurgery**	**Radiation**	**Neuro-oncology**	
Endocrinopathy management	**Endocrinology**			
Treatment of HO	**Endocrinology**	**Weight management / Metabolic medicine**	**Clinical nutrition/ Supportive care**	**Community Providers (PCP, ABOM)**

Ready to Launch Upon FDA Approval

Establish IMCIVREE as the foundational treatment for aHO

Access team engaging with payers

Patient services team engaging with patients, families

Yann Mazabraud

EVP, Head of International

IMCIVREE available in >25 countries outside the United States

Ongoing BBS, POMC/LEPR sales and Early-access aHO programs in France and Italy

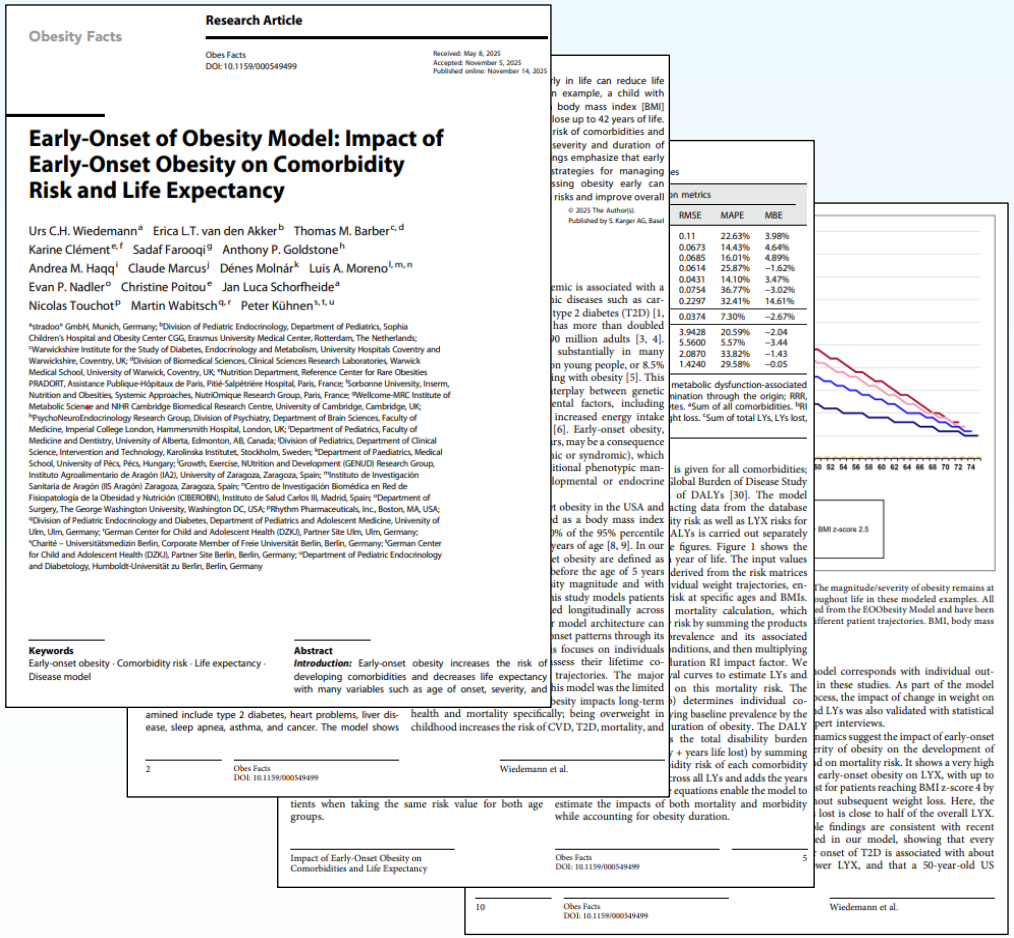
Continued execution

>100 employees in 13 countries

Eight countries added in 2025

64 abstracts at 12 international scientific congresses

Early-onset Obesity Model published in *Obesity Facts* Journal



Obesity Facts

Research Article

Obes Facts
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Early-Onset of Obesity Model: Impact of Early-Onset Obesity on Comorbidity Risk and Life Expectancy

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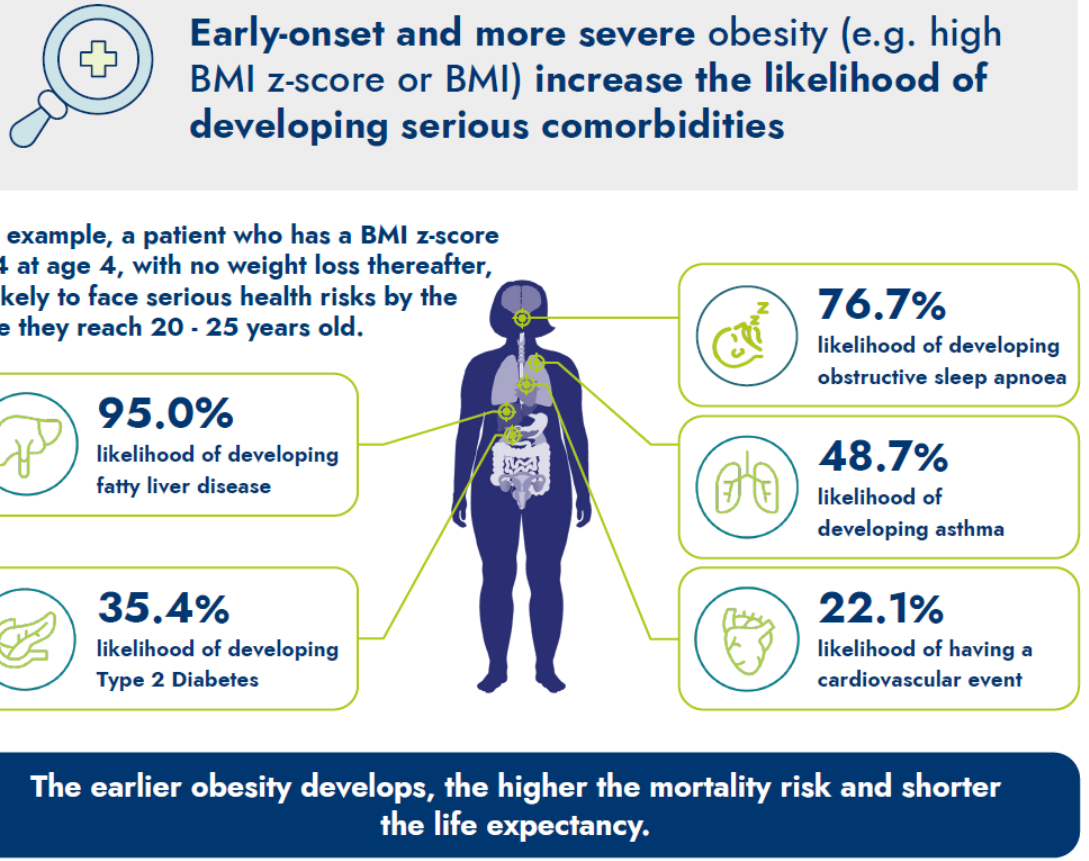
Keywords
Early-onset obesity · Comorbidity risk · Life expectancy · Disease model

Abstract
Introduction: Early-onset obesity increases the risk of developing comorbidities and decreases life expectancy with many variables such as age of onset, severity, and



Obesity Facts. 2025 Nov 14:1-15. doi: 10.1159/000549499

Preparing to Launch Setmelanotide for Acquired Hypothalamic Obesity in Japan and Europe

5,000 – 8,000

estimated Japanese prevalence[1]

Top-line Phase 3 Data expected in March 2026

~10,000

estimated European prevalence[2]

EMA Authorization expected in H2 2026

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
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 people

Hunter Smith

Chief Financial Officer

Q4 2025: Continued Growth in IMCIVREE Global Sales

$57.3M*
Q4 2025

$194.8M
FY 2025

12% **QoQ** increase from Q3 2025**

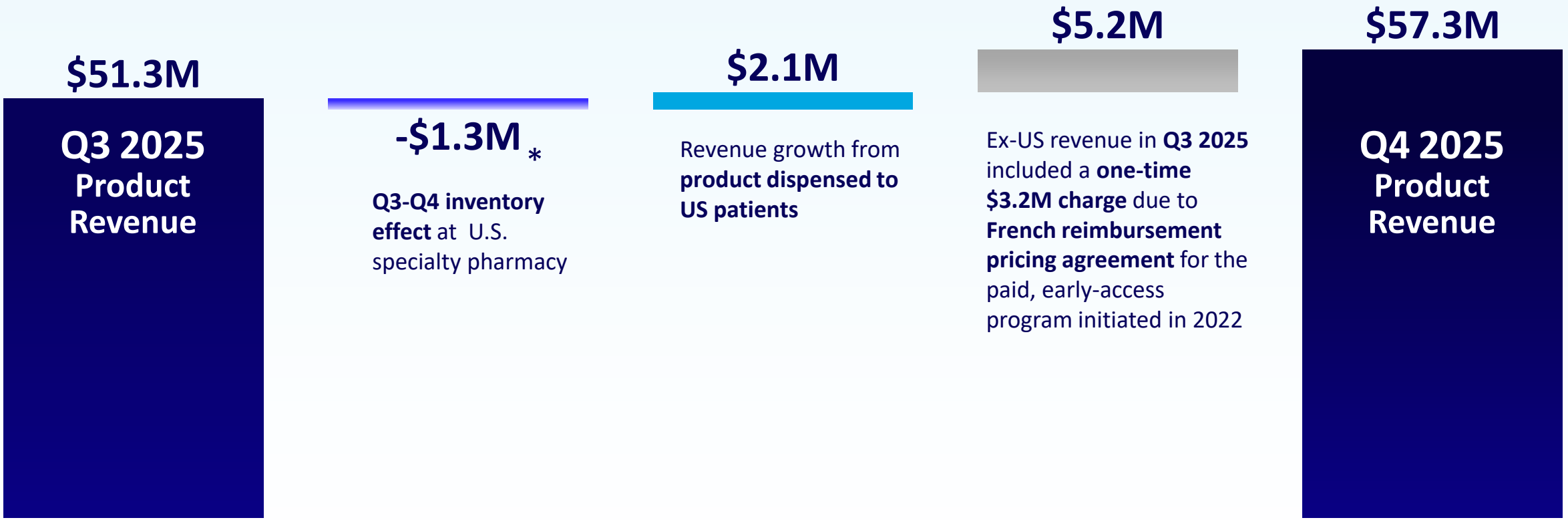
68% of **Q4 2025** revenue **from U.S.**

69% of **FY 2025** revenue **from U.S.**

~10%
increase in number of patients globally on **reimbursed therapy**

* Q4 2025 revenue from vials shipped to U.S. specialty pharmacy in excess of vials dispensed to patients was approximately $1.7M; **Reminder: During Q3 2025, Rhythm recorded a one-time $3.2 million charge following a final agreement with French authorities for reimbursement for IMCIVREE for POMC/LEPR and BBS.

Q3 to Q4 ’25: Consistent Growth in Global Patient Demand Continues



* Q4 2025 revenue from vials shipped to U.S. specialty pharmacy in excess of vials dispensed to patients was approximately $1.7M, compared to $3M in Q3 2025;

Q4, Full-year 2025 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended December 31, 2025	Three months ended December 31, 2024	Year ended December 31, 2025	Year ended December 31, 2024
Product revenue, net	$57.3M	$41.8M	$194.8M	$130.1M
R&D expenses	$42.0M	$41.2M	$167.3M	$238.0M
SG&A expenses	$57.5M	$38.1M	$194.9M	$144.3M
Net Loss attributable to common stockholders	$(48.8)M	$(44.6)M	$(201.9)M	$(264.6)M
Weighted average common shares outstanding	66,876,883	61,596,442	64,984,361	60,995,204
Net Loss per share attributable to common stockholders – basic and diluted	$(0.73)	($0.72)	$(3.11)	($4.34)
Cash, cash equivalents and short-term investments position (period end)	$388.9M	$320.6M	$388.9M	$320.6M

4Q, Full-year 2025 Financial Highlights

$362.3M

2025 GAAP OpEx, which includes **$66.8M** in stock-based compensation

$295.5M*

Non-GAAP[1] OpEx

68,285,039

Common shares outstanding[2] including

729,164

shares of common stock converted from preferred shares

* 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 $295.5 million in 2025 excludes $66.8 million in stock-based compensation; 2. As of Feb. 24, 2026.

2026 OpEx Guidance

$385M to $415M

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

R&D: $197M to $213M

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 and fixed consideration related to in-licensing and related milestone payments. For more information, see slide 3 – Non-GAAP Financial Measures

Questions