Rhythm Pharmaceuticals

Fourth Quarter/Year End 2023 Financial Results and Business Update

February 22, 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 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, 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 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 includes 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

Continued Execution on Clinical Development, Global Commercialization

Expand opportunity with hypothalamic obesity

- Ph 3 enrollment complete with 120 patients dosed
- On track for topline data in 1H 2025
- Agreement reached with Japan's PMDA on potential registration path
- 5,000 to 8,000 estimated HO patients estimated to be living in Japan

Multiple development programs advancing

- Acquired license to LB54640, oral MC4R agonist in Phase 2 trials
- IND for RM-718 accepted; Phase 1 trial on track to start 1H 2024
- Ph3 trial in pediatric patients achieved primary endpoint; Type II variation submitted to EMA for label expansion, and sNDA submission on track for 1H 2024

Strong BBS commercial execution

- $24.2 million in net revenues from IMCIVREE sales in 4Q 2023
- >100 new prescriptions, >70 approvals for reimbursement in U.S. in 4Q 2023
- Market access achieved in Spain and Italy for BBS

IMCIVREE® (setmelanotide) injection

Potential Path to Registration Set based on Feedback from Japan's PMDA

Planned Japanese clinical development

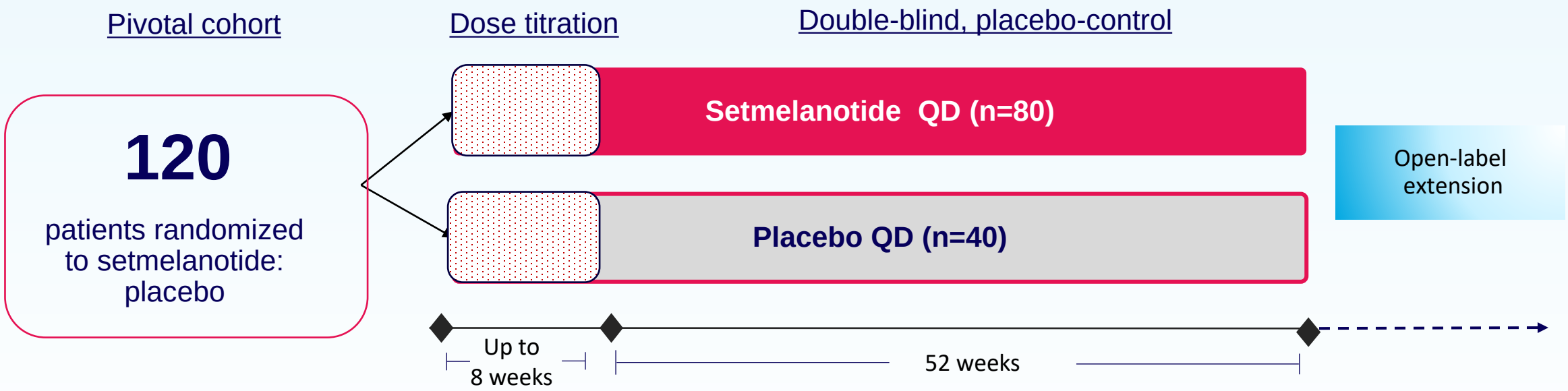
- Supplemental cohort of Ph3 trial to enroll 12 or more Japanese patients
- First patient expected to be dosed in 3Q 2024
- Pharmacokinetic data to be collected
- Bypasses earlier-stage trials in Japanese subjects

Regulatory submissions

- No anticipated impact on timing of anticipated FDA and EMA regulatory submissions
- Supplemental cohort in addition to pivotal dataset

PMDA: Pharmaceuticals and Medical Devices Agency

Phase 3 Hypothalamic Obesity Trial: Enrollment Complete, Top-line Data Expected in 1H2025



NOTE: Trial completion for patients enrolled in supplemental cohort, including 12 Japanese patients, does not affect regulatory submissions in the United States or European Union.

Primary endpoint: Mean % change in BMI from baseline to after approximately 52 weeks on a therapeutic regimen of setmelanotide compared with placebo.

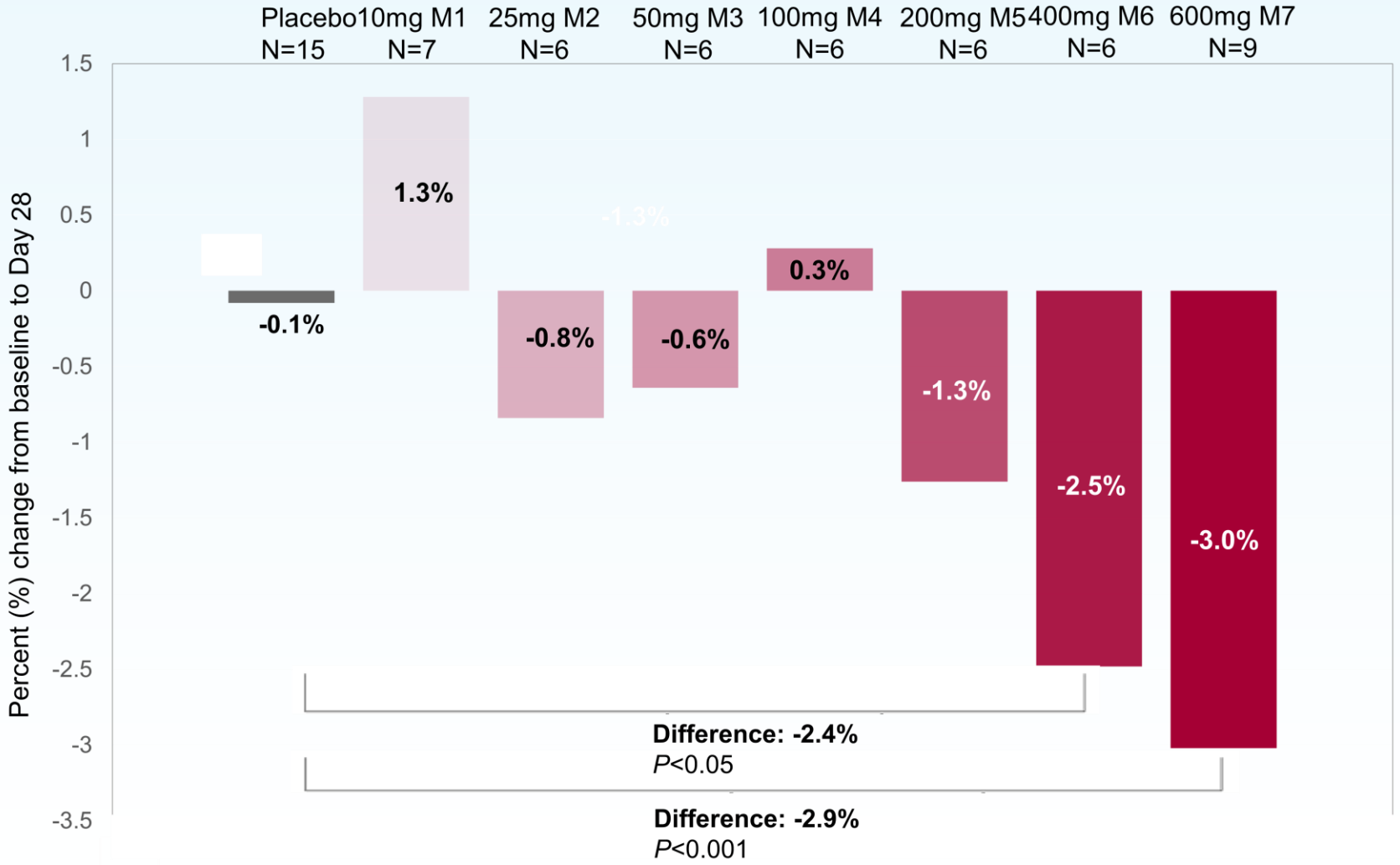
Rhythm, LG Chem Agreement Designed to Accelerate Development and Delivery of Additional Therapy Options for Patients

LG Chem
Life Sciences Company

Highly regarded global biopharma company with strong chemistry and translational science capabilities

LB54640: Oral, highly selective MC4R agonist with compelling Phase 1 data; no hyperpigmentation observed

LB54640 Showed Dose-response Body Weight Loss in Healthy Obese Volunteers



Favorable safety profile

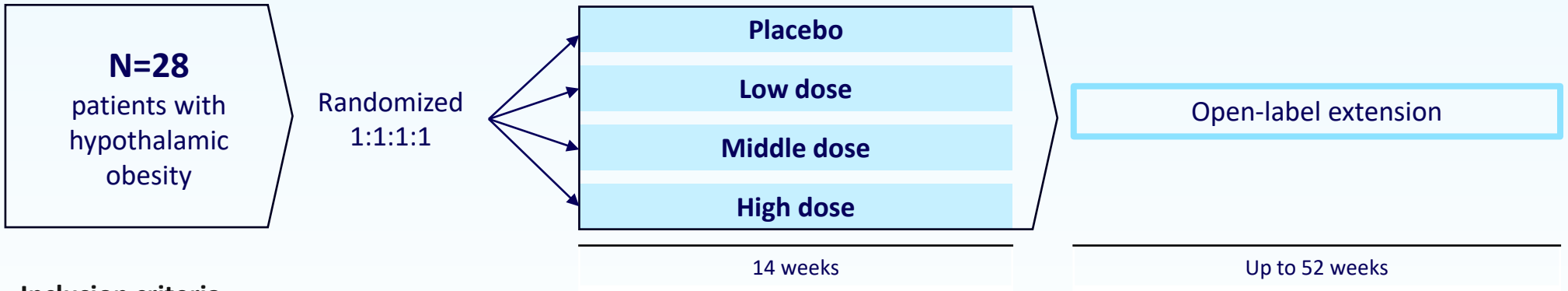
- No serious adverse events
- No skin pigmentation, adrenal, or genitourinary adverse events observed
- Mild to moderate nausea, diarrhea, vomiting most common

As presented by LG Chem at The Obesity Society's ObesityWeek® 2022.

Rhythm® PHARMACEUTICALS

SIGNAL Trial: 14-week, Phase 2 Open-label Trial Evaluating LB54640 in Patients with Hypothalamic Obesity

Transfer of sponsorship from LG Chem to Rhythm in process



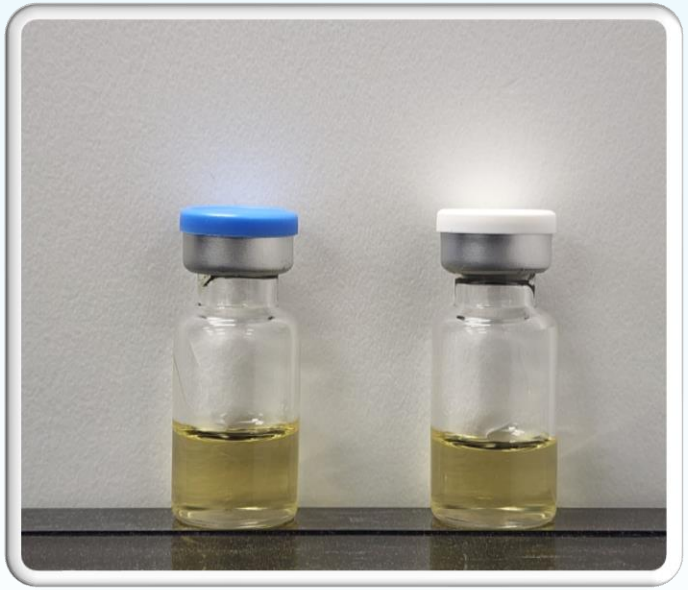
Inclusion criteria

- ≥18yo BMI ≥30 kg/m2 for adults
- 12-<18 yo ≥95th percentile for patients
- Setmelanotide-naive

Efficacy endpoint

- Mean % change in BMI from baseline at 14 weeks

RM-718 has Demonstrated Similar Safety Compared to Setmelanotide Weekly Formulation in Pre-clinical Studies



- In vivo safety results supportive of no off-target cardiovascular effects, like setmelanotide
- No hyperpigmentation observed in vivo
- In vivo results suggest potential efficacy for body weight reduction, hyperphagia reduction
- Potential for efficient development path with hypothalamic obesity

IND accepted; First in human, three-part Phase 1 study to evaluate safety, tolerability, and PK of RM-718 QW anticipated to begin in 1H 2024

Setmelanotide Achieved Clinically Meaningful Reductions in BMI and BMI-Z in 2-<6yo Patients with POMC/LEPR Deficiency or BBS

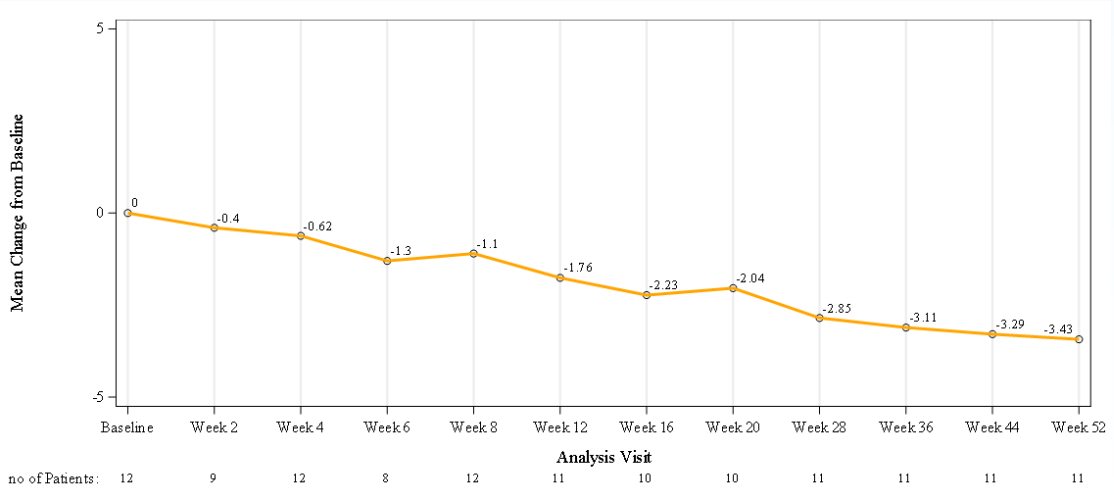
Analysis set population (N=12)

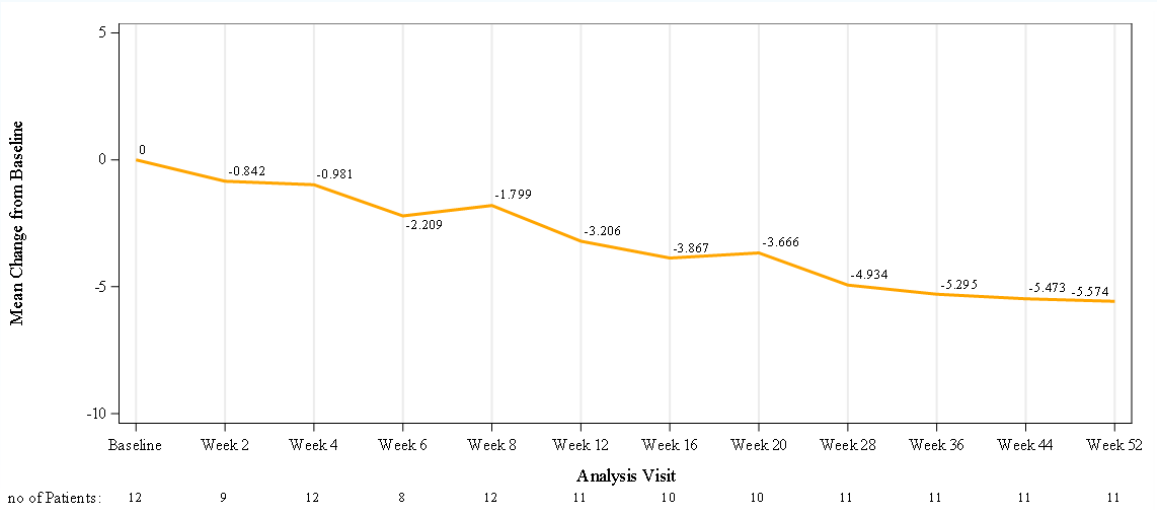
83.3% (10 of 12)

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

-18.380%

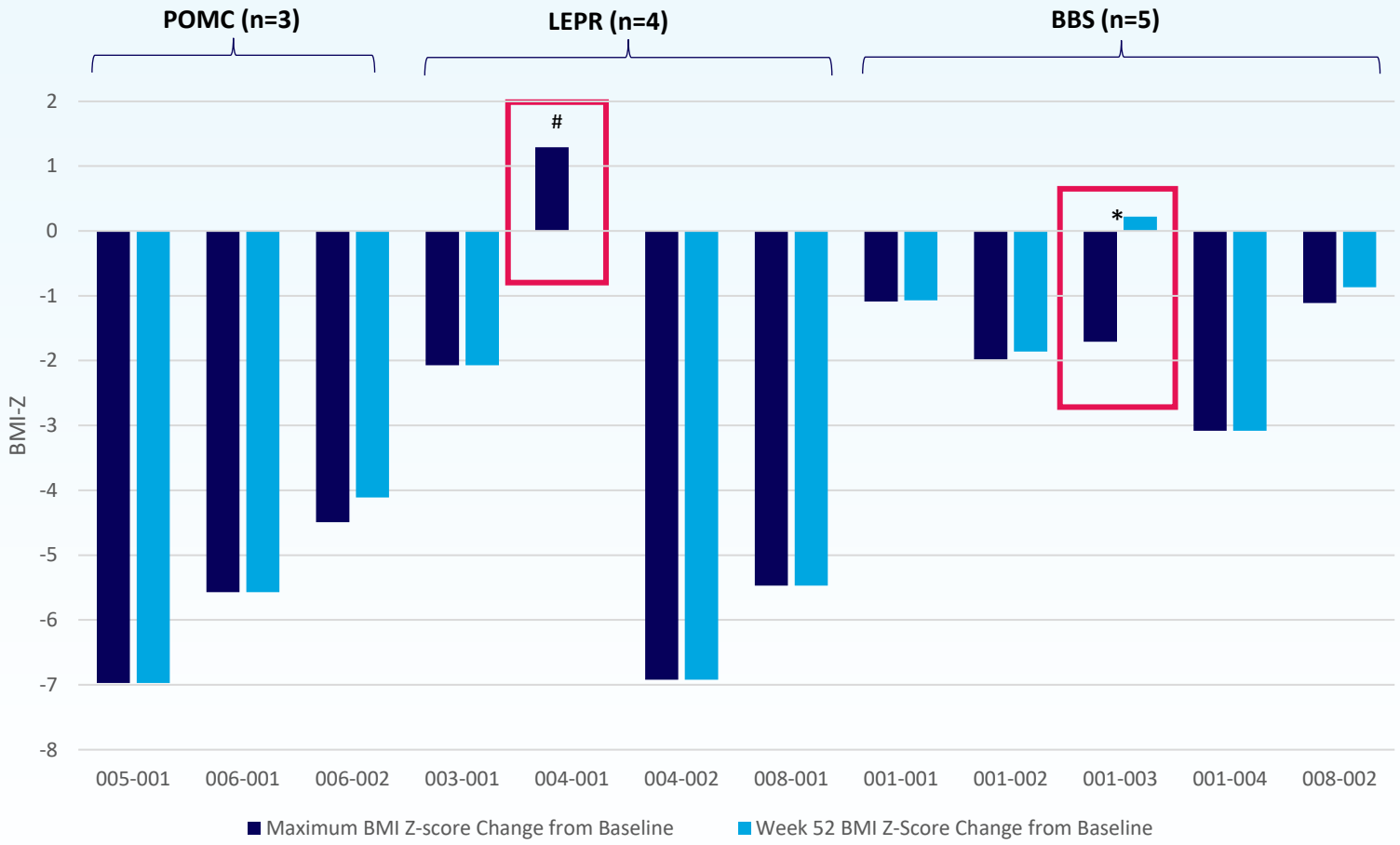
Mean percent change from baseline in BMI at Week 52





Data on file at Rhythm. To be presented at a medical conference.

Setmelanotide Achieved Consistent Reductions in BMI-Z Score



-3.04

Mean change from baseline in BMI-Z at Week 52 (N=12)

-4.3	**-1.3**
POMC/LEPR (n=7)	BBS (n=5)

11 patients completed the trial, and all remain on therapy€.

*Patient was not compliant with dosing (next slide); #Patient discontinued the study at Week 7 and was subsequently lost to follow-up; € As of Dec. 3, 2023.
For patients who did not achieve their greatest reduction from baseline n BMI-Z score at Week 52 (52-week population), the maximum reduction in Z-score at any time is presented.

Rhythm® PHARMACEUTICALS

Jennifer Lee

BBS U.S. Launch

Fourth Quarter 2023 Prescriptions and Approvals for Reimbursement

>100

Prescriptions received during 4Q 2023

>70

Approvals for reimbursement received during 4Q 2023

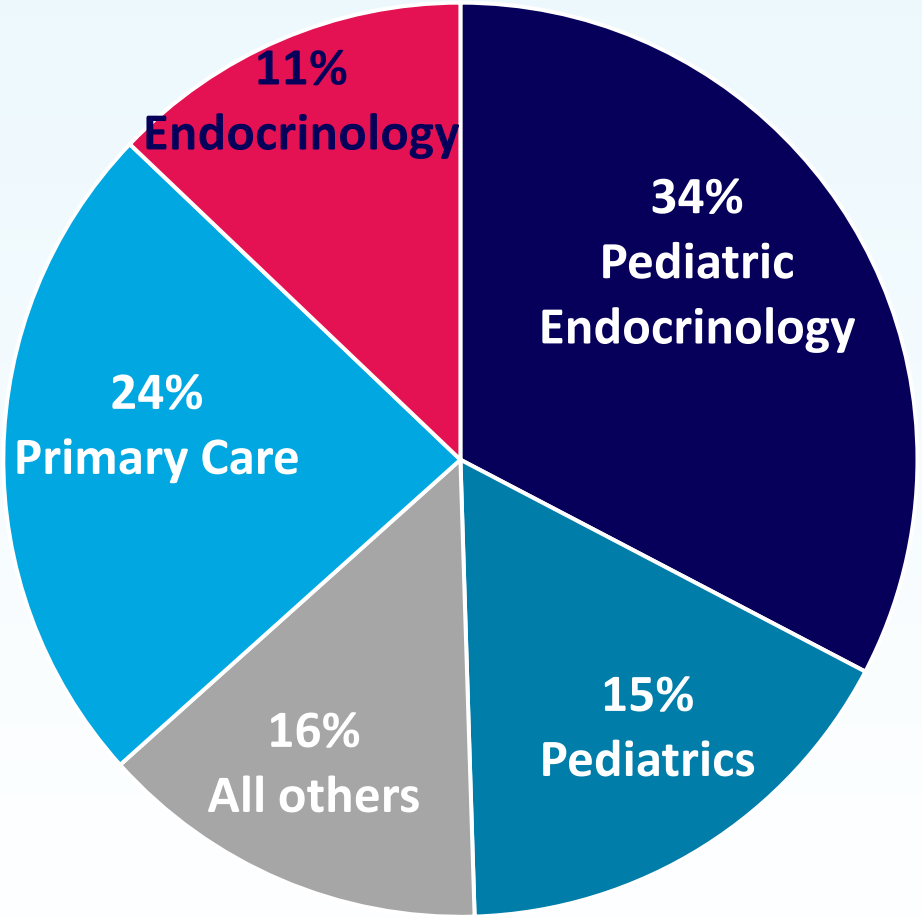
30 previously reimbursed patients were transitioned to free drug through bridge program due to a single state Medicaid program requesting additional documentation to continue reimbursement.

Snapshot of BBS Patients with Prescriptions

Age Range	Since Launch*
Adult (18+)	~59%
Adolescent (12-17)	~23%
Pediatric (6-11)	~18%

*As of December 31, 2023

Increased Depth and Breadth of BBS IMCIVREE Prescriber Base



>360*

Prescribers
as of 12/31/2023

28% of prescribers ‘new to Rhythm’

30% of prescribers have written more than one prescription

*As of December 31, 2023

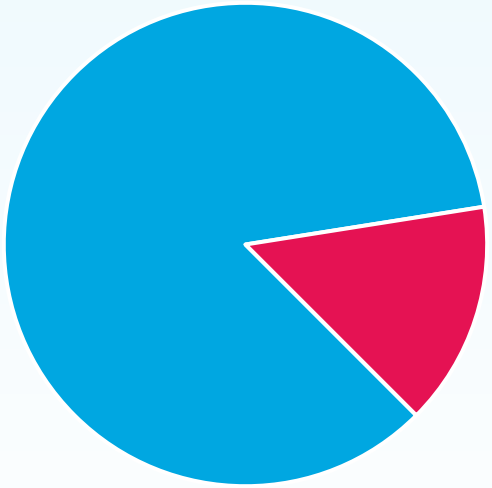
Incremental Improvement in Medicaid Access and Reimbursement with >85% of Covered Lives in States with Positive Coverage

>85%**

of covered lives split between states with:

- an IMCIVREE policy in place; or
- or a positive coverage decision in the absence of an IMCIVREE policy**

Medicaid Covered Lives
~85 million*



<15%**

of covered lives in states with:

- no IMCIVREE prescription received;
- or IMCIVREE prescription being processed;
- or no access by policy **

Payor mix remains consistent as ~90% of reimbursed BBS prescriptions since launch fall under commercial and Medicaid plans**

* According to Medicaid, there were approximately 85 million individuals enrolled in Medicaid in all fifty states, Puerto Rico and the District of Columbia, as of December 2022; ** As of Dec. 31, 2023

Vast Majority of IMCIVREE Prescription Re-authorizations Approved

110*

re-authorization approvals

(at 3-, 6- or 12-months)

>90%* approved at initial re-authorization

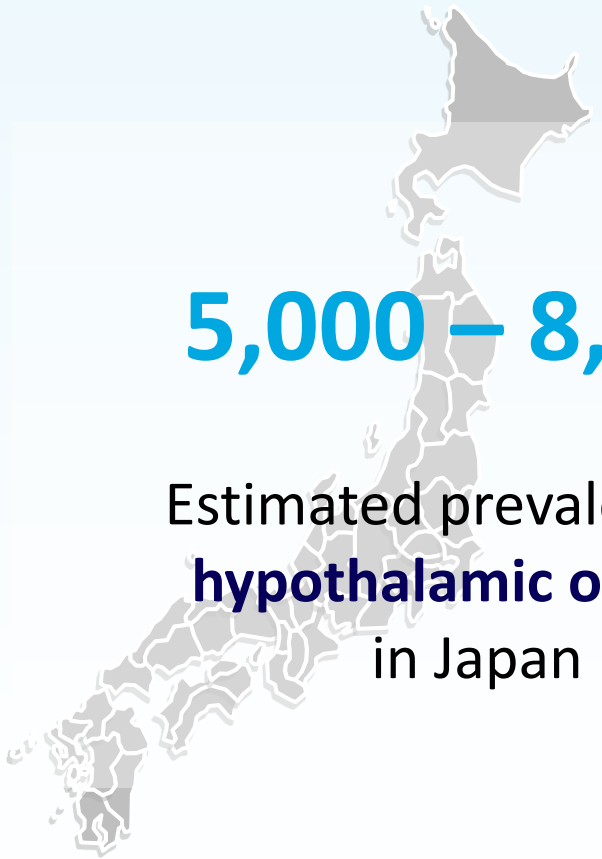
10 denials: 6 already approved**, working toward approval for remaining 4

*As of December 31, 2023; ** As of February 16, 2024

Yann Mazabraud

EVP, Head of International

Significant Opportunity in Japan with Higher Per-capita Incidence and Prevalence of Hypothalamic Obesity



5,000 – 8,000

Estimated prevalence of **hypothalamic obesity** in Japan

- Prevalence is 2-3 times higher than in the USA & Europe due to a higher frequency of craniopharyngioma been reported
- **> 100** health care centers treating patients with hypothalamic obesity
- Single-payer system with established history of recognizing rare diseases

Rhythm's Initial Hypothalamic Obesity Symposium in Japan Well Attended

Solid Start for IMCIVREE Launch for BBS in Germany

Continued focus on engaging with physicians at care centers across the country

~1,200

Estimated German prevalence*

~800

Patients diagnosed with BBS*

>250

Patients with BBS identified*

*Internal company estimates.

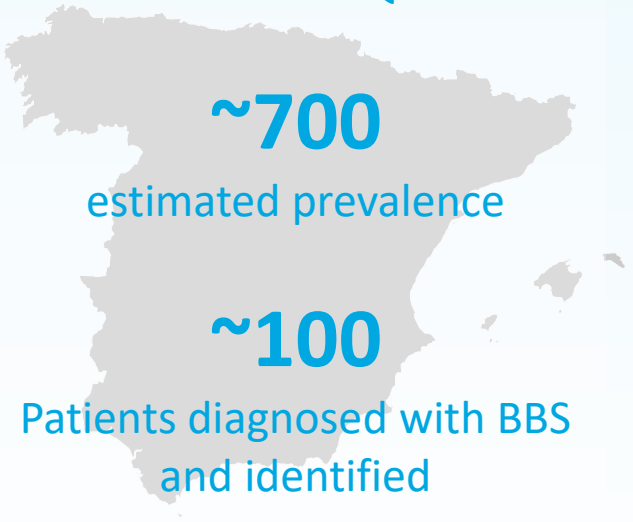
Engaging care centers, large hospitals leads to prescriptions

Rhythm@Home

Reimbursement Achieved for IMCIVREE for BBS in Two New Markets

Spain

Launched in 1Q 2024



~700

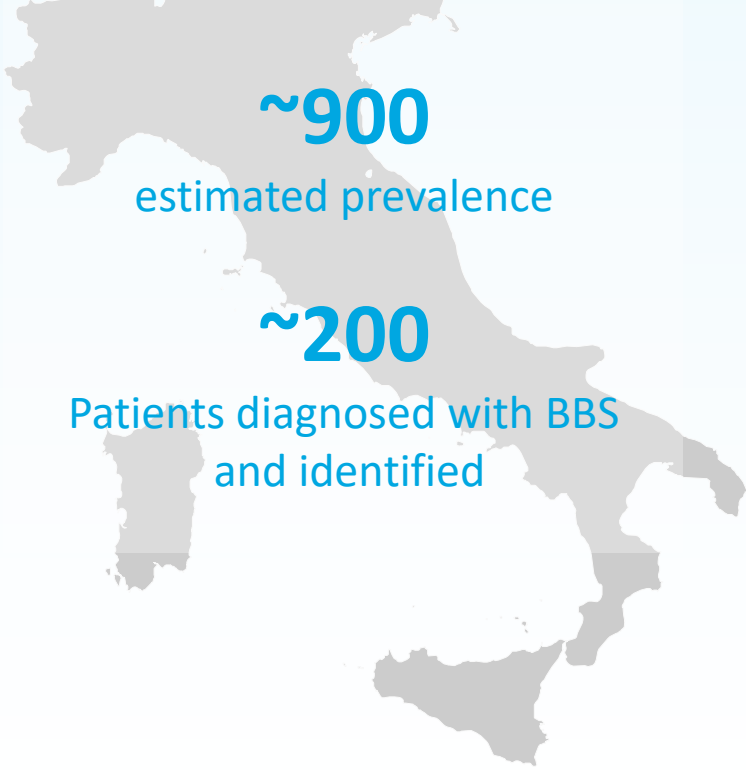
estimated prevalence

~100

Patients diagnosed with BBS and identified

Italy

Launched in 1Q 2024



~900

estimated prevalence

~200

Patients diagnosed with BBS and identified

*Internal company estimates.

Market Access Achieved for IMCIVREE for Biallelic POMC/LEPR and/or BBS in 12 Countries outside of North America

United Kingdom
Launched in POMC/LEPR; BBS launch in 2H2024

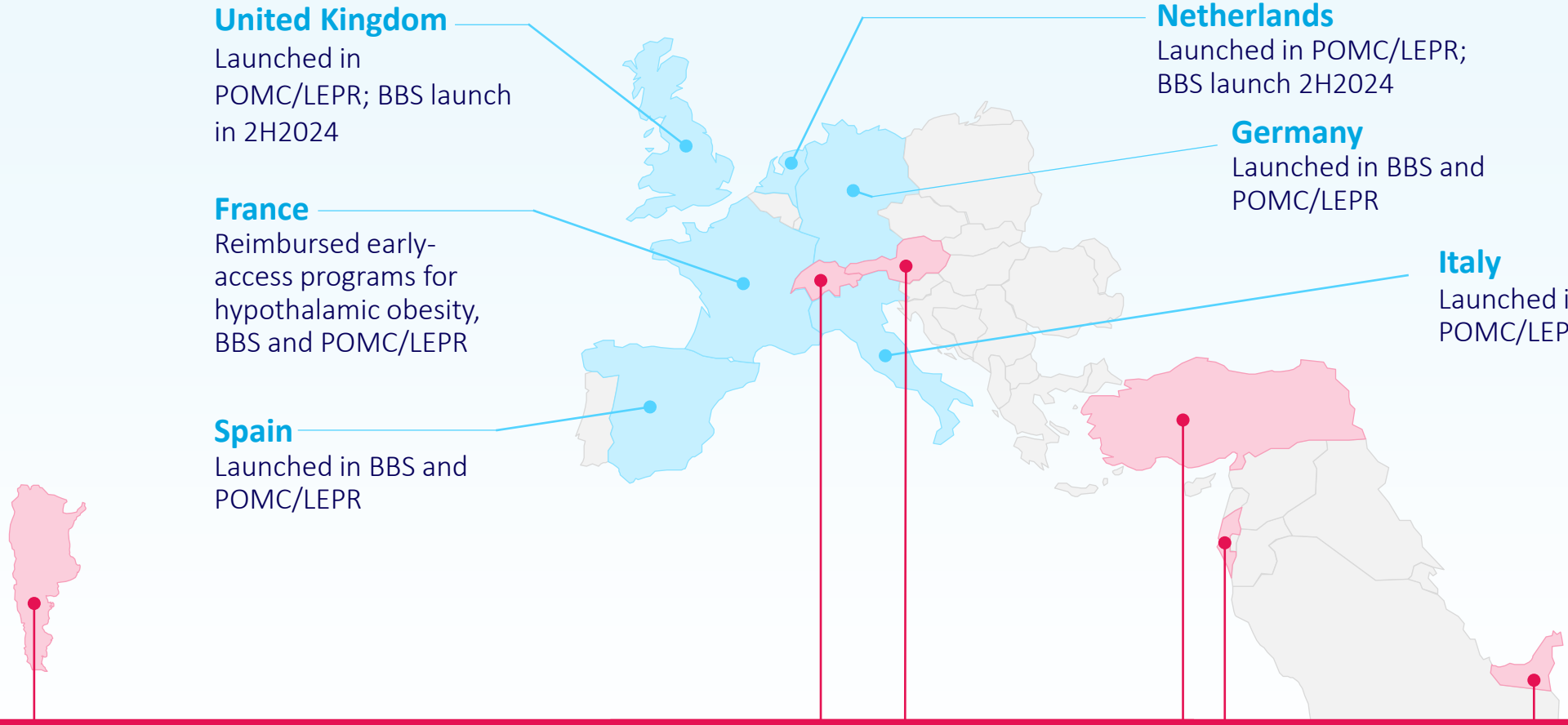
France
Reimbursed early-access programs for hypothalamic obesity, BBS and POMC/LEPR

Spain
Launched in BBS and POMC/LEPR

Netherlands
Launched in POMC/LEPR; BBS launch 2H2024

Germany
Launched in BBS and POMC/LEPR

Italy
Launched in BBS and POMC/LEPR



EARLY ACCESS OR NAMED PATIENT SALES

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

Hunter Smith
4Q 2023 Financial Results

4Q 2023 Financial Snapshot

$275.8M* cash, cash equivalents and short-term investments expected to be sufficient to fund operations into 2025

($ in millions except as noted, per share data and shares outstanding)	Three months ended December 31, 2023	Three months ended December 31, 2022	Year ended December 31, 2023	Year ended December 31, 2022
Product revenue, net	$24.2M	$8.8M	$77.4M	$16.9M
Collaboration revenue	--	--	--	$6.8M
R&D expenses	$29.9M	$23.5M	$135.0M	$108.6M
SG & A expenses	$32.4M	$26.3M	$117.5M	$92.0M
Loss from operations	$(41.3)M	$(42.1)M	$(184.4)M	$(179.2)M
Shares outstanding (basic and diluted share count, weighted average)	59,211,199	56,299,525	57,673,128	52,120,701
Net (loss) per share basic and diluted	($0.70)	($0.75)	($3.20)	($3.47)
Cash, cash equivalents and short-term investments position (period end)	$275.8M	$333.3M	$275.8M	$333.3M

* As of December 31, 2023.

4Q and Year End 2023 Financial Highlights

$275.8M
cash equivalents and short-term investments as of December 31, 2023

76%
of 4Q 2023 revenue from U.S. sales of IMCIVREE vs. 80% in 3Q 2023

GAAP OpEx of **$261.8M** includes **$32.6M** in stock-based compensation in 2023

Non-GAAP[1] OpEx for 2023 of **$219.9M***

RYTM expects cash to be sufficient to fund planned operations **into the second half of 2025**

* Does not include COGS; [1] Non-GAAP Operating Expenses is a non-GAAP financial measure. Non-GAAP Operating Expenses of $219.9 million is derived from GAAP total operating expenses of $261.8 million less $32.6 million in stock-based compensation. For more information, see slide 3.

Financial Guidance for 2024

$100 million in fixed consideration commitment to acquire LB54640 from LG Chem*

- $40 million paid in January 2024
- 432,143 shares of common stock issued to LG Chem, valued at $20 million in January 2024
- $40 million to be paid in 18 months
- Total accounted for in R&D expenses during 1Q 2024
- In future quarters, when the achievement of development and commercial milestones becomes probable, the Company will recognize R&D expense

Anticipated Non-GAAP Operating Expenses[1] for 2024:
$250M to $270M

- R&D: $145 million to $160 million, including $10M-$15M of LB54640 development costs
- SG&A: $105 million to $110 million
- Does not include stock-based compensation
- Does not include $100 million in fixed consideration related to in-licensing of LB-54640 from LG Chem

*As announced on January 4, 2024; [1]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.

David Meeker, MD
Conclusion

Continued Execution: Recent Achievements and Multiple Anticipated Milestones

Recent achievements

- ✓Licensed global rights to **oral MC4R agonist LB54640**
- ✓**Completed enrollment** in Phase 3 hypothalamic obesity trial
- ✓Achieved **positive reimbursement** decision IMCIVREE for **BBS** in **Spain and Italy**
- ✓IND application for **new pipeline product, RM-718 QW**, accepted by the FDA
- ✓**Phase 3 pediatrics trial** achieved primary endpoint; **EMA** regulatory submission completed

Anticipated milestones in 2024

- **1H2024:** Initiate Phase 1 study of RM-718 QW
- **1H2024:** Complete sNDA submission to US FDA to expand IMCIVREE label to include children between 2yo and <6yo
- **2H2024:** Announce Ph2 DAYBREAK stage 2 PBO-controlled data
- **2H2024:** Complete enrollment in 2 or more EMANATE cohorts in 2H2024
- **1H2025:** Topline data in Phase 3 hypothalamic obesity trial

Questions