Rhythm Pharmaceuticals

Third Quarter 2023 Financial Results and Business Update

November 7, 2023

On Today's Call

David Connolly, Executive Director of Investor Relations and Corporate Communications

David Meeker, MD, Chair, President and Chief Executive Officer

Jennifer Chien, Executive Vice President, Head of North America

Yann Mazabraud, Executive Vice President, Head of International

Hunter Smith, Chief Financial Officer

Important Notice

This presentation contains certain statements that are forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and that involve risks and uncertainties, including without limitations statements regarding the potential, safety, efficacy, and regulatory and clinical progress of setmelanotide, including the anticipated timing for initiation of clinical trials and release of clinical trial data, our expectations surrounding potential regulatory submissions, approvals and the timing thereof, including the anticipated IND application for RM-718, our business strategy, prospects and plans, including regarding commercialization of setmelanotide, the application of genetic testing and related growth potential, expectations surrounding the potential market opportunity for our product candidates, our participation in upcoming events and presentations, and the content of such presentations, our anticipated financial performance and financial position, including estimated Non-GAAP Operating Expenses for the year ending December 31, 2023, and the sufficiency of our cash, cash equivalents and short-term investments to fund our operations. 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 outcome of clinical trials, the impact of competition, the impact of management departures and transitions, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our expenses, the impact of the COVID-19 pandemic on our business operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q and other reports we file 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.

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. 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

High-level Execution on Global Commercialization and Market Access for BBS, Clinical Development

Strong BBS commercial execution

- Strong growth with $22.5M in global net revenue for 3Q2023
- More than 100 international patients on reimbursed IMCIVREE therapy
- Robust demand for IMCIVREE for BBS continues

IMCIVREE® (setmelanotide) injection

Hypothalamic obesity Ph3 trial progressing

- Ph3 trial on track to complete enrollment by the end of 2023
- 25.5% mean BMI reduction achieved at one-year setmelanotide therapy (n=12) in LTE trial, as presented at ObesityWeek®
- Pre-approval, paid early access granted in France

Multiple development programs advancing

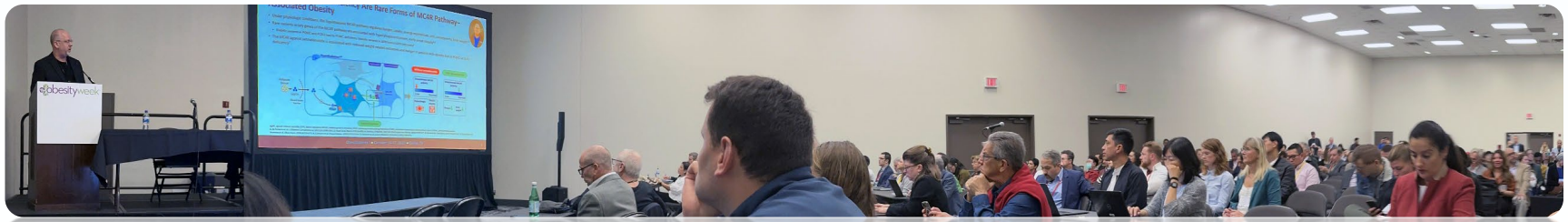
- RM-718: IND on track for submission by year-end 2023
- Multiple 2H 2023 setmelanotide data readouts with preliminary data from Ph2 DAYBREAK trial, Ph3 pediatrics and Ph3 switch
- Additional detail on MC4R pathway development programs at Dec. 6 R&D event

Six Presentations at ObesityWeek® 2023

obesityweek® | THE OBESITY SOCIETY

October 14-17, 2023 • Dallas

Weight Reduction in Patients with **Hypothalamic Obesity** Treated With Setmelanotide for **12 Months**	**3-Year** Setmelanotide Weight Outcomes in Patients with **Bardet-Biedl Syndrome** and Obesity	Cardiac, Renal, and Endocrine/Diabetes Mellitus Outcomes in Children with **Bardet-Biedl Syndrome**	Impact of Setmelanotide on Metabolic Syndrome Risk in Patients With **Bardet-Biedl Syndrome**	**4-Year** Setmelanotide Weight Outcomes of Patients With **POMC and LEPR Deficiency Obesity**	Impact of Setmelanotide on Metabolic Syndrome Risk in Patients With **POMC and LEPR Deficiency**



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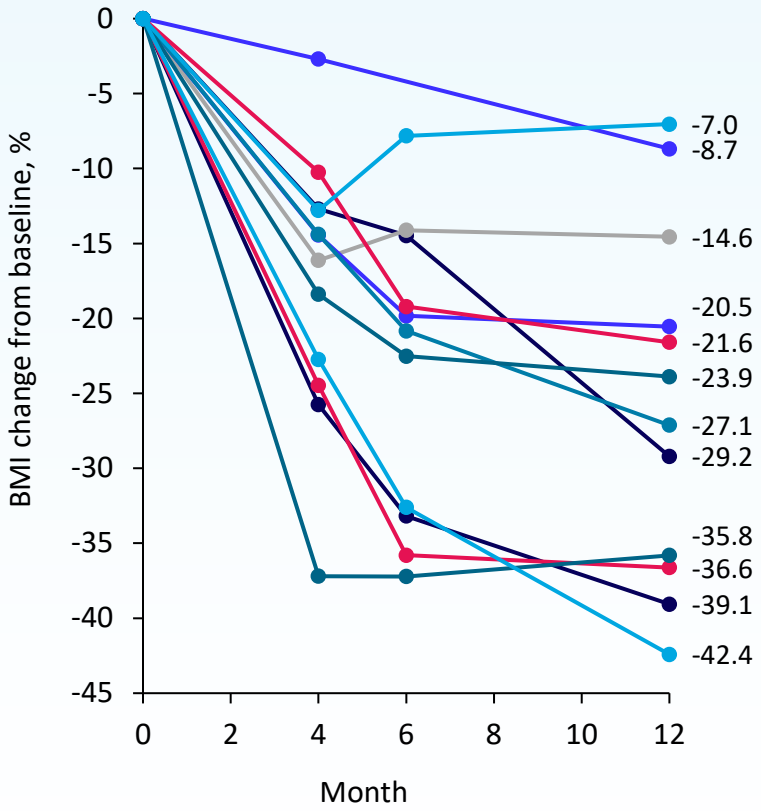
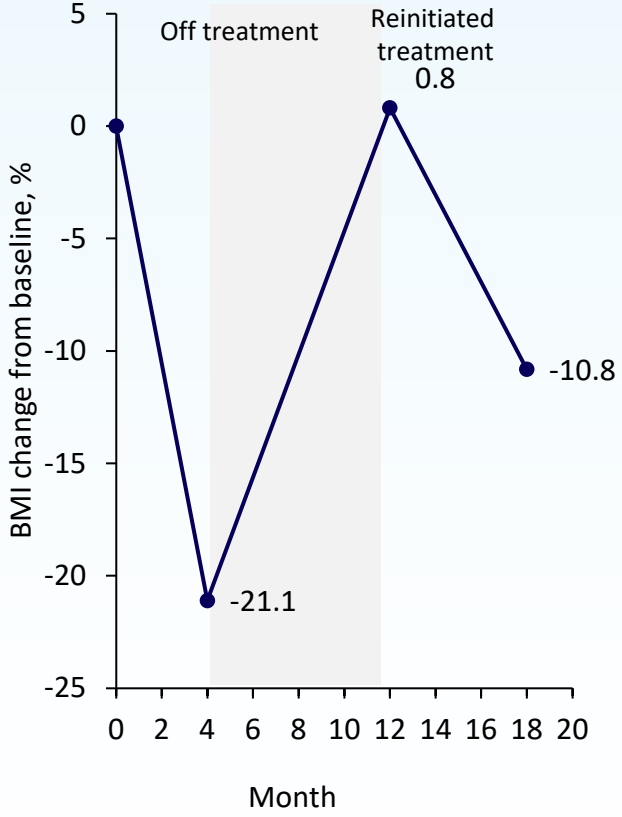
Hypothalamic Obesity: Patients Achieved 25.5% Mean BMI Reduction at One Year of Setmelanotide Therapy in Long-term Ext. Trial

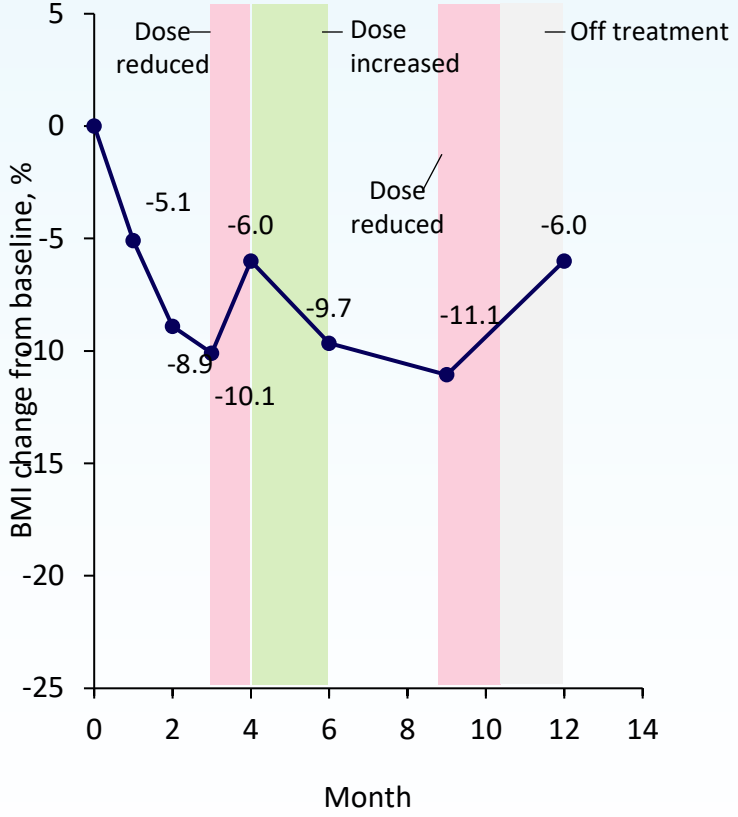
Patients on treatment at Month 12 (n=12)



Patient lost to follow-up (n=1)



Patient who discontinued treatment because of an AE (n=1)



As presented during The Obesity Society Annual Meeting (TOS 2023) on October 17, 2023, in Dallas.

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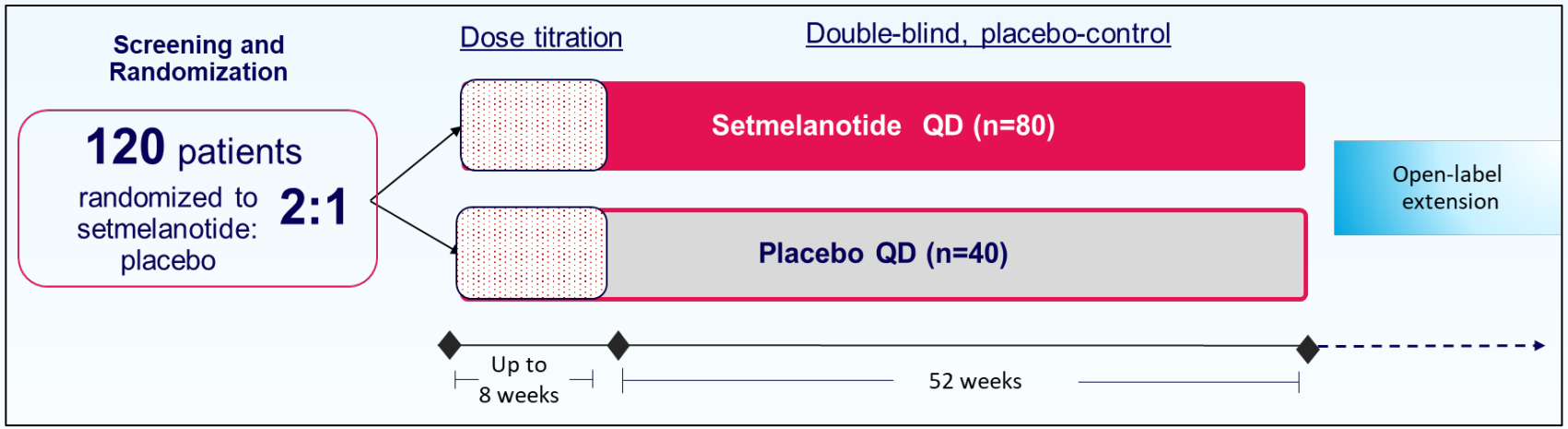
Ph3 Hypothalamic Obesity Trial on Track to Complete Enrollment by end of 2023



Starting dose for all patients is 0.5mg QD; Maximum dose for patients<6yo is between 1.5mg QD and 3.0mg QD based on body weight; maximum dose for patients >6yo with a body weight of 30 kgs or more is 3.0mg QD.

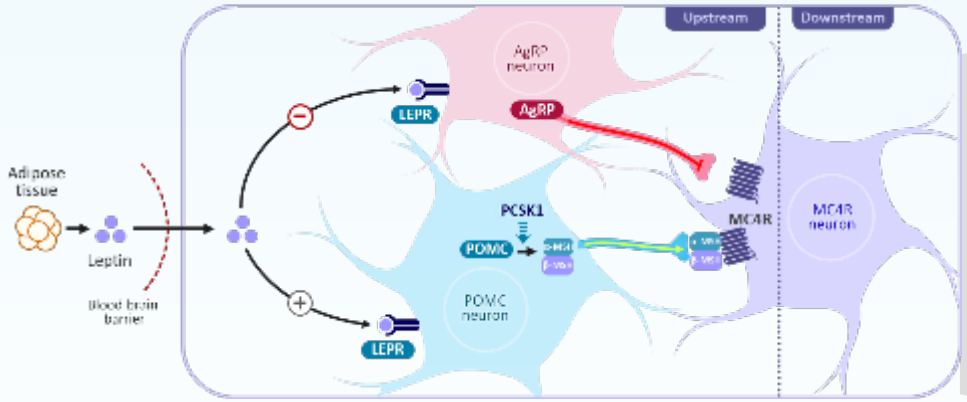
Primary endpoint: Mean % change in BMI from baseline to after approximately 52 weeks on a therapeutic regimen of setmelanotide compared with placebo.

>Two-thirds
of patients screened*

>70%
of planned sites now open*

BMI, body mass index; QD, once daily. * As of Nov. 3, 2023.

Rare MC4R Pathway Diseases Combine for Significant Opportunity



Approved for:€	
Bardet-Biedl syndrome	POMC, PCSK1 and LEPR deficiencies
4,000 - 5,000 patients in the U.S.*	**600 – 2,500 patients in the U.S.***

Phase 3 Trial Initiated
Hypothalamic obesity
5,000 – 10,000 patients in the U.S.*

Phase 3 EMANATE Trial
Heterozygous POMC/PCSK1 insufficiency
Heterozygous LEPR insufficiency
SRC1 deficiency
SH2B1 deficiency
53,000 patients in the U.S.*

*Estimated prevalence of U.S. patients based on company estimates; does not include ex-U.S. prevalence estimates.

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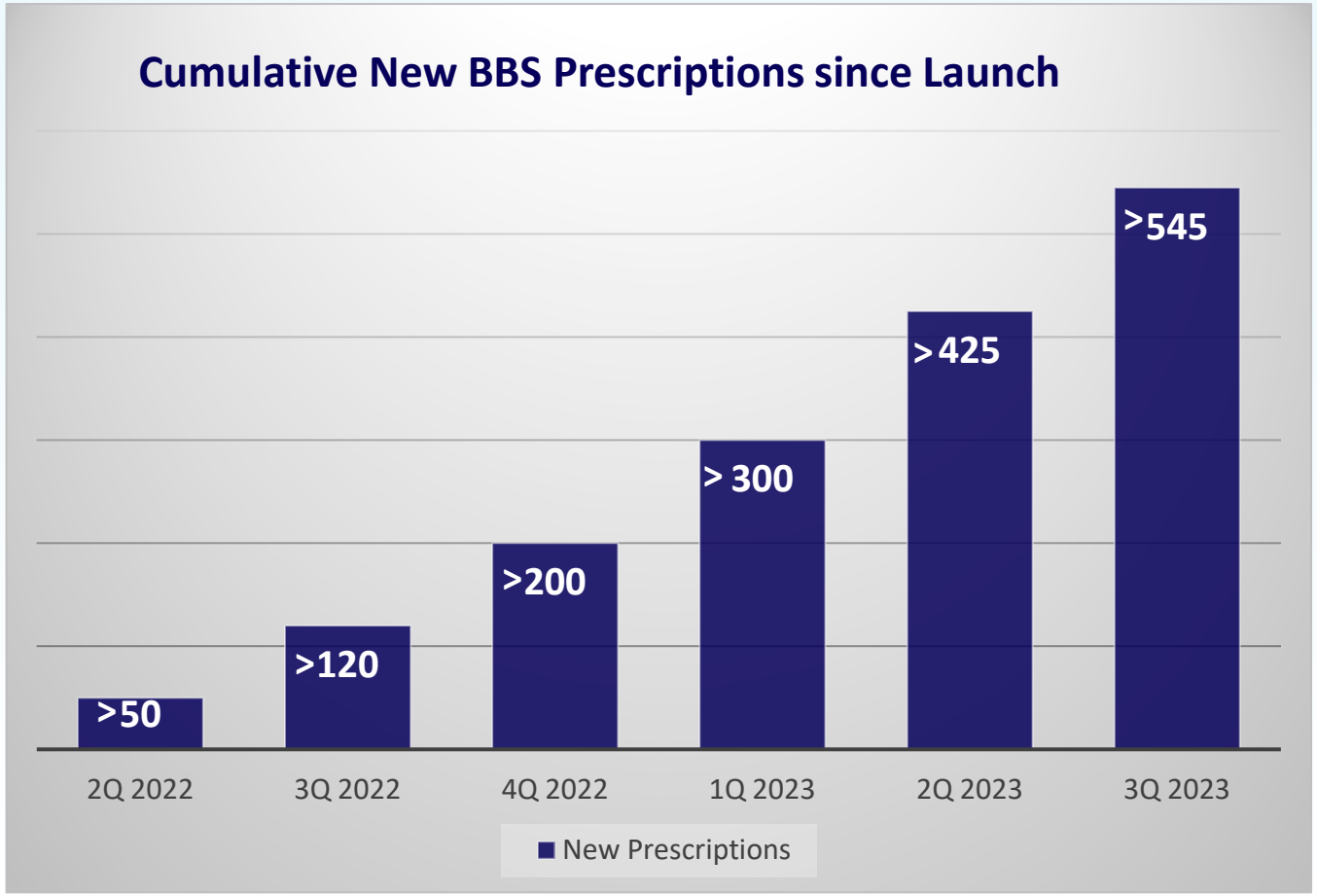
Jennifer Chien

BBS U.S. Launch

Strong U.S. Demand Continues for BBS Launch to Date



>545*

New BBS prescriptions launch to date

>300* unique prescribers

>330* reimbursement approvals

* As of September 30, 2023. IMCIVREE was approved by the U.S. FDA on June 16, 2022.

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Third Quarter 2023 Prescriptions and Approvals for Reimbursement Illustrate Continued Progress

>120

Prescriptions received during 3Q 2023

80

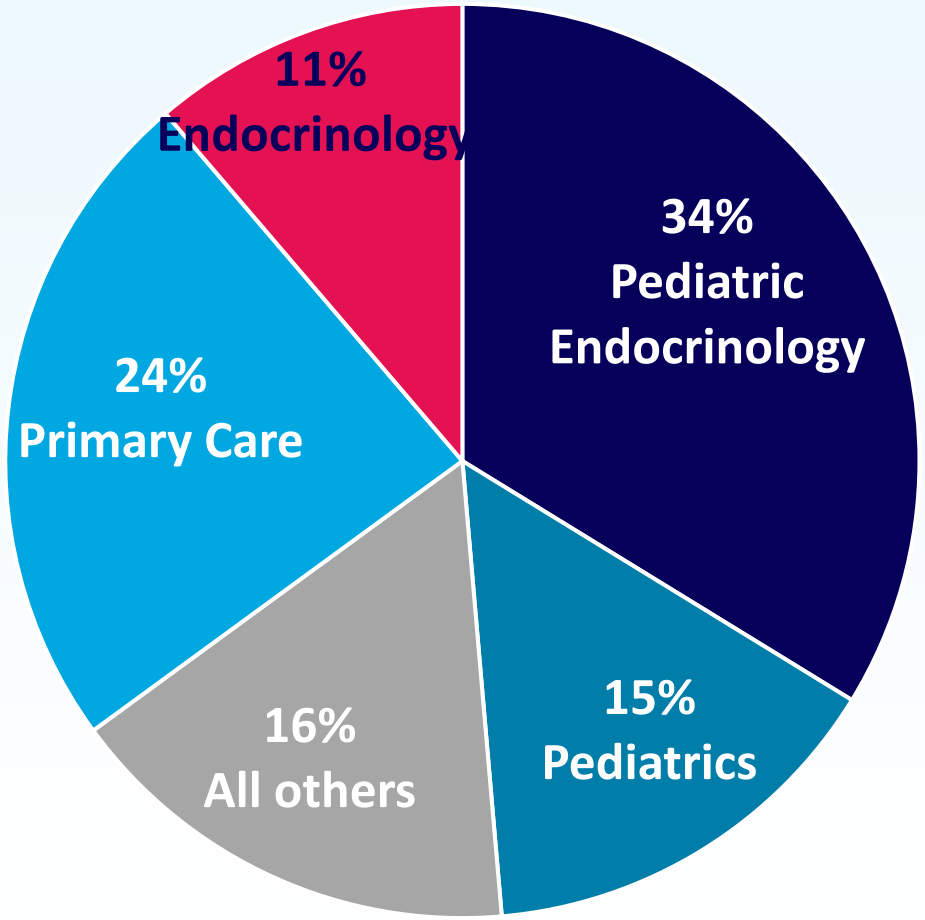
Approvals for reimbursement received during 3Q 2023

Snapshot of BBS Patients with Prescriptions

Age Range	Since Launch*
Adult (18+)	~57%
Adolescent (12-17)	~24%
Pediatric (6-11)	~19%

*As of September 30, 2023

BBS IMCIVREE Prescribers by Specialty Since Launch



>300*

Prescribers
as of 9/30/2023

28% Of prescribers ‘new to Rhythm’

28% of prescribers have written more than one prescription

*As of September 30, 2023

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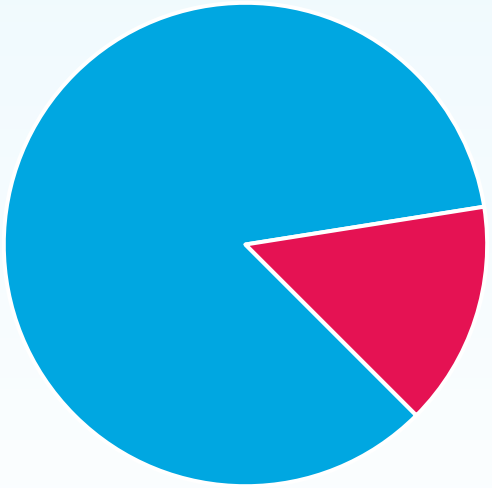
Medicaid Access and Reimbursement Consistent with 80% of Covered Lives in States with Positive Coverage Policies or Decisions

~80%**

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*



~20%**

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 Sept. 30, 2023

Vast Majority of IMCIVREE Prescription Re-authorizations Approved

~75*

re-authorization approvals

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

>90%* approved at initial re-authorization

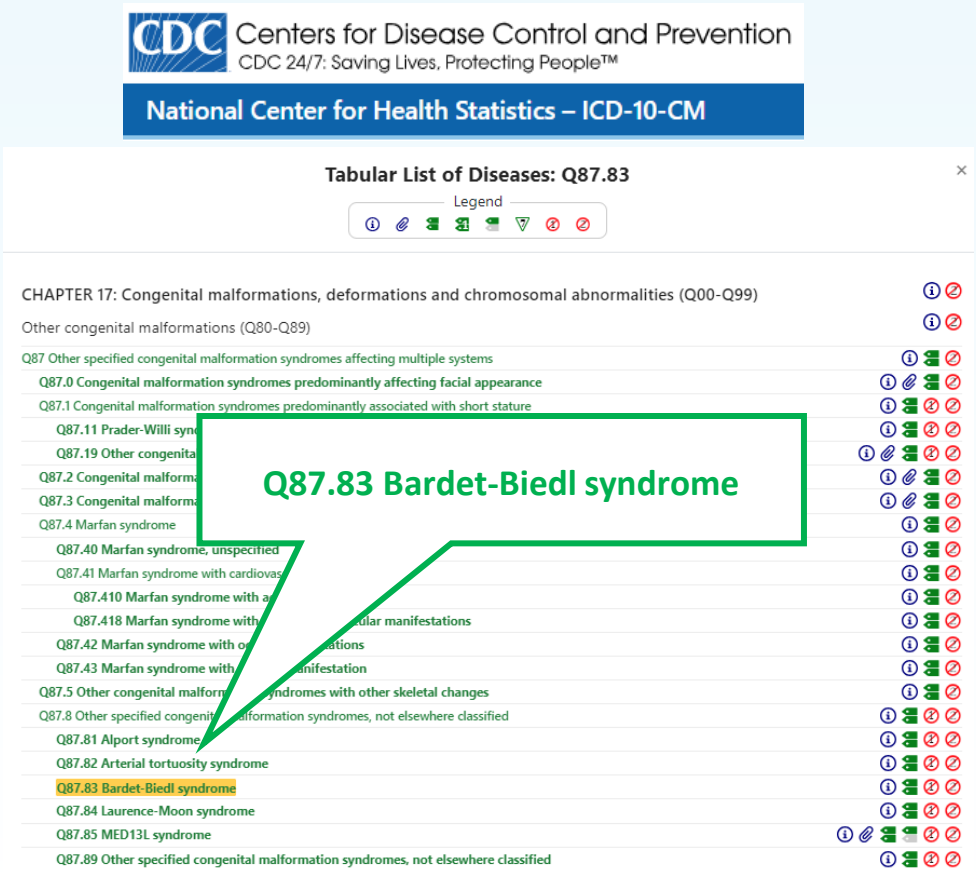
Majority of plans have **12-month** re-auth timeframes

*As of September 30, 2023

New ICD-10 Diagnosis Code Established for BBS Effective Oct. 1

Improves disease awareness, understanding and diagnosis and may enhance access to therapies

- Prior, providers limited to utilizing ICD-10 code Q87.89 - a generic code for congenital malformation syndromes
- Specific BBS ICD-10 code allows for improved patient identification
- Access to data to understand diagnostic and treatment journeys



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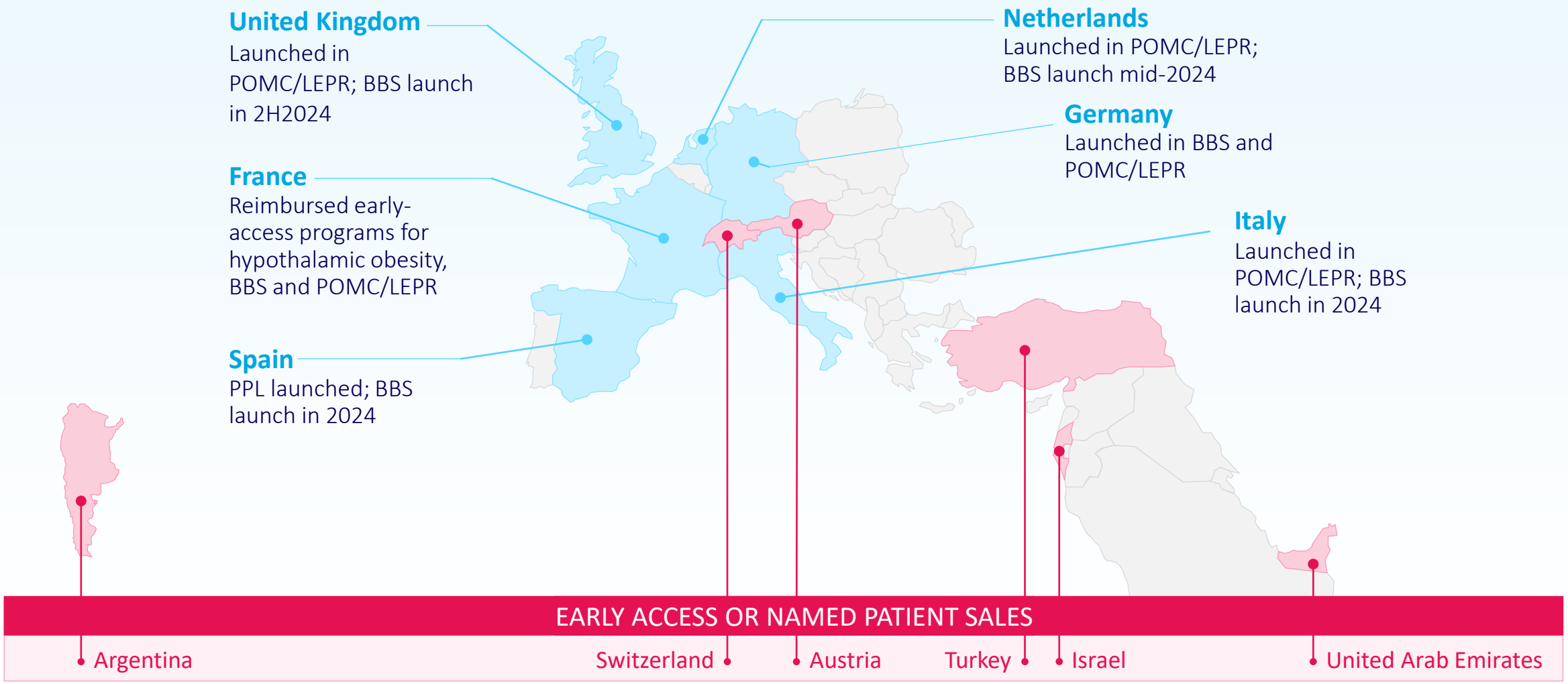
Yann Mazabraud

EVP, Head of International

More than 100 International Patients* with Biallelic POMC/LEPR and/or BBS on Reimbursed IMCIVREE Therapy



* As of Oct. 27, 2023. International patients excludes North America.

Solid Start for IMCIVREE Launch for BBS in Germany

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

Rhythm at ESPE 2023

Symposium

- Hyperphagia and early-onset, severe obesity: and the role of a personalized treatment approach of MC4R pathway diseases

Oral presentations

- Setmelanotide's potential to reduce risk of cardiovascular disease, type 2 diabetes and metabolic syndrome in pediatric patients with POMC/LEPR deficiencies, or BBS
- Sequencing results from ROAD

2nd IMPROVE Conference

Dec. 11- 13, 2023 - Paris

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Hunter Smith
3Q 2023 Financial Results

3Q 2023 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended September 30, 2023	Three months ended September 30, 2022
Product revenue, net	$22.5M	$4.3M
R&D expenses	$33.6M	$21.1M
SG&A expenses	$30.5M	$21.9M
Net Loss	$(44.2)M	$(40.9)M
Shares outstanding (basic and diluted share count)	57,874,960	51,400,922
Net Loss per share - basic and diluted	$(0.76)	$(0.79)

3Q 2023 Financial Highlights

$299.3M
cash equivalents and short-term investments as of September 30, 2023

80%
of 3Q 2023 revenue from U.S. sales of IMCIVREE vs. 86% in 2Q 2023

OpEx includes
$8.5M
in stock-based compensation in 3Q;
$23.9M
in 2023 year to date*

Non-GAAP OpEx Guidance for 2023:
$210M to $220M**

With **$25M investment tranche** from Healthcare Royalty Partners and gross proceeds from **ATM program of $50M** received during 3Q 2023, RYTM expects cash to be sufficient to fund planned operations **into 2026**

* Nine months ending on Sept. 30, 2023; ** Does not include COGS.

David Meeker, MD
Conclusion

Plans for Continued Execution: Anticipated Upcoming Milestones and Data Readouts

Save the date:

Dec. 6, 2023 R&D Event:
Update on RYTM's MC4R Pathway Program

- Update on hypothalamic obesity with KOL
- Detail data on RM-718, new weekly, MC4R agonist
- Announce preliminary data from the open-label part of the Phase 2 DAYBREAK trial
- Announce topline data from Phase 3 pediatrics trial in 2-6 yo patients with MC4R pathway deficiencies

Anticipated clinical milestones

- ✓ Early 2023: Initiate Ph 3 hypothalamic obesity trial
- ✓ 2H2023: Present data analyses from Ph2 and LTE trials in hypothalamic obesity
- 4Q23: Complete enrollment in Phase 3 hypothalamic obesity trial
- 4Q2023: Complete IND submission for RM-718
- 1H2024: Initiate Ph 1 trial of RM-718 in healthy obese volunteers

Ex-US Market Access:

- ✓ 2Q23: Germany launch for BBS
- 2H23: Launch in Spain and Italy for both POMC/LEPR and BBS

Rhythm's Strategic Priorities for 2023

Execute on global commercial strategy with **BBS launches**

Enroll and execute **Phase 3** trial to evaluate setmelanotide in **hypothalamic obesity**

Expand IMCIVREE opportunity and new product with development **assets**

Questions