Rhythm Pharmaceuticals

Second Quarter 2023 Financial Results and Business Update

August 1, 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 and our expectations surrounding potential regulatory submissions, approvals and the timing thereof, 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, the potential financial impact, growth prospects, benefits of and research and development efforts following our acquisition of Xinvento B.V., 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, Expansion of Overall Opportunity through Clinical Development

Strong BBS commercial execution

- Strong growth with $19.2M in global net revenue for 2Q2023
- Robust U.S. demand for IMCIVREE for BBS continues
- IMCIVREE now commercially available in Canada, GCC states; German BBS launch underway

IMCIVREE®
(setmelanotide) injection

Hypothalamic obesity programs progressing

- Based on rapid progress in Ph3 trial, enrollment completion now anticipated by the end of 2023
- Six-month LTE data demonstrating sustained and deepening reductions in BMI
- 12-month data planned for fall conference

Multiple development programs advancing

- RM-718: IND planned by year-end 2023
- Multiple 2H 2023 data readouts with preliminary data from Ph2 DAYBREAK trial and Ph3 pediatrics and Ph3 switch
- Additional detail on development programs at 4Q R&D event

RM-718: More Selective MC4R Agonist Extending Patent Protection

Investigational New Drug (IND) application on track to be filed by end of 2023

MC4R-specific, potentially more potent

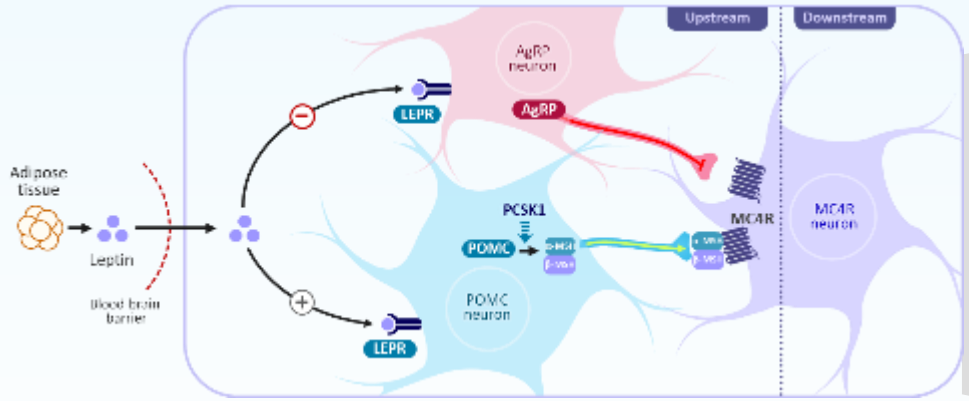
MC1R-sparing, designed to eliminate hyperpigmentation effect

Weekly formulation with composition of matter **patent protection to 2041***

More details at R&D event in Q4

*Includes patent term adjustment and patent term extension.

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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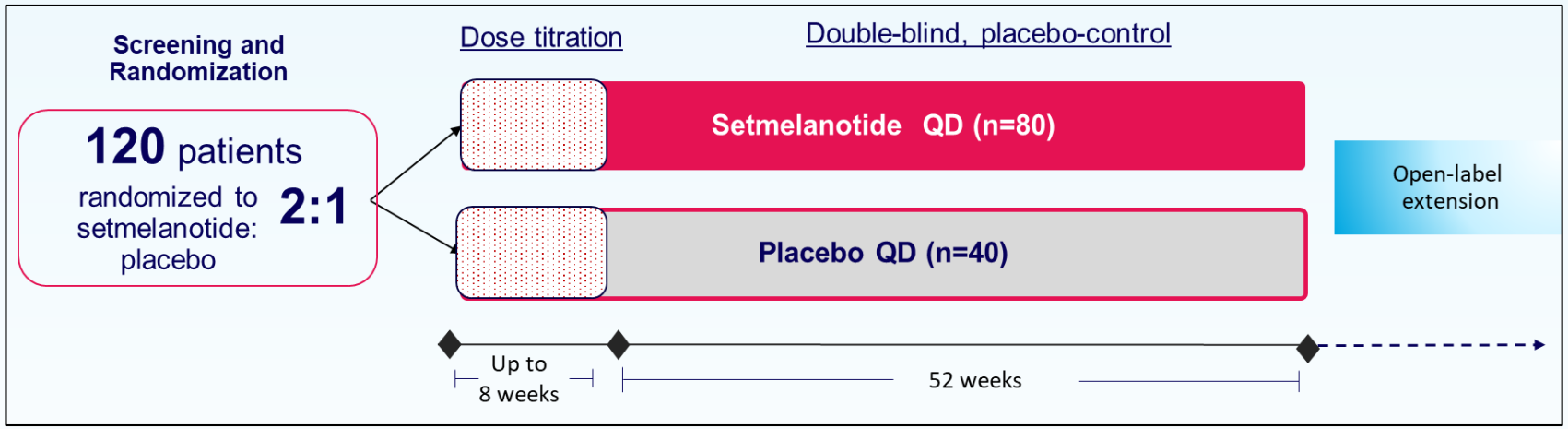
Accelerating Guidance: Now Expect to Complete Enrollment by the end of 2023 in Ph3 Hypothalamic Obesity Trial



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.

25%

patients screened as of June 30

1/3

of planned sites now open

BMI, body mass index; QD, once daily.

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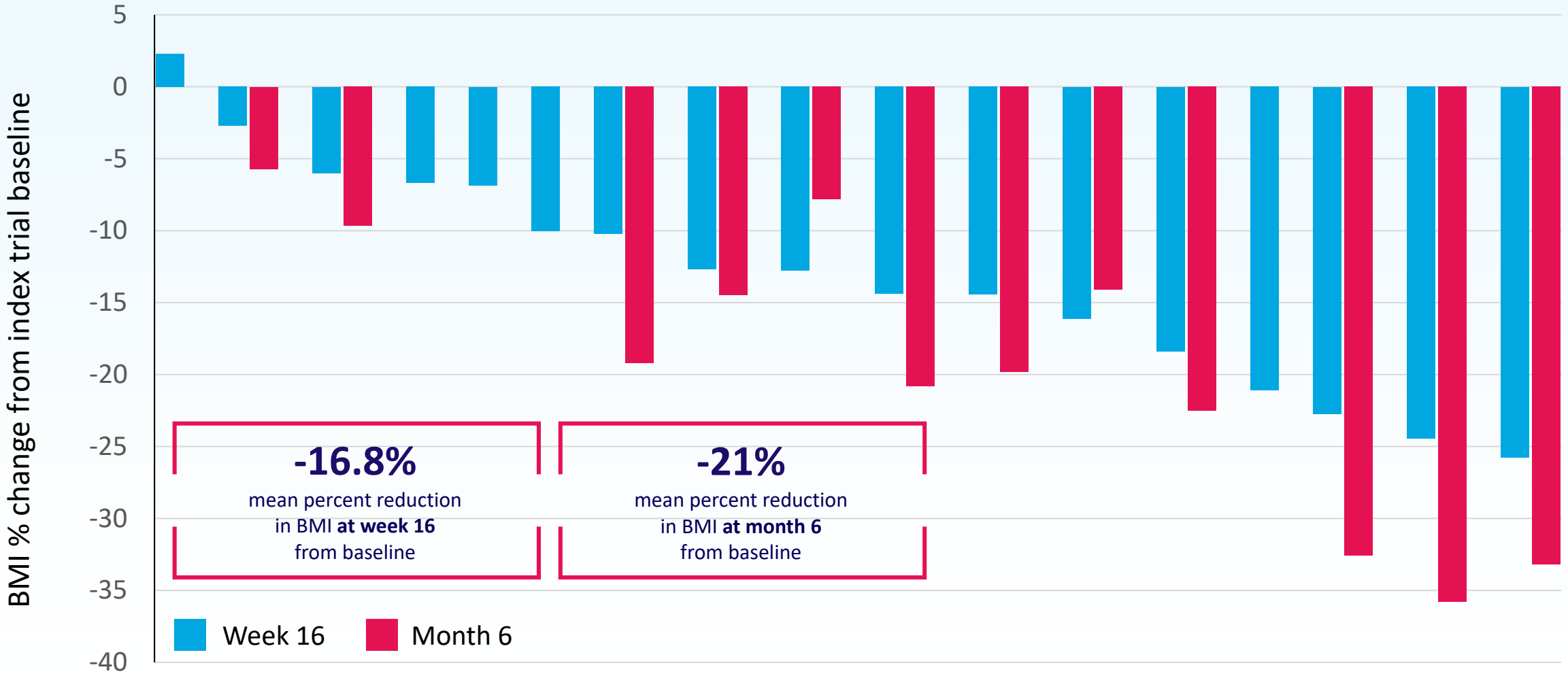
Hypothalamic Obesity: LTE Data Demonstrate Sustained, Deepening BMI Reduction over Six Months*



*Adapted from data presented during The Endocrine Society Annual Meeting & Expo (ENDO 2023) on June 17, 2023, in Chicago.

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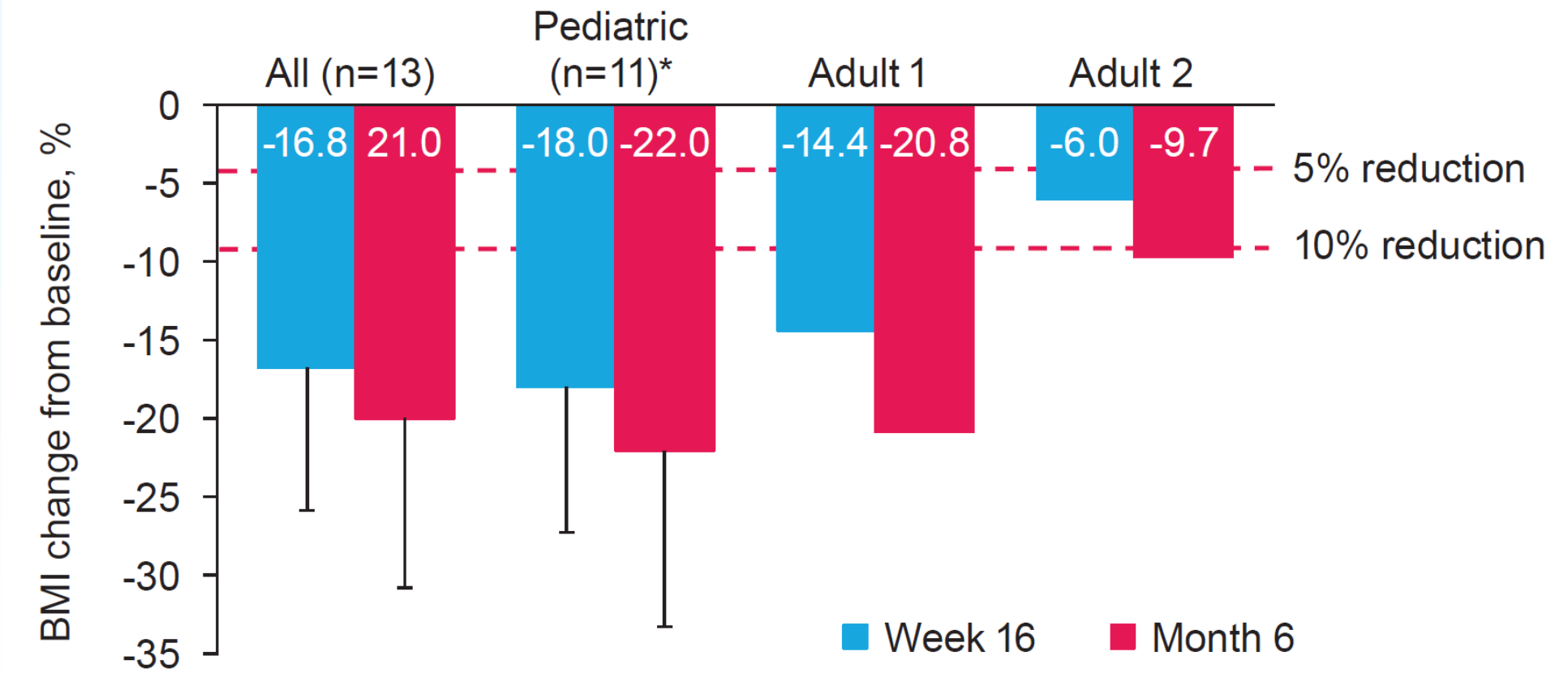
Progression in BMI Reduction Consistent Across All Patients in LTE

Mean BMI reduction of 21.0% from baseline observed in 13 patients at six months, showing progression from 16.8% mean BMI reduction at 16 weeks



Error bars are the standard deviation. *One pediatric patient did not have a Month-6 visit, and Month-9 data were used for this analysis. BMI, body mass index.
As presented at ENDO 2023.

Ongoing Programs Designed to Achieve Label and Pipeline Expansion

	Patient Population	Pre-clinical	Phase 1/2	Phase 3	Commercially Approved
IMCIVREE™ (setmelanotide) injection	POMC, PCSK1 or LEPR (PPL) deficiency				
	Bardet-Biedl syndrome (BBS)				
Setmelanotide *daily formulation*	Hypothalamic Obesity				
	Emanate Obesity and Hunger Clinical Trial				
	Pediatrics (age 2 to <6 years, POMC or LEPR deficiency obesity or BBS)				
	Daybreak Obesity and Hunger Clinical Trial				
Setmelanotide *weekly formulation*	Switch study with patients previously on setmelanotide				
	Patients with BBS naïve to setmelanotide therapy (ex-U.S.)				
RM-718	Rare MC4R pathway diseases		IND planned by year-end 2023		
Pre-clinical	Congenital Hyperinsulinism (CHI)	Lead identification underway; IND anticipated in 2024			

Complete Denotes study underway Denotes planned study

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Jennifer Chien

BBS U.S. Launch

Hyperphagia and Early-onset Obesity Have a Significant Impact on Patients with MC4R Pathway Diseases and their Families

IMCIVREE Patient Ambassador program launched with 8 patient/caregiver speakers

"I was hungry all day long. I even started sneaking food in the middle of the night because my mind was constantly on my hunger."

Kathryn, Diagnosed with BBS at 6 years old

"Prior to IMCIVREE, I didn't realize how much of my mental energy was consumed by my hunger. I'm able to free up my mind and do more enjoyable things with my life."

BORN WITH:

Autosomal recessive polycystic kidney disease (diagnosed in utero), polydactyly

2 YEARS OLD:

Visual impairment and developmental delays emerge

6 YEARS OLD:

Pronounced hyperphagia; clinical presentation prompted BBS diagnosis via genetic testing

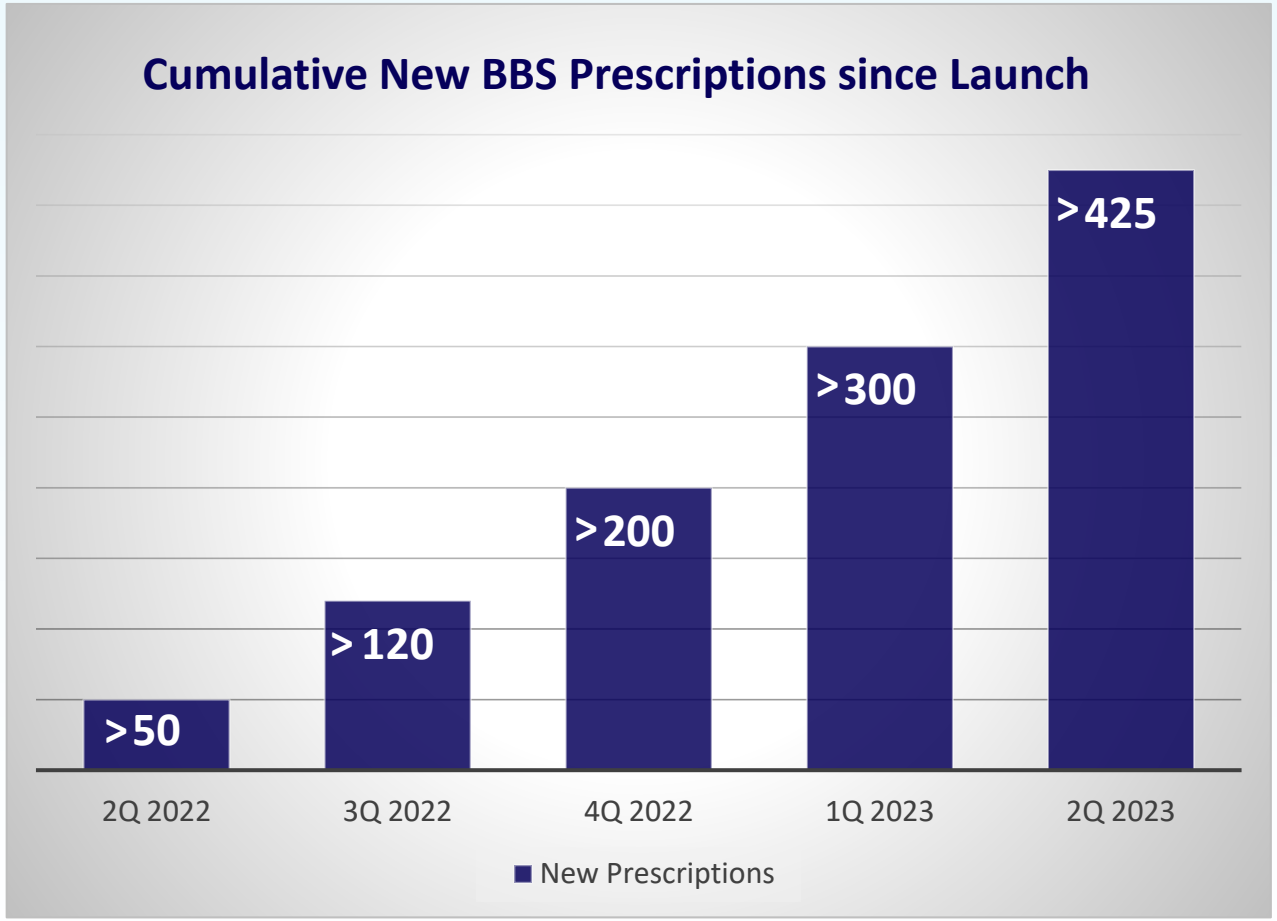
TEEN YEARS:

Hyperphagia, obesity, and visual deficits worsen

28 YEARS OLD:

IMCIVREE prescribed by PCP

Strong U.S. Demand Continues throughout First Full Year of BBS Launch



>425*
New BBS prescriptions launch to date

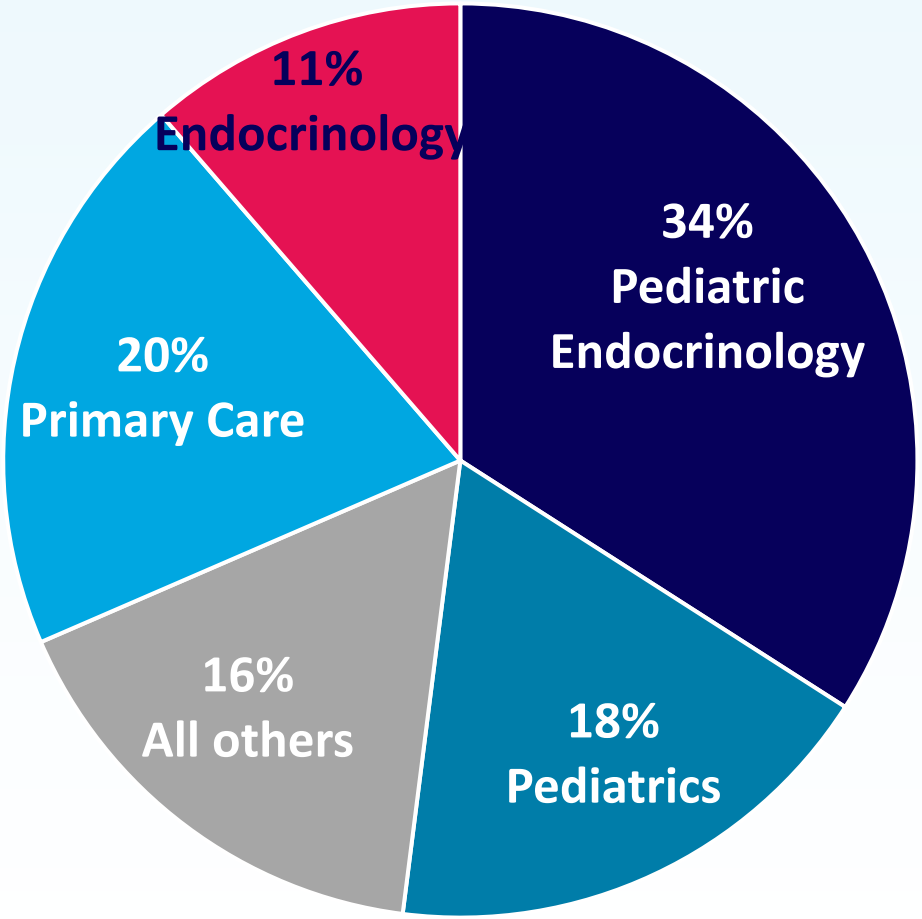
>125* received during 2Q 2023

>250* reimbursement approvals

>250* unique prescribers

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

BBS IMCIVREE Prescribers by Specialty Since Launch



>250*

Prescribers
as of 6/30/2023

26% Of prescribers ‘new to Rhythm’

>25% of prescribers have written more than one prescription

*As of June 30, 2023

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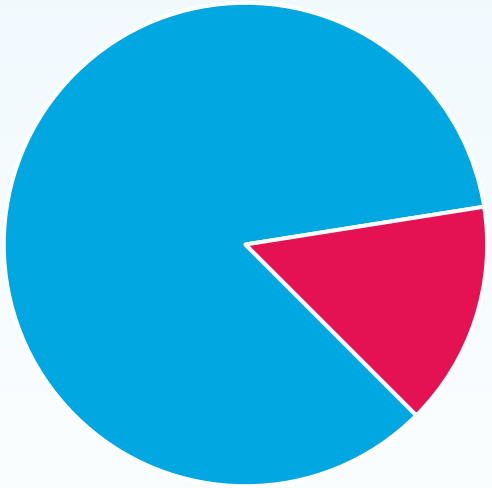
Improved Medicaid Reimbursement now with ~80% of Covered Lives in States with Positive Coverage Policies, Decisions for IMCIVREE

~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 June 30, 2023

Snapshot of BBS Patients with Prescriptions, Duration on Therapy

Age Range	Since Launch
Adult (18+)	~54%
Adolescent (12-17)	~25%
Pediatric (6-11)	~21%

Re-authorizations

50

re-authorization approvals to date (at 3-, 6- or 12-months)

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

*As of June 30, 2023

Patient Identification, Physician Engagement and Community Building

Patient Identification

- Uncovering Rare Obesity genetic testing
- Non-personal promotion
- Ambassador programs and webinars

Physician Engagement

- Increased depth and breadth of prescribers with direct engagement
- Medical conference presentations and events

Community Building

- Rhythm InTune
- Patient advocacy engagement
- Non-personal promotion
- Speaker programs and webinars

Rhythm® PHARMACEUTICALS

Yann Mazabraud

EVP, Head of International

Important Market for IMCIVREE for BBS, POMC and LEPR Deficiencies

POMC, PCSK1 and LEPR Deficiency Obesities

Estimated European prevalence

600 - 2,500

~100

individuals identified in **EU4 + UK**

Bardet-Biedl Syndrome

Estimated European prevalence

4,000 – 5,000

>1,500

individuals identified in **EU4 + UK**
(~20 academic medical centers with >40 BBS patients)

IMCIVREE for Biallelic POMC/LEPR and/or BBS to be Available in More than Ten Countries Outside United States in 2023

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

United Kingdom
NICE BBS discussions encouraging; BBS launch anticipated in 2H2024

Italy
'Innovation' rating from AIFA; ongoing price negotiation; BBS launch end of 2023

Netherlands
BBS pricing negotiations ongoing, with recent administrative changes, BBS launch mid-2024

Spain
Ongoing PPL & BBS pricing negotiations; Launch planned end of 2023

Early access or named patient sales

Austria

Turkey

UAE

Argentina

Initiated the reimbursement process in Belgium and the Nordic Countries

Strong Start for IMCIVREE Launch for BBS in Germany

Leveraging KOL engagement, BBS patient advocacy and patient support programs

~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

Patient support system tailored to each patient, designed to educate patients and caregivers, to set expectations and to maintain adherence

Hunter Smith
2Q 2023 Financial Results

2Q 2023 Financial Snapshot

($ in millions, except per share data and shares outstanding)	Three months ended June 30, 2023	Three months ended June 30, 2022
Product revenue, net	$19.2M	$2.3M
R&D expenses	$33.5M	$31.5M
SG&A expenses	$30.0M	$22.3M
Net Loss	$(46.7)M	$(45.0)M
Shares outstanding (basic and diluted share count)	56,867,662	50,398,003
Net Loss per share - basic and diluted	$(0.82)	$(0.89)
Cash, cash equivalents and short-term investments position (period end)	$253.6M	$235.6M

2Q 2023 Financial Highlights

$278.0M
pro forma cash, cash equivalents and short-term investments as of June 30, 2023, together with anticipated HCR milestone

~86%
of 2Q 2023 revenue from U.S. sales of IMCIVREE vs. 83% in 1Q 2023

2Q 2023
OpEx includes
$8.9M
in stock-based compensation vs. $6.4M in 1Q 2023

Non-GAAP OpEx Guidance for 2023:
$200M to $220M*

In July 2023, achieved sales milestone making Rhythm eligible for **$25M investment tranche** from Healthcare Royalty Partners

Cash expected to be sufficient to fund planned operations **into 2025**

* Does not include COGS.

David Meeker, MD
Conclusion

Plans for Continued Execution: Anticipated Upcoming Milestones and Data Readouts

Anticipated clinical milestones

- ✓ Early 2023: Initiate Ph 3 hypothalamic obesity trial
- ○ 2H2023: Present data analyses from Ph2 and LTE trials in hypothalamic obesity at medical conferences
- ○ 2H23: Announce preliminary data from Phase 2 DAYBREAK trial in 2H2023
- ○ 2H23: Announce topline data Ph3 open-label pediatrics trial in patients between 2 and 6 years old
- ○ 2H23: Announce PK and tolerability data Ph3 weekly switch trial
- ○ 2H23: Provide update on early-stage programs, including RM-718 and CHI program, at R&D event
- ○ 2H23: Complete enrollment in Phase 3 hypothalamic obesity trial
- ○ 1H24: Initiate a Ph 3 weekly “de novo’ study

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