Rhythm Pharmaceuticals

Third Quarter 2022 Financial Results and Business Update

November 8, 2022

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

Forward Looking Statements

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 in various geographic markets, expectations surrounding the potential market opportunity for our product candidates, the potential for coverage and reimbursement of our product candidates by third-party payers, 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.

David Meeker, MD

Executing on our Global Strategy to Deliver a Precision Medicine Addressing Unmet Medical Needs

Strong Start to U.S. BBS Launch

- >120 prescriptions written
- >80 physicians
- >40 patient reimbursement approvals

International Market Access Advancing

- EC* authorization for BBS granted on September 6, 2022
- UK POMC, LEPR launch underway
- Access POMC, LEPR achieved in Germany, France
- Access in Netherlands and Italy expected by end of 2022

Potential for Meaningful Label Expansion

- Received FDA Breakthrough Therapy Designation for hypothalamic obesity
- Ph 3 trial initiation planned for early 2023
- Full Ph 2 data presented at ObesityWeek®
- EMANATE, DAYBREAK, pediatrics trial and weekly formulation trials ongoing

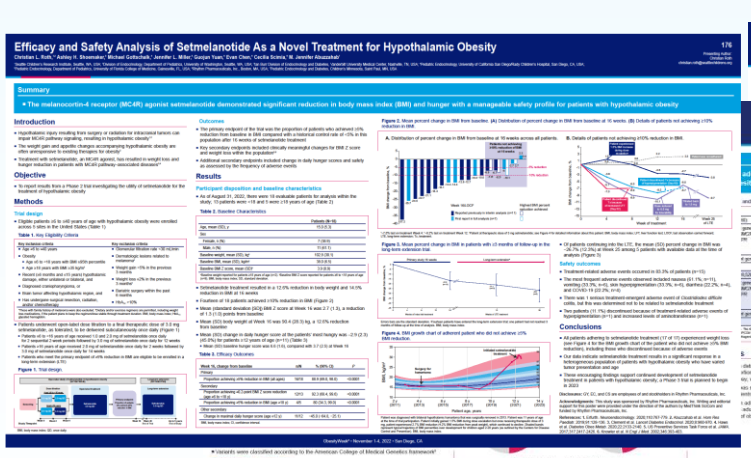
Well-capitalized, with cash to fund operations into 2025

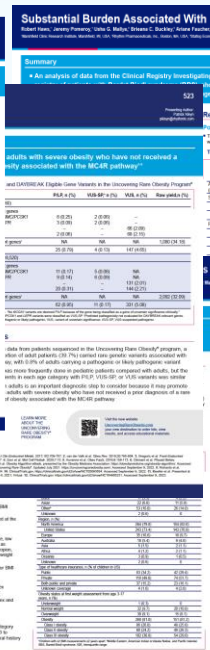
*EC is European Commission

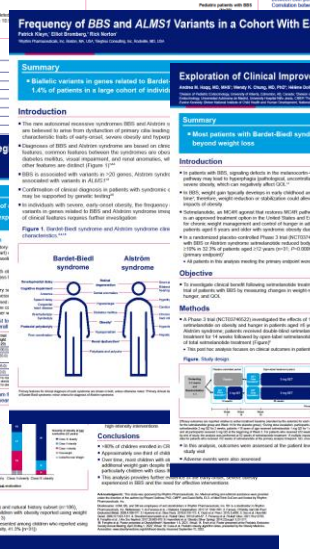
11 Presentations Delivered at ObesityWeek® 2022

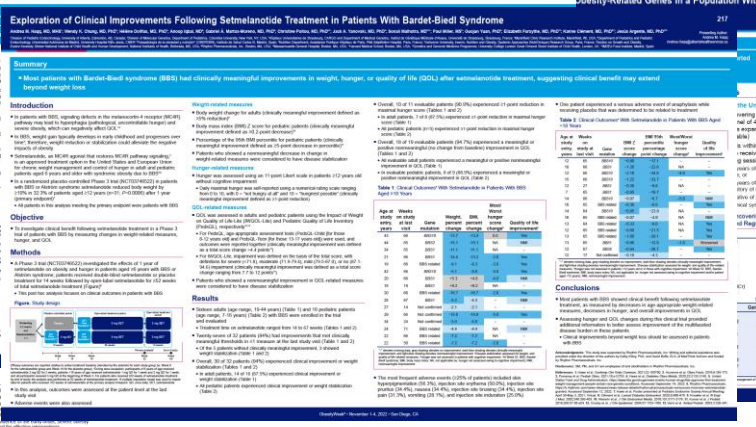
obesityweek® | THE OBESITY SOCIETY

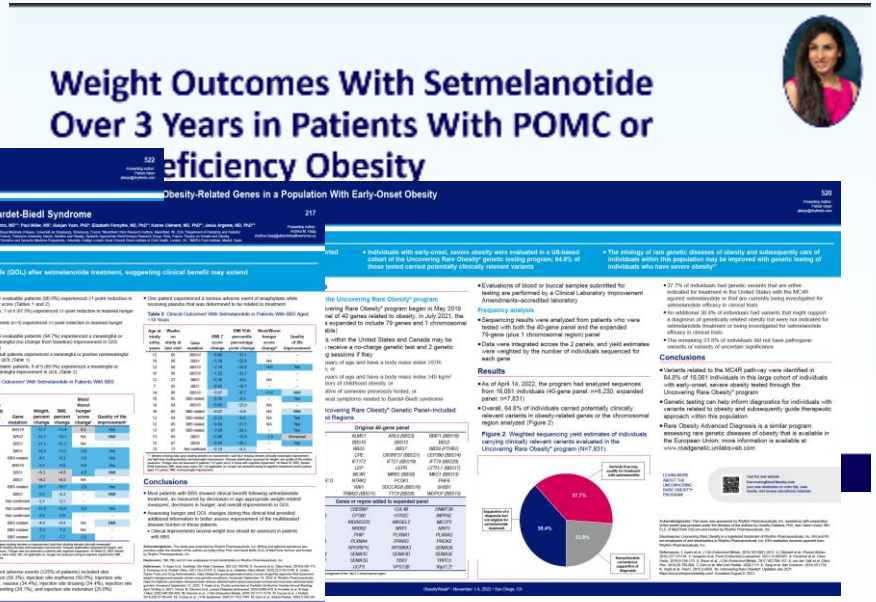
November 1-4, 2022 • San Diego











Rhythm® PHARMACEUTICALS

Setmelanotide and Hypothalamic Obesity: A Transformative Opportunity for Rhythm

5,000 – 10,000*

patients

Estimated U.S. prevalence

~500* additional cases diagnosed in U.S. each year

- ✓ Unmet medical need is high; no approved therapies
- ✓ MC4R pathway deficiency following injury to hypothalamic region
- ✓ Patients are identified; no genetic testing required
- ✓ Patients are engaged with the system receiving specialist care for pituitary complications

*To estimate the number of patients with incident and prevalent craniopharyngioma and astrocytoma with obesity, Rhythm analyzed the literature and used the number of new cases of each per year in the United States, overall survival rates after a diagnosis of each brain tumor type and obesity rates among those patients at diagnosis or post-diagnosis. See appendix for details.

Setmelanotide Achieved Significant BMI Reduction at 16 Weeks in Patients with Hypothalamic Obesity in Phase 2 Trial

Full analysis set population (N=18)

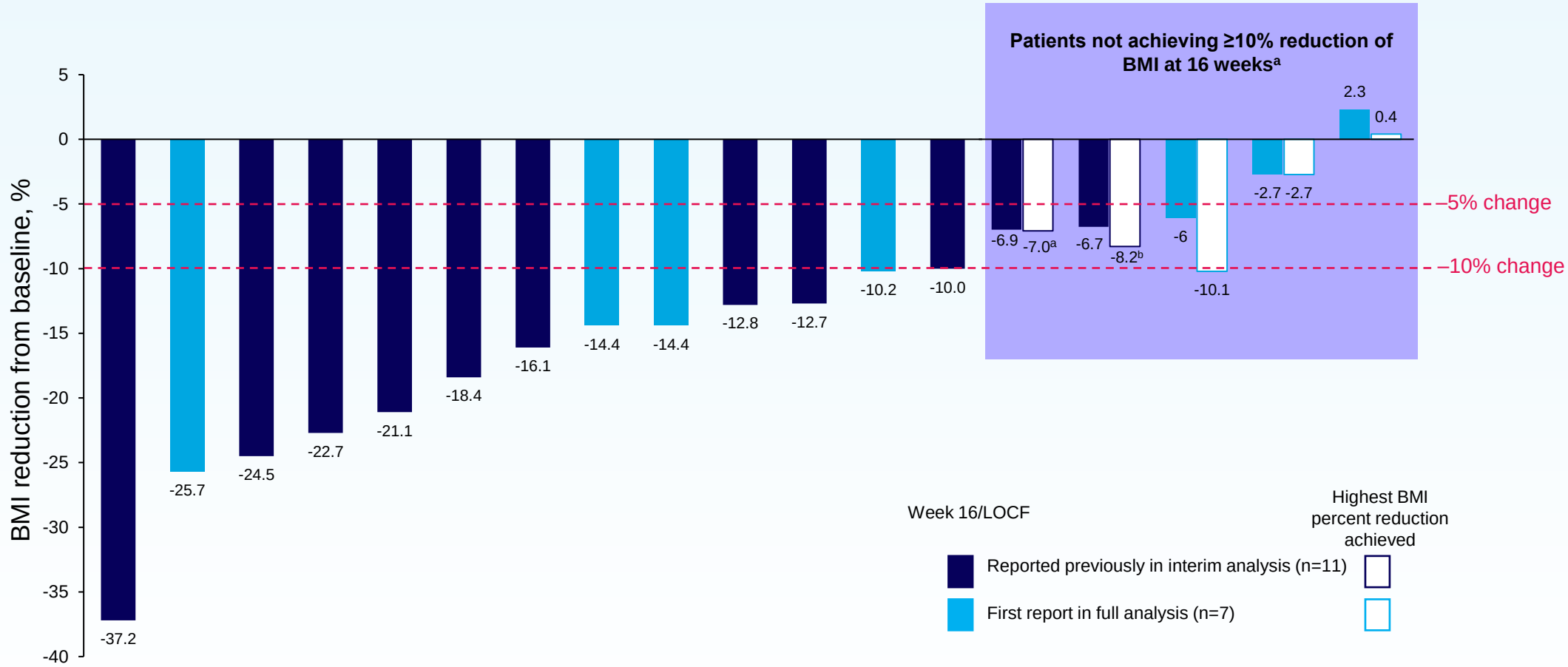
16 of 18
patients achieved
primary endpoint
of ≥5% reduction in BMI
(P<0.0001)

14 of 18
patients achieved
≥10% reduction
in BMI

–14.5%
mean change
in **BMI** at 16 weeks

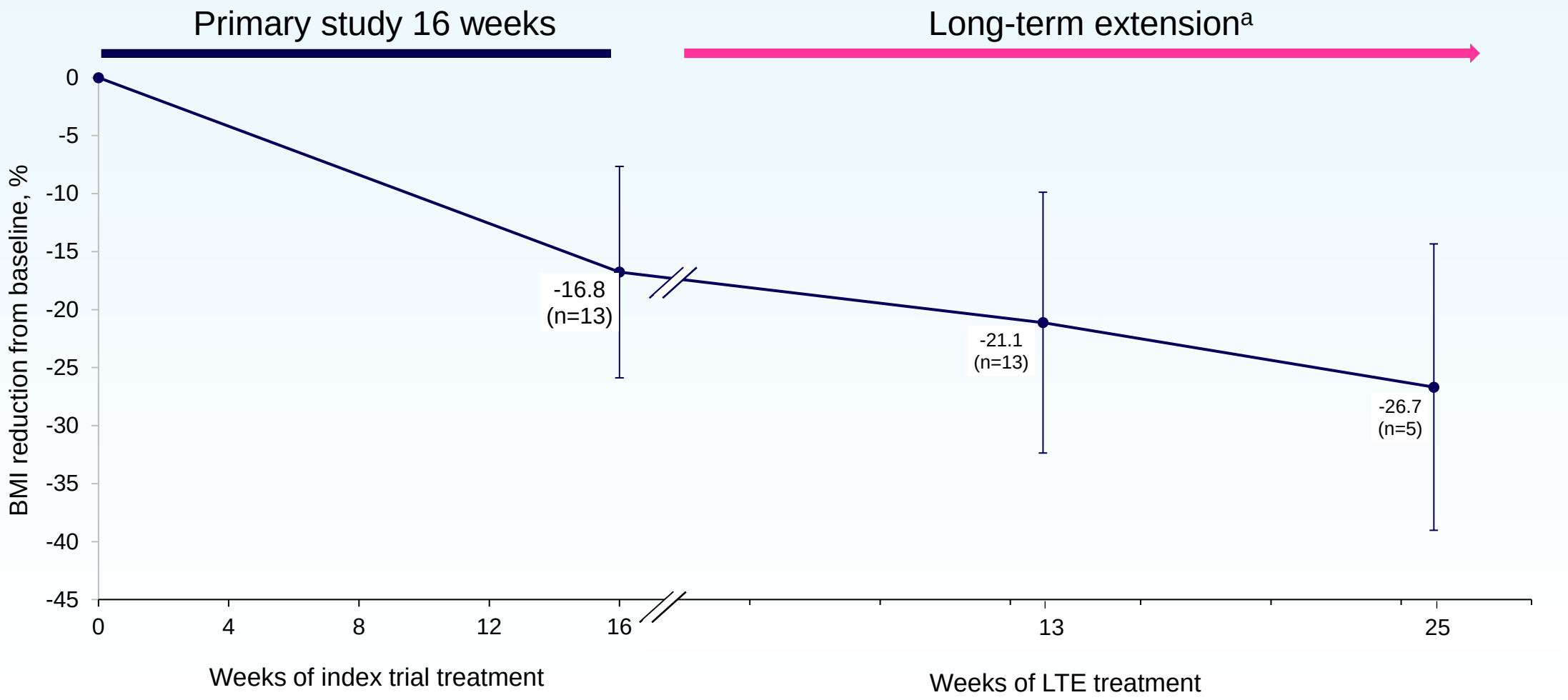
As presented during The Obesity Society's ObesityWeek® 2022, November 1-4, 2022 in San Diego, CA

Setmelanotide Achieved Consistent BMI Reduction at 16 Weeks



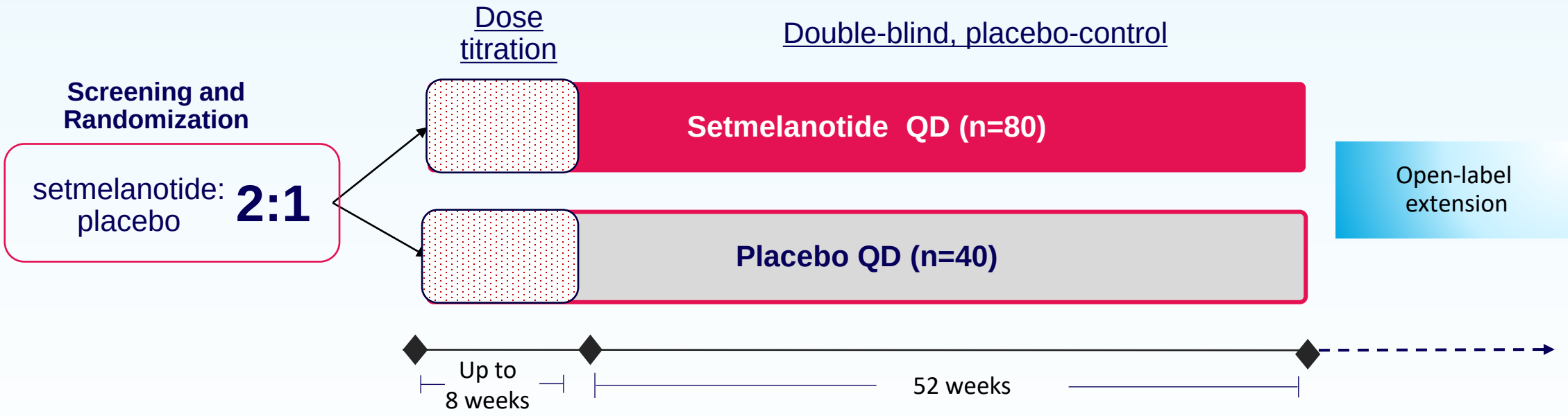
[a]–7.0% last on treatment Week 4. [b]–8.2% last on treatment Week 12. BMI, body mass index; LOCF, last observation carried forward.

Mean Percent Change in BMI in Patients With ≥3 Months of Follow-up in the Long-term Extension Trial



Errors bars are the standard deviation. [a]Fourteen patients have entered the long-term extension trial; one patient had not reached 3 months as of a cut-off date of September 23, 2022. BMI, body mass index.

Phase 3 Double-blind, Randomized Controlled Trial with 120 Patients Expected to Begin in Early 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.

BMI, body mass index; QD, once daily.

Multiple Clinical Trials Ongoing to Expand IMCIVREE Label and Overall Opportunity

Pediatrics Trial
Phase 3
Patients aged 2 to <6 years

Weekly Formulation
Phase 3
Switch Trial

Emanate
Phase 3 Trial

Daybreak
Phase 2 Trial

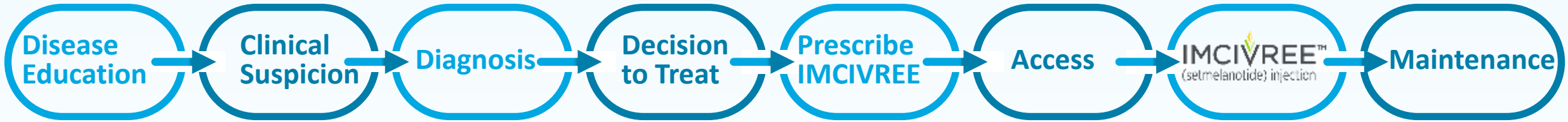
Hypothalamic obesity
Phase 3 Trial planned for early 2023

Jennifer Chien

BBS U.S. Launch

The Journey To Treatment with IMCIVREE and Beyond

PATIENTS & CAREGIVERS



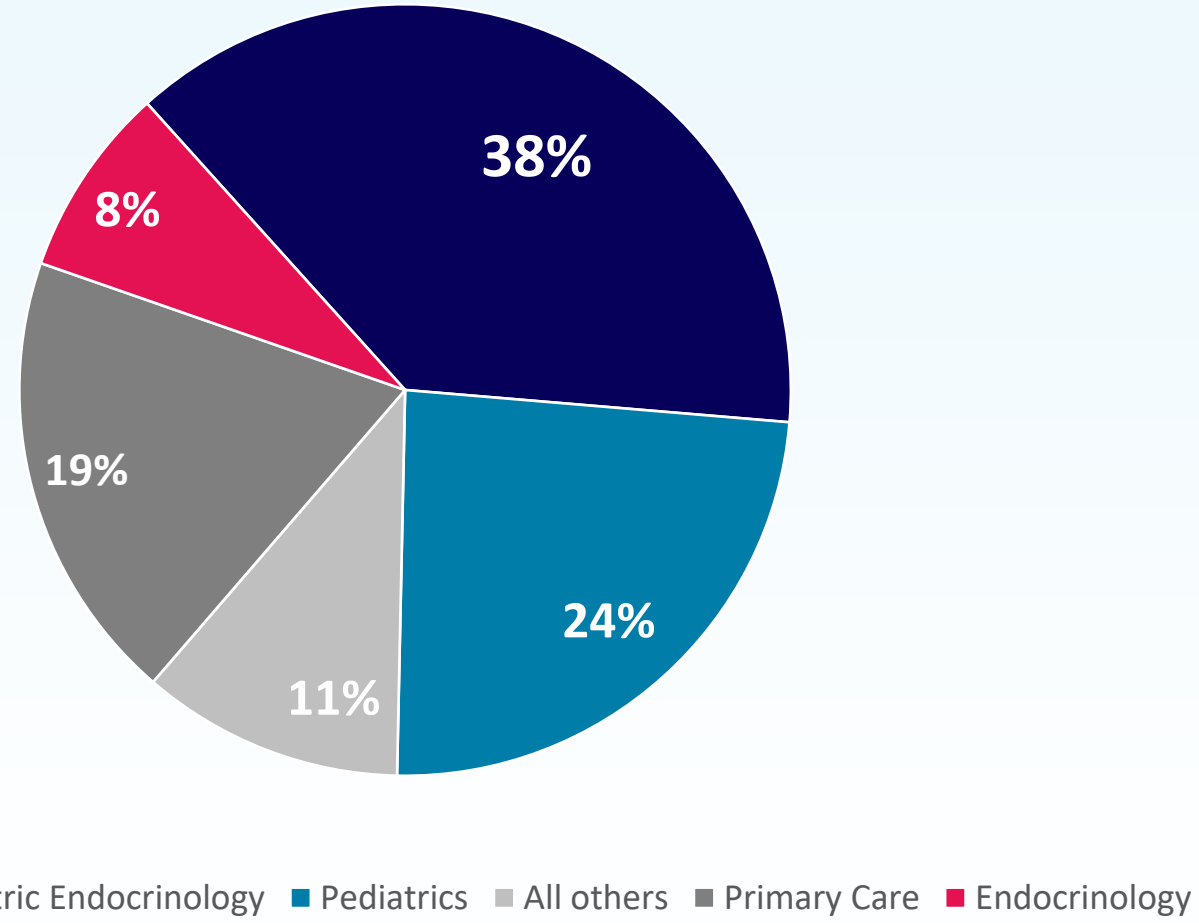
PHYSICIANS

Rhythm® PHARMACEUTICALS

Continued Momentum Across First Full Quarter of Launch

*Cumulative as of September 30, 2022

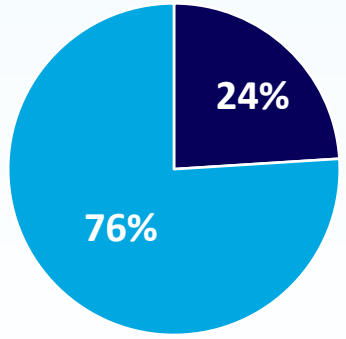
BBS IMCIVREE Prescribers by Specialty



>80*

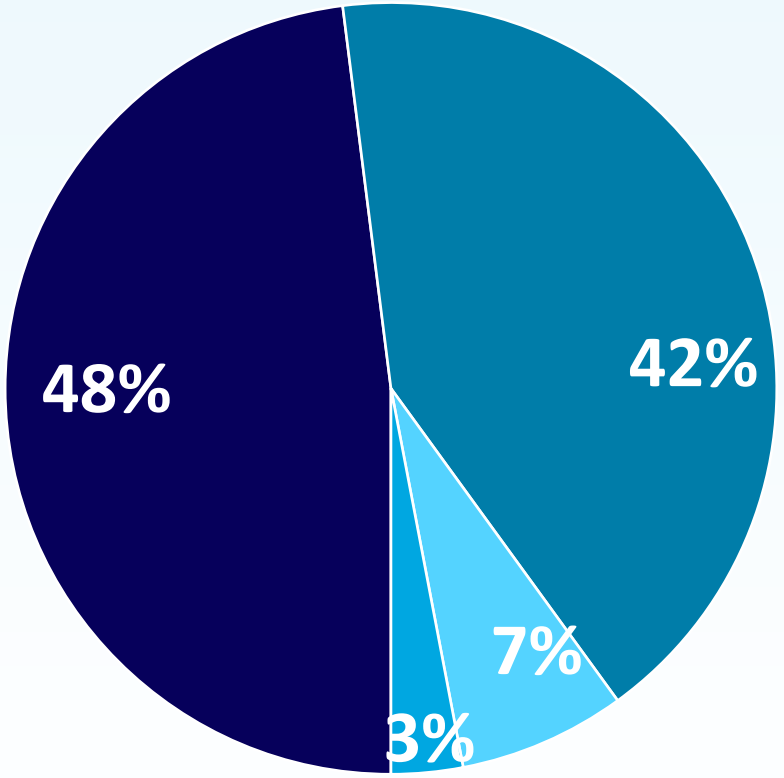
unique prescribers

Source of prescriptions



*As of September 30, 2022

Approximately 90% of Initial BBS Prescriptions Fall Under Commercial and Medicaid Plans



*As of September 30, 2022

>40 approvals for reimbursement

- Reimbursement process takes between **one to three months**
- Following initial approvals, subsequent approvals are faster

Rhythm® PHARMACEUTICALS

Snapshot of Patient Prescriptions Received in First Full Quarter

Age Range	%
Adult (18+)	~43
Adolescent (12-17)	~27
Pediatric (6-11)	~30

Rhythm InTune
Support made personal

>90%

of BBS prescriptions are written for patients who have consented to **InTune**

*As of September 30, 2022

Patients Benefiting from IMCIVREE Therapy

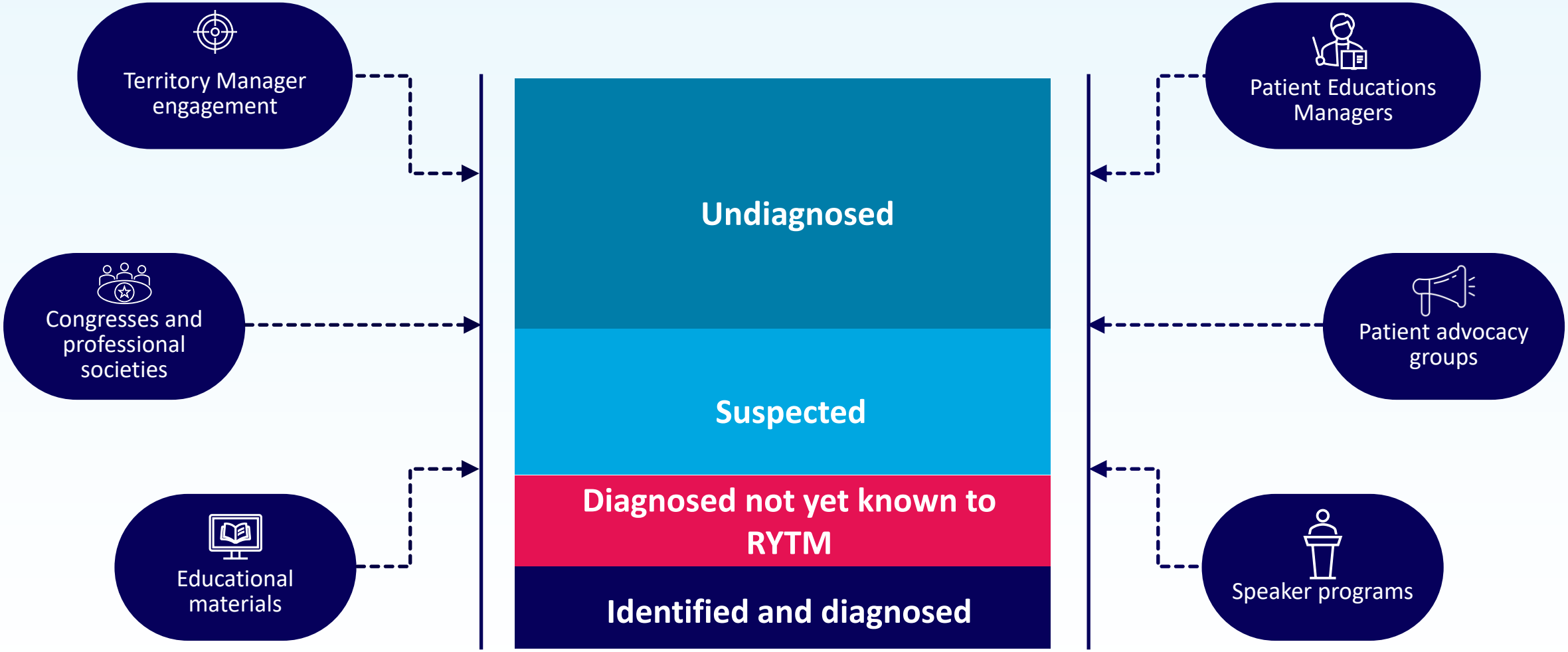
*My daughter has reached her maintenance dose and is feeling good, has **more energy, is less hungry and has already lost 10 pounds.”***

*My son used to sleep all day and stay up all night, since he has been on IMCIVREE he is wide awake during the day and sleeps through the night. **My son rarely smiled before; He now smiles all day long.***

*My **son is more confident**, his clothes are too big, and he doesn’t ask for snacks between meals anymore. What a wonderful change.*

*We **almost stopped treatment** due to side effects early on but understanding what to expect and titrating more slowly, **we were able to continue**. We have seen a great decrease in hunger and food stealing behaviors and noticeable changes at school. The **support and education from my PEM (patient education manager) is truly a gift to our family.***

Multi-channel Engagement to Continue Identifying Patients with BBS



Yann Mazabraud

EVP, Head of International

Significant Market Opportunity for BBS and POMC, PCSK1 and LEPR Deficiencies in Europe

POMC, PCSK1 and LEPR Deficiency Obesities

~100

individuals identified in **EU4 + UK**

Estimated European prevalence

600 - 2,500

Bardet-Biedl Syndrome

>1,500

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

Estimated European prevalence

~2,500

European Launch Update for POMC, PCSK1 and LEPR Deficiency

✓ **United Kingdom**
Commercial launch in October 2022 following UK NICE recommendation

✓ **Germany**
Launched, first sales in 2Q22 following exemption from G-BA lifestyle drug exclusion list

✓ **France**
Reimbursed since March 2022 via early access program

- **Italy**
  On track for launch by year end 2022
- **Netherlands**
  On track for launch by year end 2022
- **Israel**
  On track for launch by year end 2022
- **Launch anticipated in 2023**
  Spain, Sweden and Argentina

IMCIVREE for Treatment of Obesity and Control of Hunger in Patients with Bardet-Biedl Syndrome

EC Marketing Authorization Received Sept. 6, 2022

France
Reimbursed early-access program achieved in July 2022

Germany
G-BA exemption procedure ongoing
Launch expected 1H2023

United Kingdom
Submission through Reliance Procedure completed
NICE HST evaluation initiated

Italy
On track for dossier submission by year end

Spain
On track for dossier submission by year end

Netherlands
On track for dossier submission by year end

1st International Meeting on Pathway-Related Obesity (IMPROVE 2022) Welcomes ~100 Physicians and Scientists in October 2022 in Berlin

Hunter Smith
3Q 2022 Financial Results

3Q22 Financial Highlights: Strong Cash Position

$347.8 million[a]

Cash, cash equivalents and short-term investments

$140 million[b]

Successfully completed public offering with exercise of underwriters' option

$37.5 million[c]

Secured second of two tranches from HealthCare Royalty Partners following EC marketing authorization for IMCIVREE in BBS

[a] Partial exercise of the underwriters' option to purchase additional shares as part of public offering, which resulted in additional net proceeds of $14.2, not included in cash on-hand as of Sept. 30, 2022; [b] Gross proceeds including shoe; [c] Remain eligible for additional $25M upon achievement of certain sales milestones

3Q 2022 Financial Snapshot

($ in millions except as noted, per share data and shares outstanding)	Three months ended September 30, 2022	Three months ended September 30, 2021
Product revenue, net	$4.3M	$1.0M
License revenue	--	_
R&D expenses	$21.1M	$27.5M
SG & A expenses	$21.9	$17.5M
Net (loss)	$(40.9)	$(35.1)M
Shares outstanding (basic and diluted share count)	55,756,256	50,268,312
Net (loss) per share basic and diluted	$(0.79)	($0.70)
Cash, cash equivalents and short-term investments position (period end)	$347.8M	$328.4M

Cash on hand expected to be sufficient to fund operations into 2025

David Meeker, MD
Conclusion

Rhythm's Strategic Priorities for 2022 and 2023

Execute on U.S. commercial strategy with **BBS launch**

Achieve access and launch IMCIVREE **for both BBS and POMC, PCSK1 and LEPR** in select international markets

Initiate **Phase 3** trial to evaluate setmelanotide in **hypothalamic obesity** in early 2023

Expand IMCIVREE opportunity through additional studies**:**

- EMANATE Ph 3
- Pediatrics Ph 3
- Weekly Ph 3
- DAYBREAK Ph 2

Questions