# Rhythm Pharmaceuticals

## Second Quarter 2022 Financial Results and Business Update

**August 2, 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, the application of genetic testing and related growth potential, expectations surrounding the potential market opportunity for our product candidates, 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: A Precision Medicine Addressing Unmet Medical Needs

## Strong Start to U.S. BBS Launch

- IMCIVREE approved for BBS on June 16, 2022
- >50 prescriptions written
- >35 physicians
- Initial payer mix receptive to IMCIVREE for BBS

## International Market Access Advancing

- CHMP* positive opinion on BBS; EC authorization expected in 4Q22
- Early access in France for BBS
- UK launch for IMCIVREE for POMC, LEPR deficiencies anticipated in September
- Access for IMCIVREE for POMC, LEPR achieved in Germany and France

## Potential for Meaningful Label Expansion

- Proof of concept achieved in hypothalamic obesity with full data in fall 2022
- End of Ph 2 meeting requested; Ph 3 trial initiation planned for 1H2023
- Completed enrollment in Ph 3 pediatrics (2yo-<6yo) trial in POMC, PCSK1 and LEPR and BBS
- EMANATE, DAYBREAK and weekly formulation trials ongoing

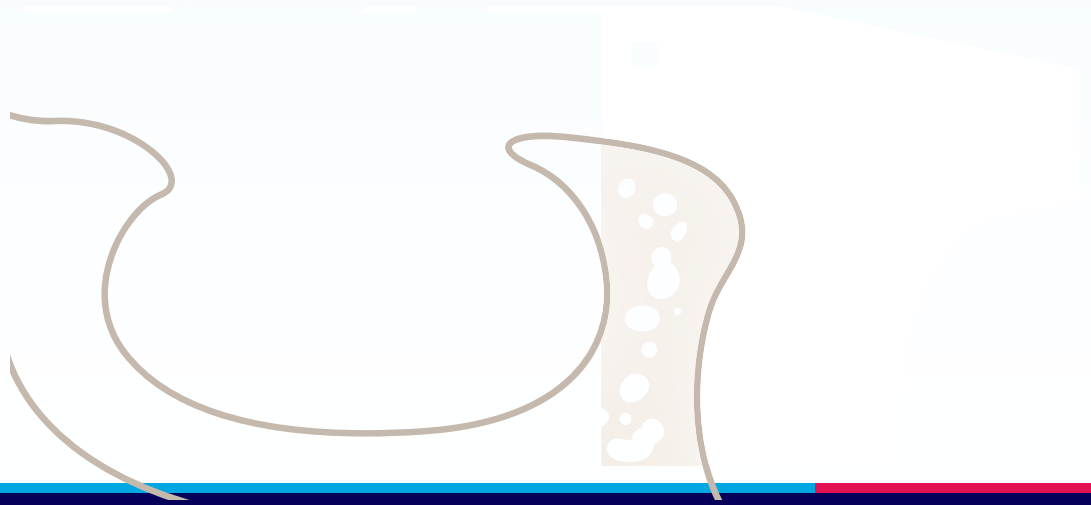
*CHMP is the European Medicines Agency's Committee for Medicinal Products for Human Use (**CHMP**); EC is European Commission.

# Hypothalamic Obesity: A Rare, Acquired Form of Obesity Following Injury to the Hypothalamic Region

**Craniopharyngioma** and **other suprasellar brain tumors** and treatment
– tumor resection surgery and radiation
– is most common cause

**MC4R pathway** deficiency following injury to hypothalamic region causes reduced energy, hyperphagia and rapid-onset, severe obesity

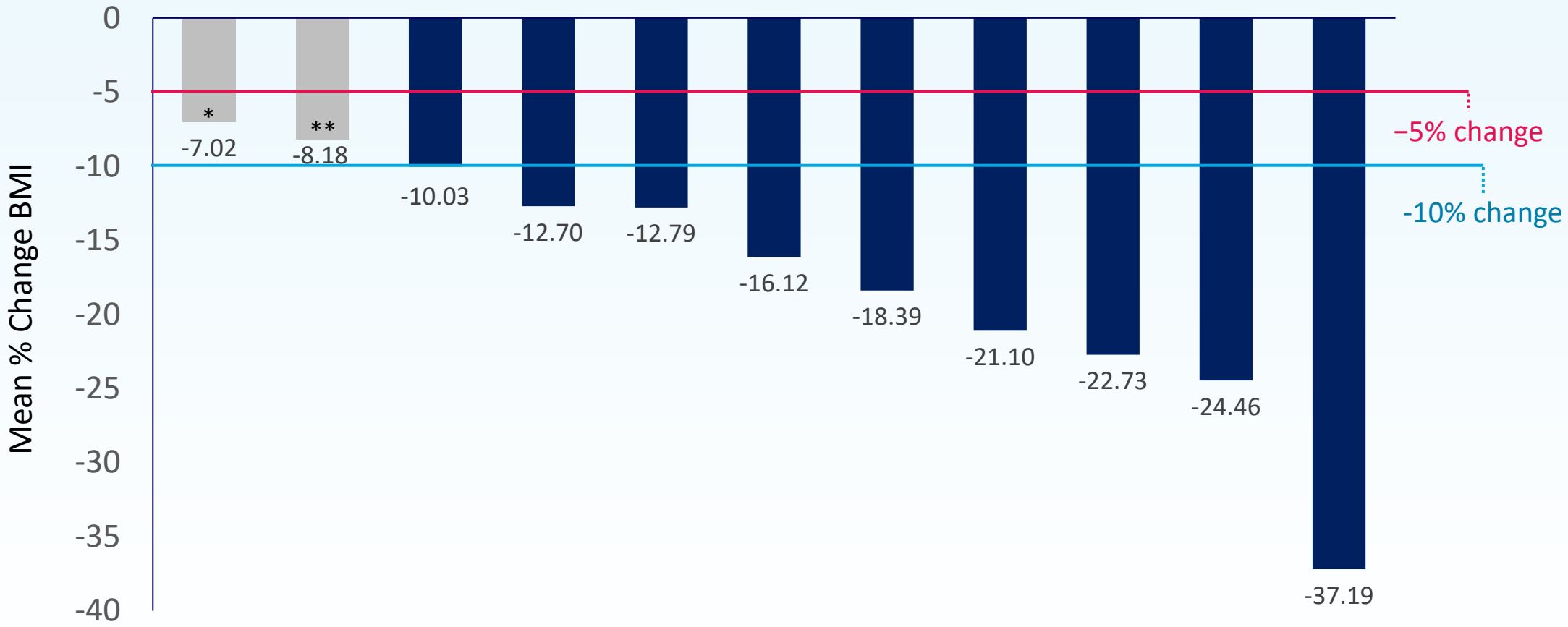
**No approved treatments available**





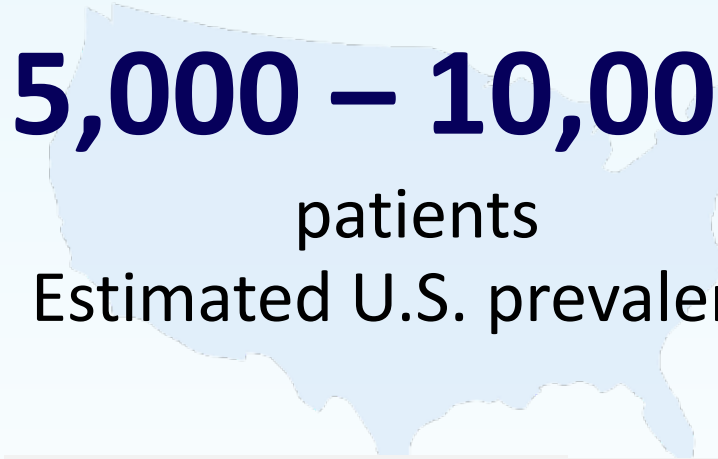
van Iersel et al. *Endo Rev.* 2020 (PMID: 30247642)

# Clinically Meaningful Reductions Observed in All Patients by 16 Weeks




Interim analysis as of the data cutoff date of May 6, 2022, as disclosed on July 12, 2022; BMI, body mass index. Two patients discontinued drug early (grey bars): * last on-treatment visit at Week 4 (-7.02%) and last visit (off-treatment) at Week 8 (-6.85%); ** last on-treatment visit at Week 13 (-8.18%) and last visit (off-treatment) at Week 16 (-6.67%). Grey bars show the BMI % reduction at last on-treatment visit.

# Setmelanotide and Hypothalamic Obesity



**5,000 – 10,000*** patients
Estimated U.S. prevalence

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

## What's Next?

- Planning to present **full data** from 18 patients in Phase 2 trial in fall of 2022
- Request submitted for **End of Phase 2 meeting with FDA,** anticipated in 2H2022
- Initiate **Phase 3 trial in 1H2023** to support potential registration

*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 and Hypothalamic Obesity: Potentially a Transformative Impact

## Hypothalamic Obesity as an MC4R Pathway Disease

- Phase 2 data reinforces the importance of the MC4 pathway as a key driver in some forms of obesity
- Setmelanotide - targeted to the MC4R - provides key insights into the underlying pathophysiology of hypothalamic obesity
- Potential evidence supporting the importance of the energy expenditure in hypothalamic obesity

## Meaningful Opportunity for Rhythm

- Patients are identified; no genetic testing required
- Patients are engaged with the system requiring specialist care (endocrinologists) to manage the other complications of pituitary and hypothalamic injury
- Unmet medical need is high; no approved therapies although many have been tried

# Multiple Ongoing Clinical Trials Evaluating Setmelanotide

***Enrollment complete***

**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 1H2023

# Jennifer Chien

## BBS U.S. Launch

# IMCIVREE Approved in BBS on June 16, 2022; Commercial Launch Efforts Well Underway

**Now approved**

IMCIVREE® (setmelanotide) injection

First and only **FDA-approved** therapy that targets a root cause of **hyperphagia** and early-onset, **severe obesity** in patients with **Bardet-Biedl syndrome**

Physicians are writing IMCIVREE **prescriptions** for BBS

Initial **payer mix** receptive to IMCIVREE for BBS

Patients with BBS are **initiating therapy** with IMCIVREE

# Foundation Set and Momentum Building at BBS Launch

## Foundation laid 2021 to 2022

- Commercial availability for POMC, PCSK1 and LEPR deficiency
- Territory Managers engaging with physicians since Sept. 2021
- Rhythm InTune established

## Momentum building at approval for BBS

- U.S. commercial launch meeting
- ENDO 2022
- Continued physician engagement
- Series of BBS Foundation meetings in summer 2022

# Initial Six Weeks of Launch off to a Strong Start

- Territory manager engagement with physicians
- Clinical trial conversions
- Patient advocacy groups and associations
- CRIBBS registry at Marshfield Clinic
- Non-personal promotional efforts to reach physicians and patients

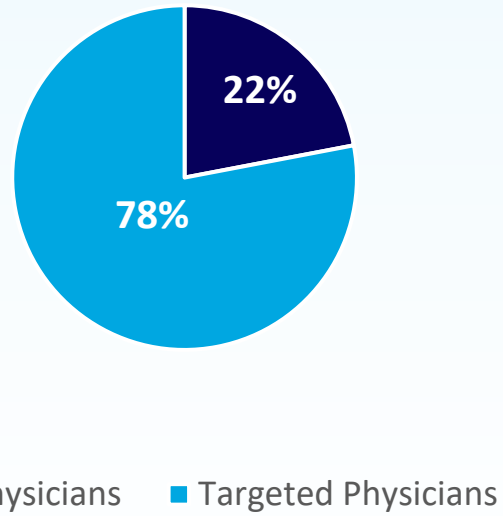


*As of July 28, 2022

# Snapshot of Patient Prescriptions Received in First Six Weeks


| Age Range | % |
|---|---|
| Adult 18+ | 29% |
| Adolescent 12-17 | 34% |
| Pediatric 6-11 | 37% |

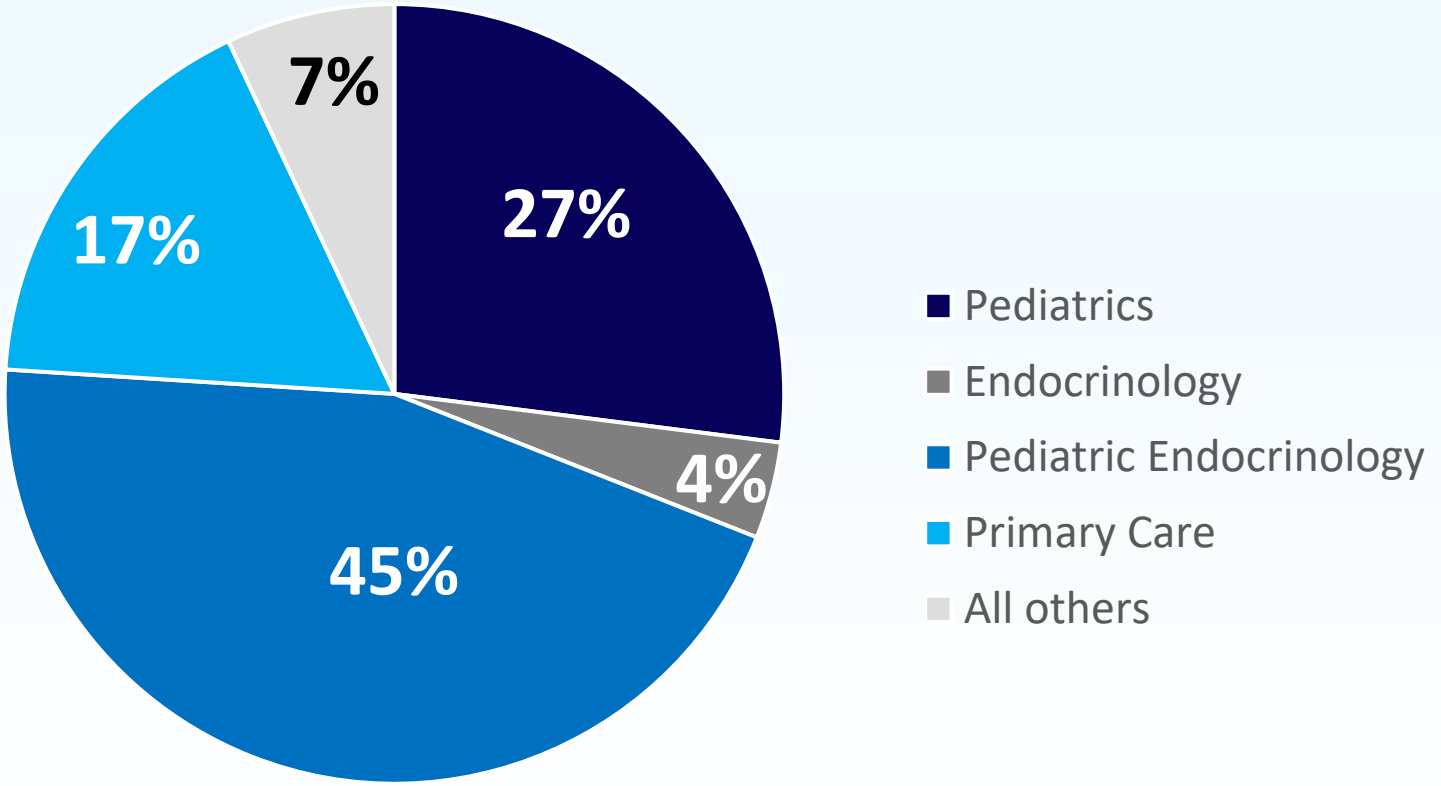
## Source of prescriptions




*As of July 28, 2022

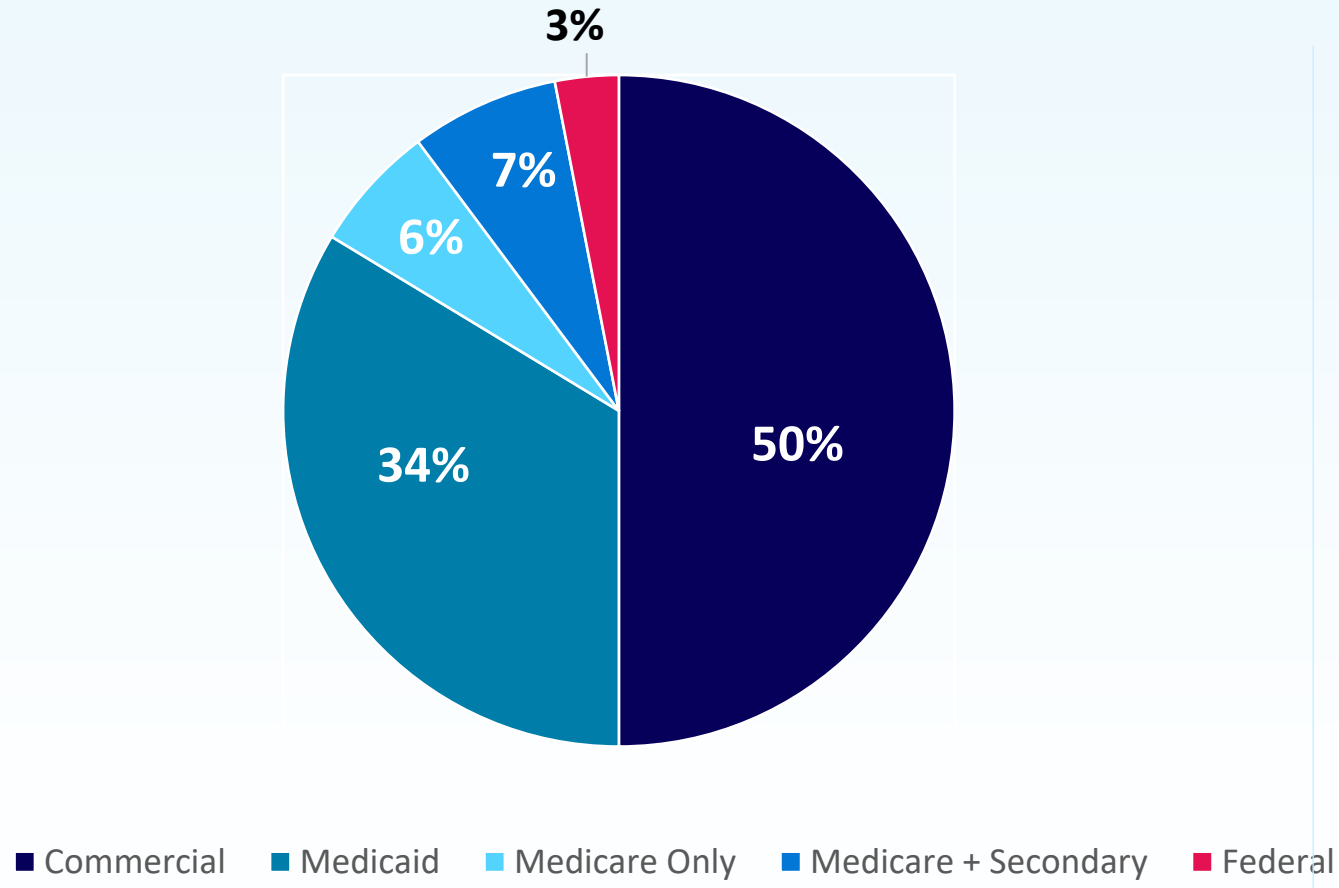
# BBS IMCIVREE Prescribers by Specialty

**>35*** unique prescribers




*As of July 28, 2022

# More than 80% of Initial BBS Prescriptions Fall Under Commercial and Medicaid Plans




- Pull-through of prescriptions in line with expectations
- Many Medicare patients have secondary insurance

*As of July 28, 2022



***Data through** Panther:7/19/2022*

Rhythm® PHARMACEUTICALS

# Rhythm InTune Support Services

Personalized program to achieve access, set treatment expectations and support patient adherence and continuity of therapy

Rhythm InTune
Support made personal

**Introduce IMCIVREE**

**Set expectations**

**Injection tips**

**Goal setting**

**Treatment support**

**Adherence**

**Discuss therapy with physician**



Rhythm® PHARMACEUTICALS

# Positive Early Signals in Launch

# 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**

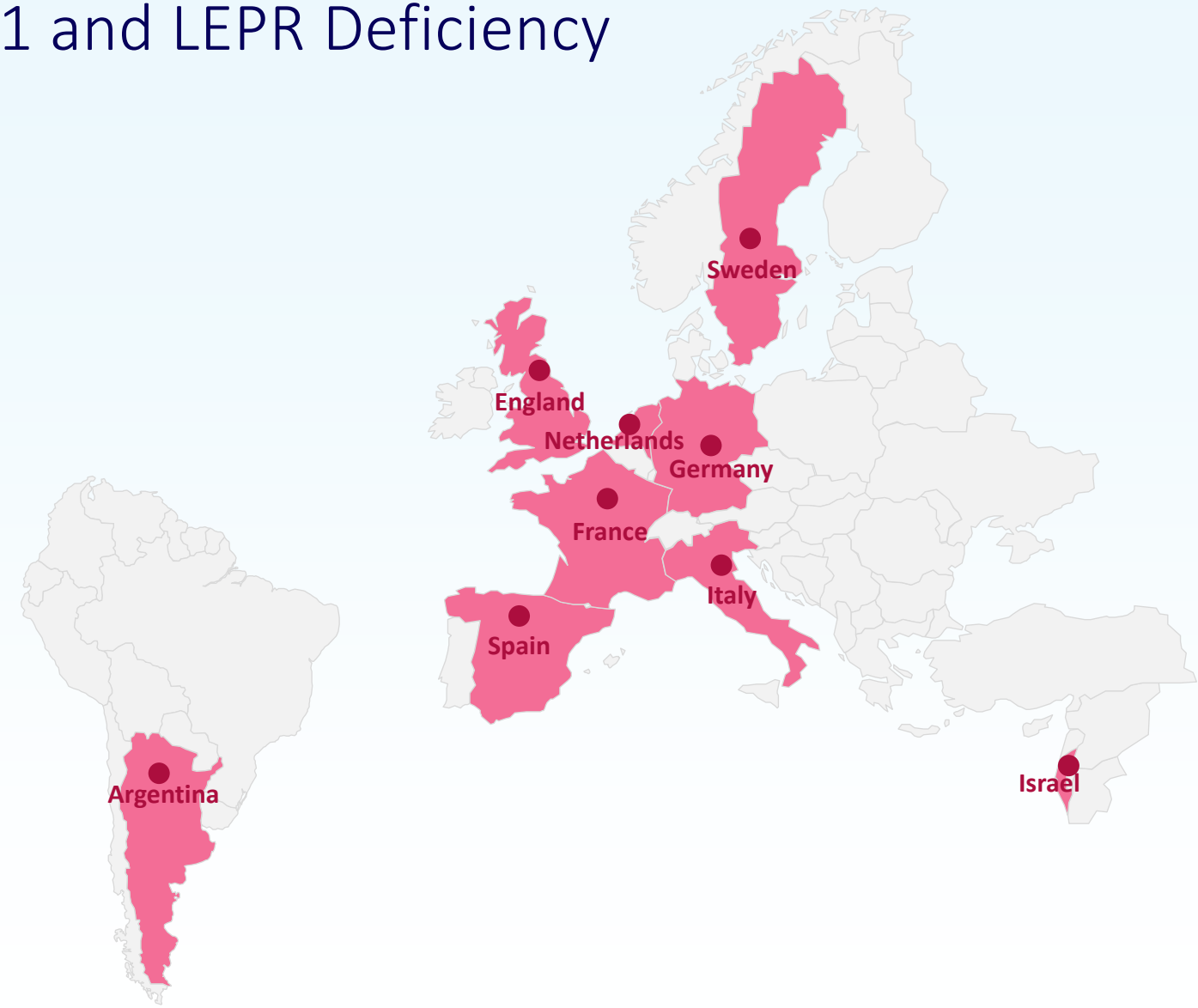
individuals identified in **EU4 + UK**
(~20 academic medical centers with >40 BBS patients)

Estimated European prevalence

**~2,500**

# Market Access for POMC, PCSK1 and LEPR Deficiency

- **Germany**
  Launched, first sales in 2Q22 with exemption from GBA lifestyle drug exclusion list
- **France**
  Reimbursed since March 2022 via early access program
- **United Kingdom**
  Commercial launch set for October 2022 following UK NICE recommendation
- **Italy**
  On track for launch by year end 2022
- **Netherlands**
  On track for launch by year end 2022
- **Launch anticipated in 2023**
  Spain, Sweden, Israel and Argentina



# EMA's CHMP Recommends IMCIVREE for Treatment of Obesity and Control of Hunger in Patients with BBS

## EC decision on Marketing Authorization Anticipated in 4Q2022

**France**
Reimbursed early access program achieved in July 2022

**United Kingdom**
Submission through Reliance Procedure completed

**Germany**
Seek GB-A exemption and launch in 1H2023

**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

### Strong Support for IMCIVREE among Leading European BBS Experts

"**Patients living with BBS** are looking for a transformational treatment that can significantly reduce hunger and body weight. If approved, setmelanotide could change the treatment paradigm for these patients and their families, providing them an option that not only has the potential to address the physical aspects of the disease, but also its negative effects on overall health, well-being and quality of life."

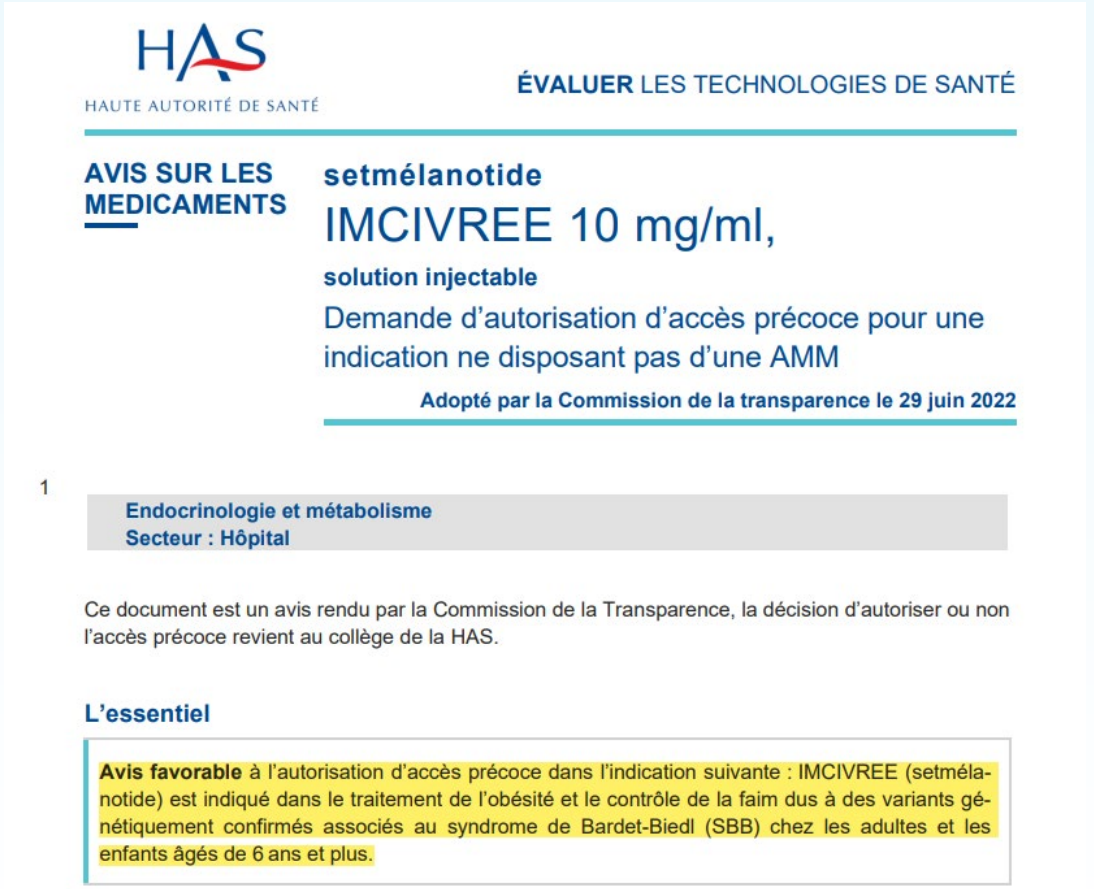
**Philip Beales, M.D.**
University College London,
Institute of Child Health,

# French ANSM and HAS Grant Pre-marketing Authorization for IMCIVREE for Patient with BBS

Ahead of **CHMP** recommendation and **EMA** authorization

32 days following the **US FDA approval**

No restriction to label



HAS
HAUTE AUTORITÉ DE SANTÉ

**ÉVALUER** LES TECHNOLOGIES DE SANTÉ

**AVIS SUR LES MEDICAMENTS**

**setmélanotide**

IMCIVREE 10 mg/ml,

**solution injectable**

Demande d'autorisation d'accès précoce pour une indication ne disposant pas d'une AMM

**Adopté par la Commission de la transparence le 29 juin 2022**

1

**Endocrinologie et métabolisme**
**Secteur : Hôpital**

Ce document est un avis rendu par la Commission de la Transparence, la décision d'autoriser ou non l'accès précoce revient au collège de la HAS.

**L'essentiel**

**Avis favorable** à l'autorisation d'accès précoce dans l'indication suivante : IMCIVREE (setmélanotide) est indiqué dans le traitement de l'obésité et le contrôle de la faim dus à des variants génétiquement confirmés associés au syndrome de Bardet-Biedl (SBB) chez les adultes et les enfants âgés de 6 ans et plus.

# Hunter Smith
# 2Q 2022 Financial Results

# 2Q22 Financial Highlights: Cash Runway Extended into 2H 2024 with Revenue Interest Financing Agreement with HealthCare Royalty

**Non-dilutive, capped RIFA provides financial flexibility with investment of up to $100M**

## To Rhythm:

- $37.5M received upon approval of IMCIVREE for BBS
- $37.5M following EC marketing authorization for IMCIVREE in BBS, anticipated in 2H 2022
- $25M upon achievement of certain sales milestones

## HCR: tiered royalty based on global net product sales:

- Low double digits decreasing to low single digits upon achievement of certain annual revenue thresholds
- Total royalty capped between 185-250% of investment, depending on aggregate royalties paid between 2028-2032

# 2Q2022 Financial Snapshot

| ($ in millions except as noted, per share data and shares outstanding) | Three months ended June 30, 2022 | Three months ended June 30, 2021 |
|---|---|---|
| Product revenue, net | $2.3M | $0.3M |
| License revenue | $6.8 | _ |
| R&D expenses | $31.5M | $25.1M |
| SG & A expenses | $22.3M | $15.5M |
| Net (loss) | $(44.7)M | $(35.4)M |
| Shares outstanding (basic and diluted share count) | 50,398,003 | 50,209,484 |
| Net (loss) per share basic and diluted | $(0.89) | ($0.70) |
| Cash, cash equivalents and short-term investments position (period end) | $235.6M | $368.2M |

**Cash on hand, together with second investment tranche under RIFA with Healthcare Royalty Partners expected in 2H22, expected to be sufficient to fund operations into at least 2H 2024**

# 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**

**Expand IMCIVREE opportunity through additional studies:**

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

# Questions