

# Rhythm Pharmaceuticals, Inc.

Targeting MC4R pathway and transforming the care of  
patients with rare genetic diseases of obesity

**June 16, 2022**



# Forward Looking Statements

This presentation contains certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, and that involve risks and uncertainties, including without limitation 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 timing thereof, our business strategy, prospects and plans, including regarding commercialization of IMCIVREE, the application of genetic testing and related growth potential, expectations surrounding the potential market opportunity for IMCIVREE or any other product candidates, anticipated benefits of and activities under our financing agreement with HealthCare Royalty, and our expected use of proceeds from the transaction with HealthCare Royalty. Statements using words such as "expect", "anticipate", "believe", "may" 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 ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our liquidity and expenses, the impact of the COVID-19 pandemic on our business and 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.

# Agenda

- David Meeker, MD  
Chair, Chief Executive Officer and President
- Jennifer Chien  
EVP, Head of North America
- Hunter Smith  
Chief Financial Officer
- Q&A

David Meeker, MD  
Chairman, CEO and President

# Focused on Continued Label Expansion for IMCIVREE to Transform the Care of Patients with Rare Genetic Diseases of Obesity

**2020-2021**



IMCIVREE approved for chronic weight management for obesity due to **POMC**, **PCSK1** or **LEPR** deficiency:

**Commercial availability in U.S.** meeting expectations and market access advancing in key **international markets**

**TODAY**



IMCIVREE approved by FDA for chronic weight management and control of hunger for obesity due to **Bardet-Biedl syndrome**

**TOMORROW**



Late-stage clinical studies ongoing to drive **significant expansion** of addressable patient population

Now **funded into 2H 2024\***

\* Rhythm announced on June 16, 2022 that it has entered into a revenue interest financing agreement with HealthCare Royalty Partners® for up to \$100 million. Rhythm intends to use the proceeds from the agreement and its cash on hand to support global commercialization efforts for IMCIVREE® (setmelanotide) and ongoing clinical development.

Now Approved:

First and Only FDA-approved Therapy that Targets a Root Cause of Early-onset, Severe Obesity and Hyperphagia Associated with BBS



IMCIVREE™  
(setmelanotide) injection

IMCIVREE is a melanocortin 4 (MC4) receptor agonist indicated for chronic weight management in adult and pediatric patients 6 years of age and older with **monogenic or syndromic obesity** due to:

- Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).
- **Bardet-Biedl syndrome** (BBS).

# Favorable IMCIVREE Label Expansion to Include BBS

'Monogenic or syndromic obesity' included in the indication statement

Patients  $\geq$  6 years old

Clinical diagnosis of BBS

Stopping rule:

- 5% weight loss or 5% BMI reduction after one year

Expanded renal population

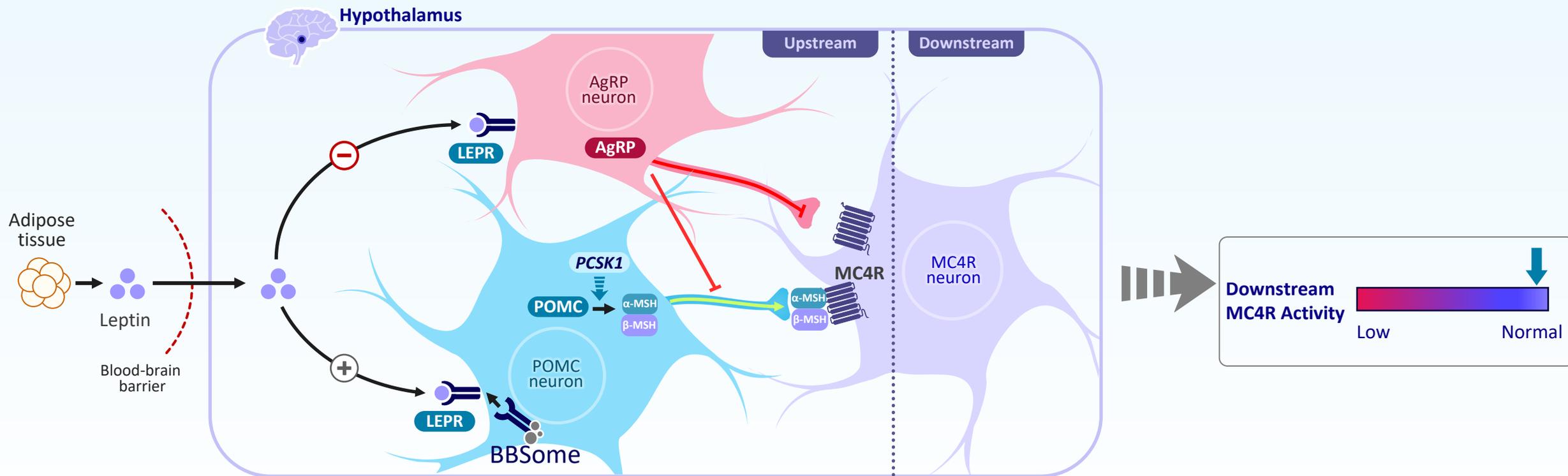
- Patients with mild to moderate renal impairment included
- Prescribed dosing titration regimen for patients 12yo or older with severe renal impairment

No contraindications

No new safety concerns

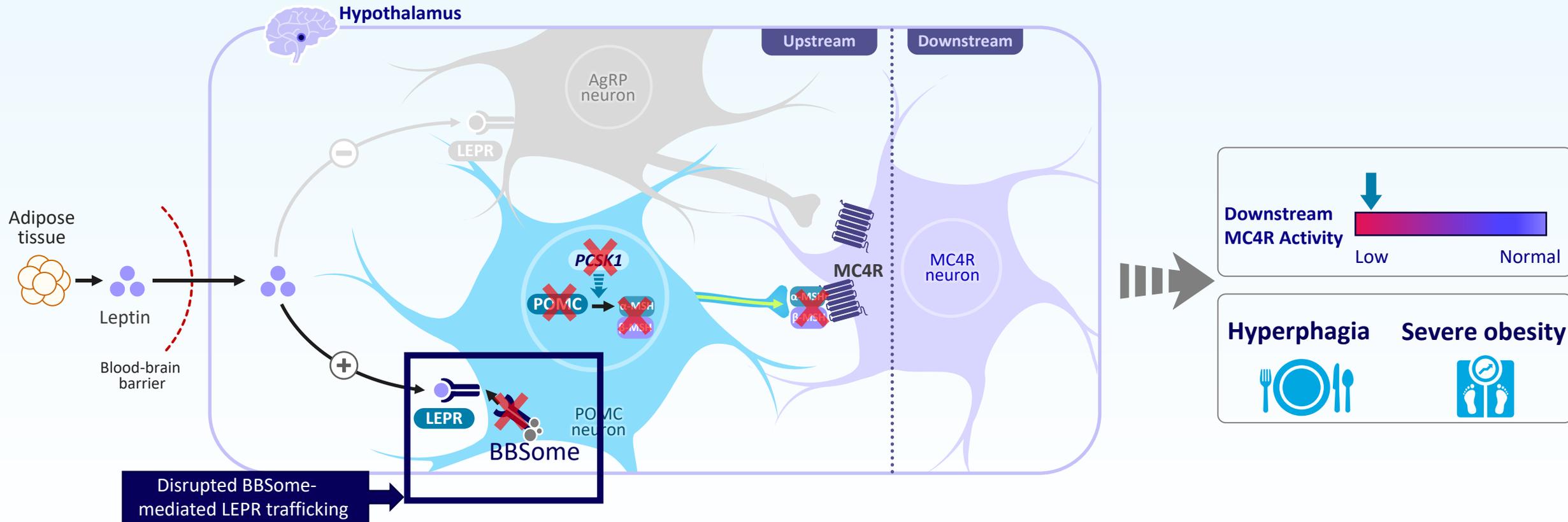


# MC4R Pathway Biology: Regulates Hunger, Satiety, and Energy Expenditure, Consequently Affecting Body Weight<sup>1-4</sup>



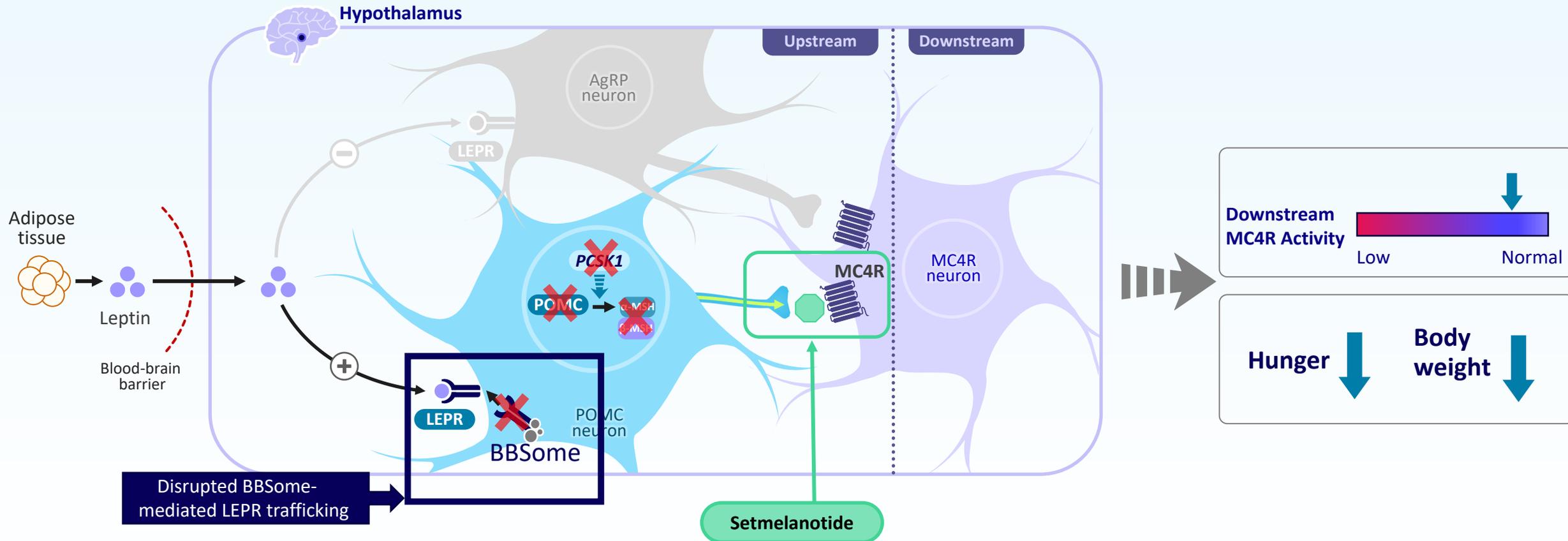
AgRP, agouti-related peptide; BBSome, complex of 8 Bardet-Biedl syndrome proteins; LEPR, leptin receptor; MC4R, melanocortin-4 receptor; MSH, melanocyte-stimulating hormone; PCSK1, proprotein convertase subtilisin/kexin type 1; POMC, proopiomelanocortin.

# Variants in BBS Genes May Disrupt MC4R Signaling, Leading to Hyperphagia and Early-Onset, Severe Obesity<sup>1-9</sup>



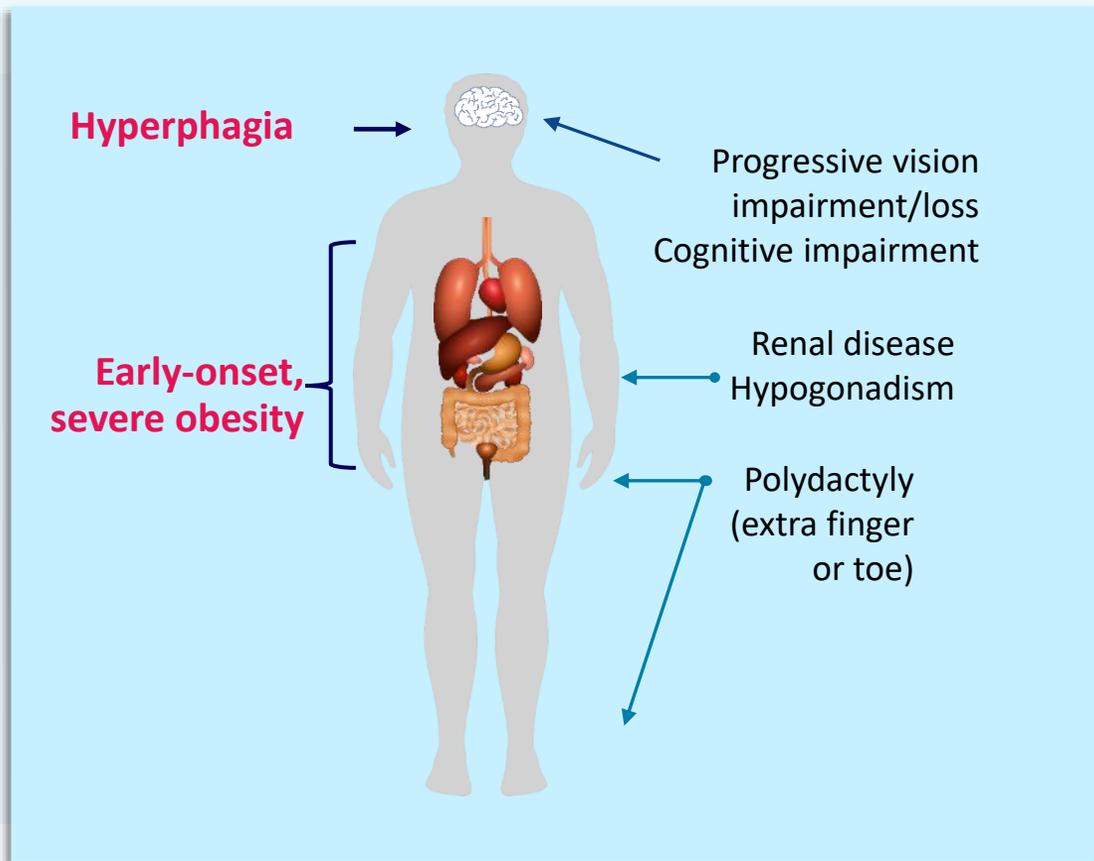
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# IMCIVREE (setmelanotide): MC4R Agonist Shown to Restore MC4R Pathway Signaling, Reduce Hunger, and Promote Weight Loss in BBS<sup>1-6</sup>



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# Bardet-Biedl is Associated with Hyperphagia and Early-onset, Severe Obesity, which Have a Significant Impact on Patients and their Families



*“My weight is my biggest challenge, and it affects every aspect of my daily activities. When I’m hungry, I can’t stop it because I don’t have the signal from my stomach to my brain.”*

Izzy, who was diagnosed with BBS when she was 5 years old

*“The [weight and hunger] most prevalent issue in Izzy’s life and our family’s life.”*

Leigh, Izzy’s mom



References: 1. From market research interviews.

# Bardet-Biedl is Associated with Hyperphagia and Early-onset, Severe Obesity, which Have a Significant Impact on Patients and their Families

*“The hunger is the most challenging part of living with BBS. It is beyond any intensity that we could ever imagine. It is everlasting, never going away and all-consuming.”*

*“When we go out, it’s like a helicopter parent... I have to shadow my kid because he will take food from people.”*

*“He can finish dinner and he’s asking about a snack 5 minutes later. It’s literally all day to anybody – me, dad, nanny – requesting whatever the next food is.”*

*“If he discovers a Costco size box of granola bars, he will eat the whole thing... He will drink so much chocolate milk that he will throw up. If there’s a box of something, he will not have a snack of it. He will have it. The whole box.”*

Source: Rhythm Patient Advisory Board, December 2021.

# Safety Information with updated IMCIVREE Prescribing Information

The most common adverse reactions (incidence  $\geq 20\%$ ) included skin hyperpigmentation, injection site reactions, nausea, headache, diarrhea, abdominal pain, vomiting, depression, and spontaneous penile

<b>Adverse event</b>	<b>Setmelanotide-treated patients (N=43<sup>1</sup>), %</b>
<b>Hyperpigmentation Disorders <sup>2</sup></b>	63
<b>Injection Site Reactions <sup>3</sup></b>	51
<b>Nausea</b>	26
<b>Spontaneous penile erection <sup>4</sup></b>	25
<b>Vomiting</b>	19
<b>Diarrhea</b>	14
<b>Headache</b>	7
<b>Skin striae</b>	7
<b>Aggression</b>	5
<b>Fatigue</b>	5

<sup>1</sup> 43 patients were treated with at least 1 dose of IMCIVREE, 1 patient initially randomized to placebo withdrew from the study prior to receiving IMCIVREE and is not included

<sup>2</sup> Includes skin hyperpigmentation, hair color changes, melanoderma, melanocytic nevus

<sup>3</sup> Includes injection site erythema, pruritis, induration, pain, bruising, edema, reaction, hemorrhage, irritation, mass

<sup>4</sup> Of the 43 patients treated with at 1 dose of IMCIVREE, 20 were male; 5 of 20 (25%) male patients treated with IMCIVREE reported an event of spontaneous penile erection

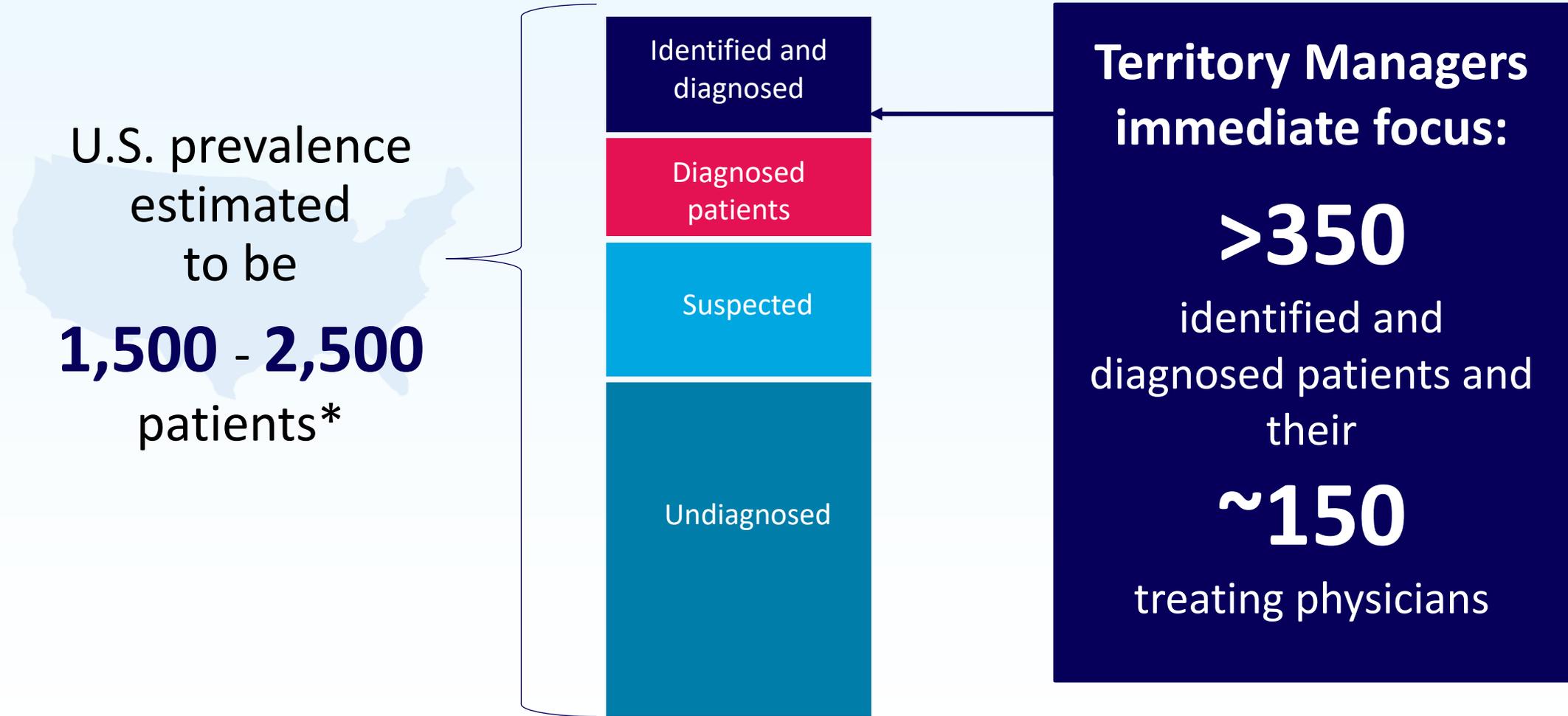
# Jennifer Chien

## EVP, Head of North America

# Rhythm is Ready to Launch Today

- ✓ Foundation for BBS launch has been set with IMCIVREE commercial availability
- ✓ BBS community is waiting; physicians are engaged; and patients are identified
- ✓ Payers are receptive to IMCIVREE for BBS with strong coverage expected
- ✓ Rhythm InTune in place to provide personalized support and education

# Bardet-Biedl Community is Established and Patients are Identified



\* Company estimate based on published prevalence estimates of one in 100,000 in North America.

# Targeted Approach to Educate Physicians with Direct Engagement and Personal and Non-personal Promotion

**Territory Manager-  
Driven Personal  
Promotion**  
*~3,500 physicians*

- Core Visual Aid
- “What to Expect” Brochure
- Specialty Flashcards
- KOL Video
- MOA Video

**Expanded Reach  
Personal Promotion**  
*Up to ~11,000  
physician targets*

- Speaker Programs
- Specialty Modules
- Conference Booth
- Symposia at Key Conferences  
(ENDO, PES, OMA, TOS)

**Broad Reach  
Non-Personal  
Promotion**  
*~22,000 physician  
targets*

- IMCIVREE Website
- Medscape Initiatives
- Targeted Banner Ads
- Search
- CRM Email Deployment
- On-Demand Educational Content

# Payers are Receptive to IMCIVREE for BBS

Perception of Disease	Product Profile	Anticipated Coverage
<ul style="list-style-type: none"><li>✓ Extreme burden of hyperphagia differentiating from general obesity</li><li>✓ Recognition of early-onset obesity and need in pediatric population</li></ul>	<ul style="list-style-type: none"><li>✓ Positive perception of efficacy and safety</li><li>✓ Understanding the value of treating hyperphagia and obesity</li></ul>	<ul style="list-style-type: none"><li>✓ Payers currently covering IMCIVREE anticipate covering for BBS upon approval</li><li>✓ Expect prior authorization</li><li>✓ Clear pathway via appeal for those not covering</li><li>✓ Genetic testing may be required by some payers</li></ul>

*Ongoing active engagement of Corporate Accounts Team with payers*

# Actively Engaging with Patient Advocacy Groups



**Bardet Biedl Syndrome Foundation**  
& FAMILY ASSOCIATION

- 48k members, both HCPs and patients
- Efforts underway to understand how many living with BBS
- Share our BBS Patient/Caregiver programs
- Share our BBS Ophthalmology programs for HCPs
- Local chapter engagements by Rhythm

- Facebook Membership - 1,765
- Active membership - 500
- Partner on educational programming
- National Virtual Meeting July 10
- Five confirmed regional meetings
  - ❑ 20-30 individuals per event
  - ❑ June 25 – July 23
  - ❑ Rhythm Presence

# Rhythm InTune: First 120 Days of Patient and HCP Engagement



Phase 2:  
Future CRM  
cadence  
additions



Patient Support Outreach

	Consent Received	Post BI	Approval	Day 0	Day 1	Day 4	Day 10	Day 30	Day 60	Day 90	Day 120
Welcome Call		<b>Ship 'Getting Started Kit'</b>	Payor approval		Post 1 <sup>st</sup> Shipment check in	Assess Barriers/Goals for treatment	Assess barriers check in call	Treatment Check In	Connect Call	Connect Call	Connect Call
Needs Assessment		Family Onboarding	Tx Expectations		Confirm start date	Injection check-in		Goal Setting	Patient Program Invite	Nutrition Wellness	Goals check-in
Expectations setting of partnership with InTune		Pathway Education Tx expectations	Injection training							Life Challenges	Empowerment Series invites
				Schedule 1st ship & RPH Tx expectations/ Injection training			RPH checks in to reinforce Tx expectations, titration, etc.	Refill calls monthly	Refill calls monthly	Refill calls monthly	Refill calls monthly
									Continuing education to mitigate discontinuation / drop-out		
	New prescriber check in TM/PEM	Treatment expectations (clinically) – what to expect			TM check in with provider						

Pharmacy Calls (Panther)\*

TM HCP Outreach

\*Monthly Pharmacy re-fill calls  
Missed shipment follow up calls

# Coordinated Patient-Centered Approach

## Patient Education Manager

- Patient Focused
- Coordinates treatment access related activities
- Provides individualized education and engagement

## Territory Manager

- Provider Focused
- Educates on enrollment process and InTune
- Resolves issues as needed

## Pharmacy (Panther)

- Distributes IMCIVREE
- Flags delays in shipments
- Completes BI's, facilitates PAs and appeals

## Market Access

- Payor Focused
- Develops pathway for IMCIVREE
- Provides policy specific support



# Ready to Launch Today!



# Hunter Smith

## Chief Financial Officer

# Revenue Interest Financing Agreement with HealthCare Royalty Partners® for up to \$100M

**Non-dilutive financing agreement extends anticipated cash runway into 2H 2024**

Rhythm to receive:

- \$37.5M today 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 will receive tiered royalty based on global net product sales:

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



David Meeker, MD  
Chairman, CEO and President

# Continued Transformational Progress in 2022

## Recently achieved milestones

- ✓ Initiated Phase 2 DAYBREAK trial
- ✓ Initiated Phase 3 “switch study” of weekly formulation
- ✓ Initiated Phase 3 trial in pediatric patients aged 2-6 years old
- ✓ Initiated Phase 3 EMANATE trial
- ✓ Achieved first European sales of IMCIVREE
- ✓ PDUFA for IMCIVREE in BBS and U.S. launch

## Anticipated milestones in 2022

- ✓ **June (ENDO):** Long-term data in BBS; SRC1; SH2B1, heterozygous and biallelic POMC/PCSK1/LEPR
- ✓ **Q2:** IMCIVREE PPL launch in Germany
- Mid 2022:** Initial Ph 2 data from in hypothalamic obesity
- Mid 2022:** Initial Ph 2 data in MC4R rescuable patients
- 2H:** CHMP decision on BBS
- 2H:** IMCIVREE PPL launch in UK and Italy
- 2H:** Initiate Phase 3 “de novo study” of weekly formulation

Rhythm<sup>®</sup>  
PHARMACEUTICALS