Rhythm Pharmaceuticals

Bardet-Biedl Syndrome

February 16, 2022

Welcome and Overview

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 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 expectations regarding payer coverage. 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.

Today's Speakers

Special Guest

Mary Morris
Patient Mother, BBS Advocate

BBS Key Opinion Leaders

Rushika Conroy, MD, MS
Pediatric Endocrinology
Baystate Children's Hospital
Associate Professor of Pediatrics
Chan Medical School, University of Massachusetts
COLUMBIA UNIVERSITY MEDICAL CENTER
NEW YORK MEDICAL COLLEGE

Robert Haws, MD
Pediatric Nephrology
Marshfield Clinic
UNIVERSITY OF TEXAS, SOUTHWESTERN MEDICAL CENTER
UNIVERSITY OF UTAH

Rhythm Pharmaceuticals Management

David Meeker, MD
Chairman, President, & CEO

Jennifer Chien
EVP, North America

Sarah Ryan
VP, Sales & Marketing

Hunter Smith
CFO

Transforming Care of Patients with Rare Genetic Diseases of Obesity

IMCIVREE® (setmelanotide) injection

FDA-approved in November 2020

EC marketing authorization received July 2021

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

Poised to deliver on **Bardet-Biedl**

Clinical development **meaningfully expands** addressable patient population

Rhythm® PHARMACEUTICALS

Rhythm is Commercial Ready

Unmet need in BBS

Solution

Rhythm is ready to launch in BBS

Ready to launch at PDUFA goal date of March 16

Mary Morris

Mary Morris and her husband are Bardet-Biedl Syndrome (BBS) caregivers and parents to six children. Their youngest daughters, Ashley (28) and Carly (21), are diagnosed and living with BBS. Mary has been a prominent advocate in the BBS community and involved with the US patient advocacy group, the BBS Foundation and Family Association, since its formation, serving as President, Vice president and secretary in the past. Mary is a Nationally Board Certified High School math teacher and spent her career teaching before her retirement.

Disclosures

Mrs. Morris was compensated by Rhythm Pharmaceuticals for the time and expense associated with today's presentation. She is a stockholder of Rhythm Pharmaceuticals.

Mary Morris

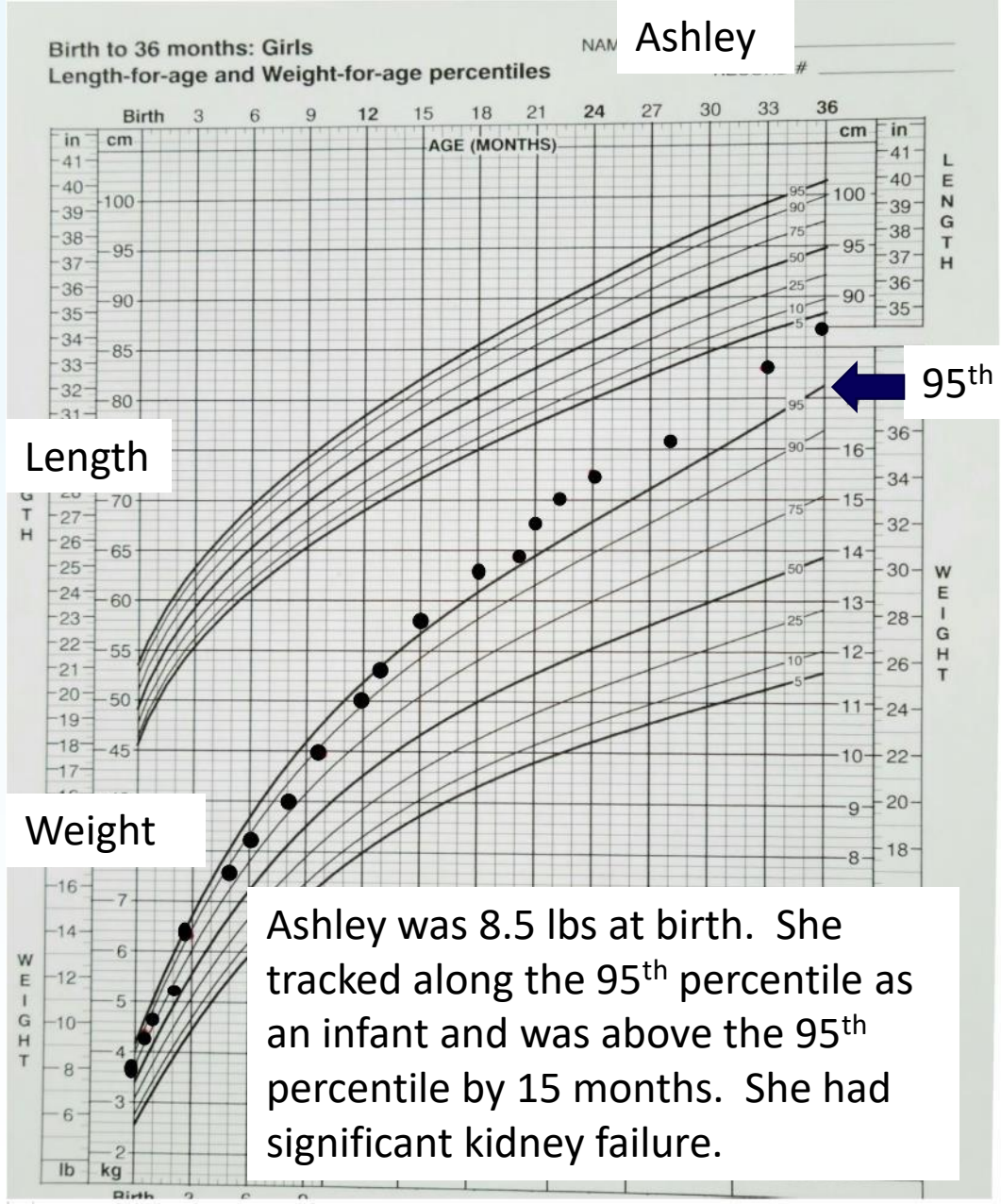
Mom of Carly and Ashley

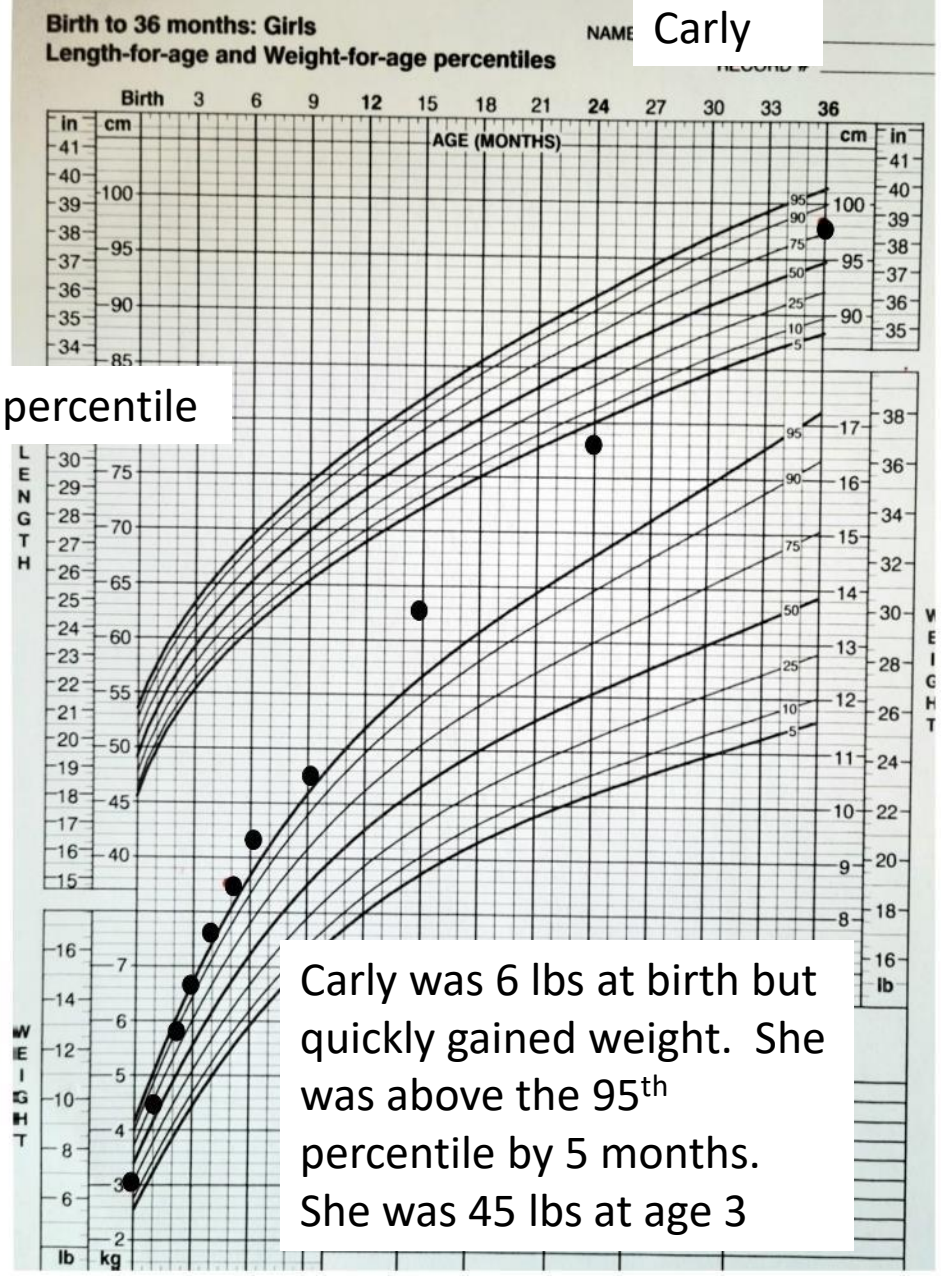
THE MORRIS FAMILY

Our Life with BBS

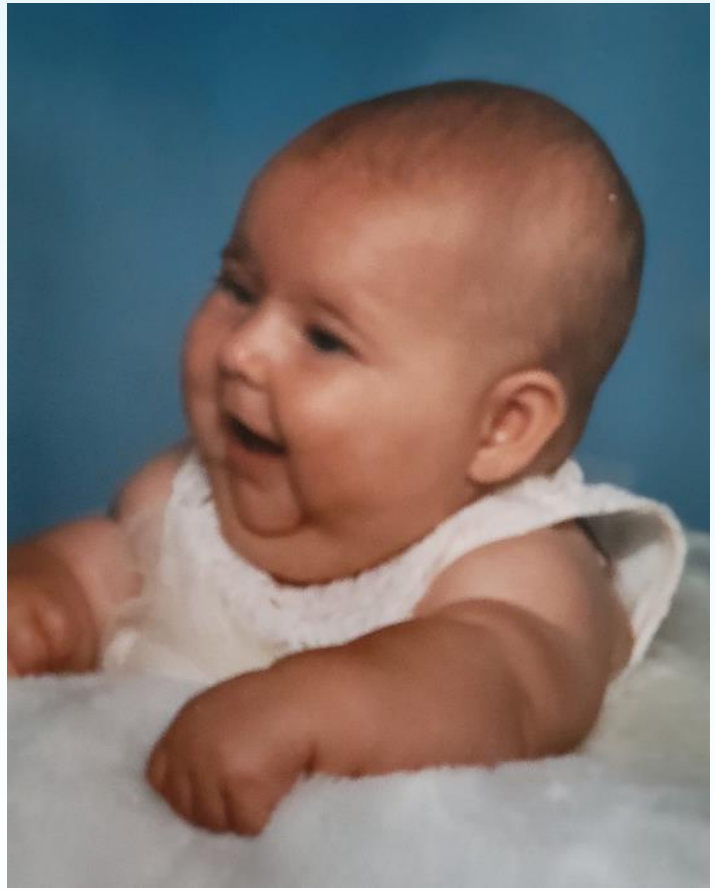

CATS
02.25.2010

Both girls gained weight very quickly as infants.

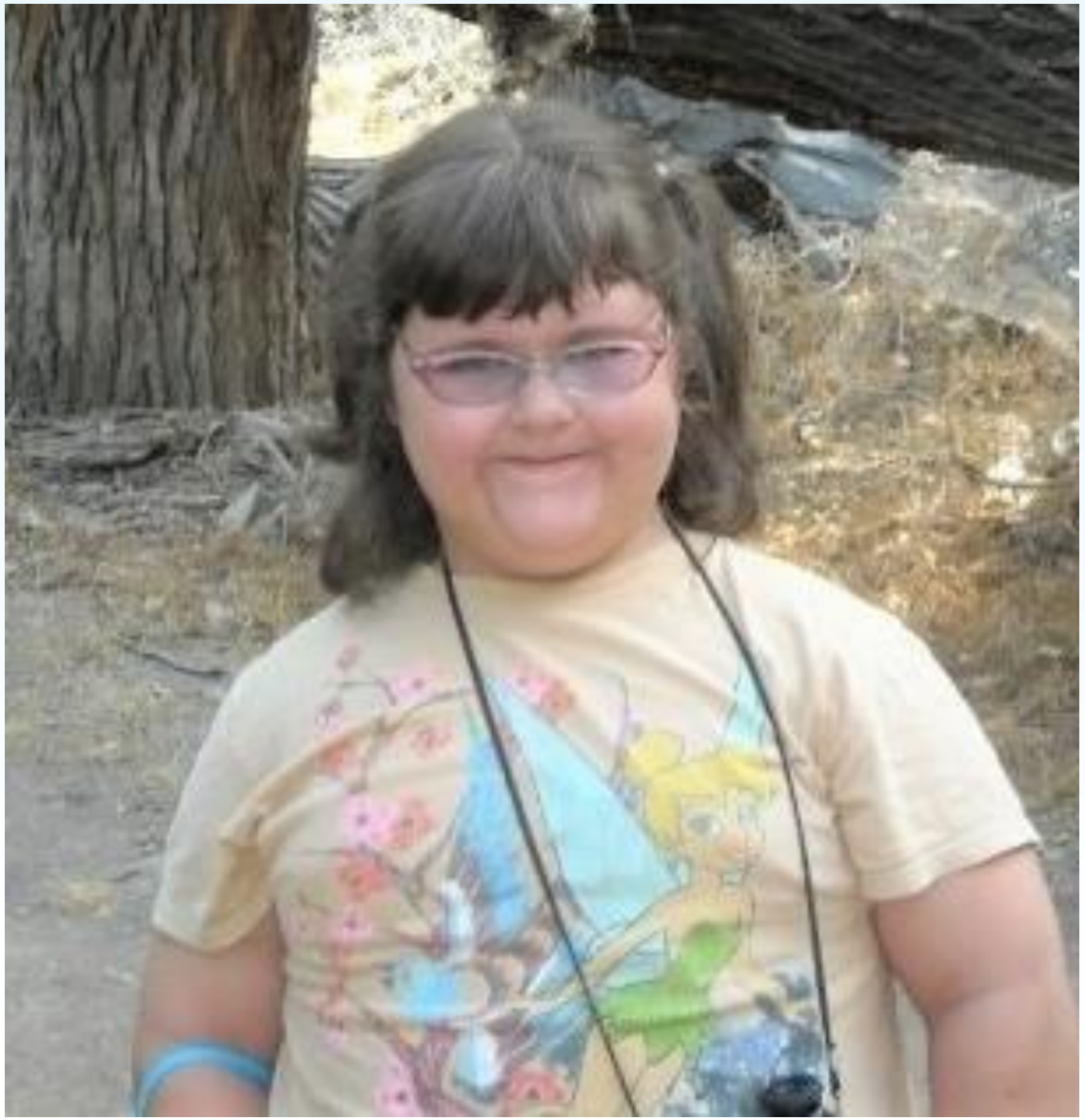




Ashley

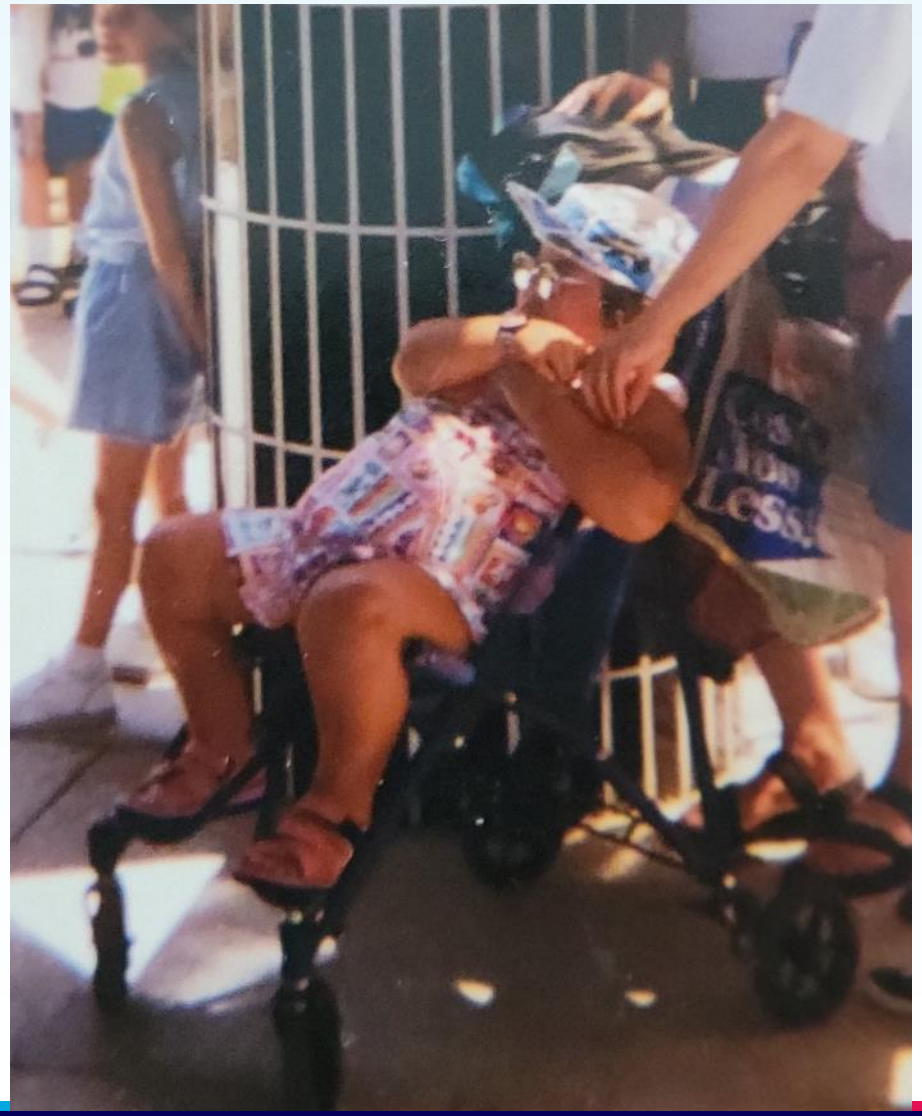


Carly



Carly 4 months

Ashley 3 years



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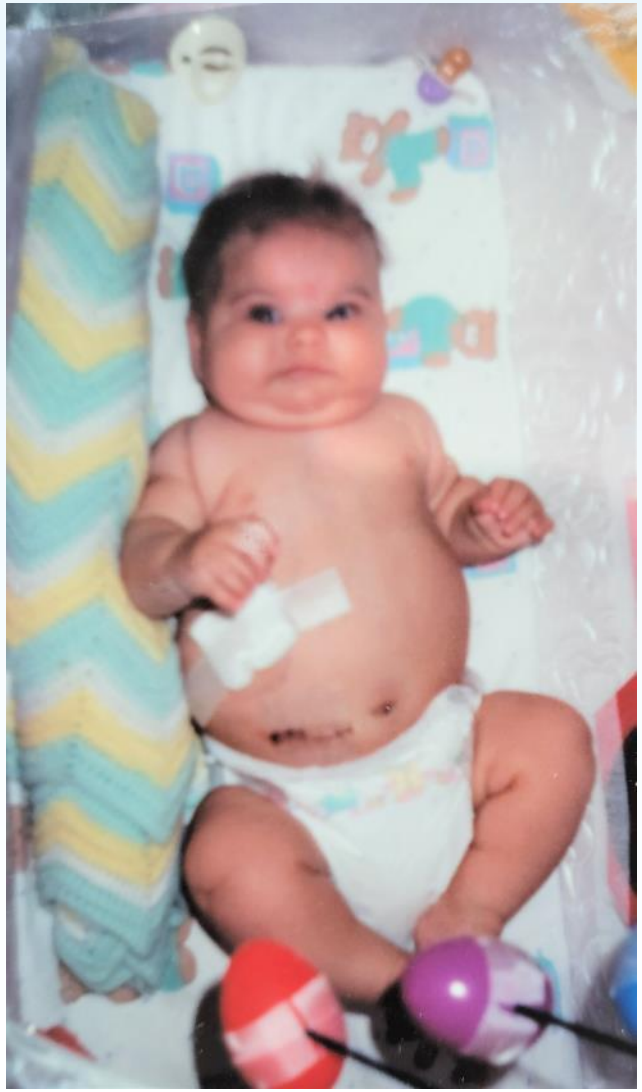
While our older kids, focused on each other,

Ashley was focused on her treat

When the girls began to lose vision, they were able to get services to help them live a full life. They had braille offered starting in kindergarten and cane training. There are many services available to the visually impaired. We were assured that blindness was not our fault.



When Ashley’s kidneys failed, she was put on dialysis and services were offered to get her through to transplant. She is able to live well with kidney failure. We were assured that kidney failure was not our fault.

When the girls became obese there were no services in place to treat it as an illness. Their obesity was seen as a personal failure.

Somehow, we had caused it to happen.

Our BBS Community

Rhythm® PHARMACEUTICALS

Rushika Conroy, M.D., M.S.
Bio and Disclosures

Dr. Rushika M. Conroy is a Pediatric Endocrinologist in the Division of Pediatric Endocrinology at Baystate Children's Hospital in Springfield, Mass. She also serves as Medical Director for Baystate's Pediatric Weight Management Program and Baystate's Pediatric Type 2 Diabetes Program.

Dr. Conroy also is Associate Professor of Pediatrics at University of Massachusetts Medical School and Adjunct Professor of Pediatrics at Tufts University School of Medicine. Dr. Conroy earned her medical degree from New York Medical College in Valhalla, New York. She trained at Schneider Children's Hospital in New Hyde Park, New York, where she was Chief Resident of Pediatrics, and completed a fellowship in pediatric endocrinology at Columbia University Medical Center. She is board certified in obesity medicine and pediatric endocrinology. In 2011, she was nominated for fellow of the year at Columbia University College of Physicians and Surgeons.

Disclosures

Dr. Conroy was compensated by Rhythm Pharmaceuticals for the time and expense associated with today's presentation. She has also been compensated by Rhythm Pharmaceuticals for the time and expense associated with serving as member of the faculty for Rhythm's GOLD program, serving as an advisor to Rhythm Pharmaceuticals and serving as a Principal Investigator on clinical trials of setmelanotide.

Rushika Conroy, M.D., M.S.

Division of Pediatric Endocrinology, Medical Director, Pediatric Weight Management and Type 2 Diabetes programs, Baystate Children's Hospital, Associate Professor of Pediatrics, UMASS-Chan Medical School – Baystate

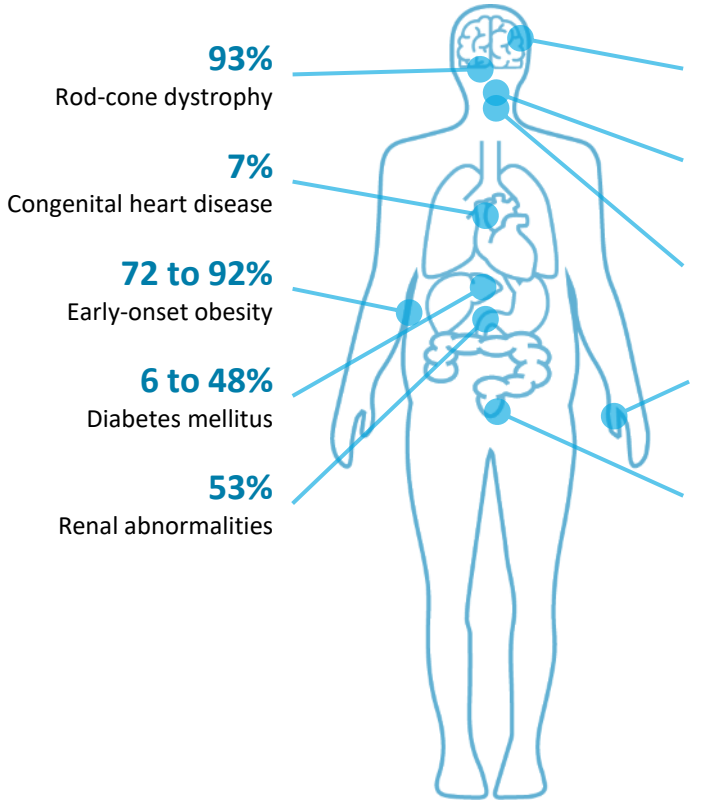
Clinical Presentation of Bardet-Biedl Syndrome

Early-onset, severe obesity

>55%

of children with BBS were overweight or have obesity by 2 years of age[1]

Additional Features[2]



References: 1. Pomeroy J et al. *Pediatr Obes*. 2021;16(2):e12703. **2.** Forsythe E et al. *Front Pediatr*. 2018;6:23.

Rhythm® PHARMACEUTICALS

Cross-sectional Analysis of CRIBBS Data Shows Obesity Appears Early in Patients Living with BBS

	<2 years	6-11 years	12-19 years
Obesity[1]	23%	83%	77%
Overweight[1]	33%	11%	15%

CRIBBS: Clinical Registry Investigating Bardet-Biedl Syndrome**; References:** 1. Pomeroy J et al. *Pediatr Obes*. 2021;16(2):e12703. Data are based on analysis of 628 patients the Clinical Registry Investigating Bardet-Biedl Syndrome (CRIBBS) with measurements from 119 participants less than 2 years of age (not including birthweight) and height and weight measurements in 509 participants 2 years of age and older. Without overweight/obesity, overweight, and obesity defined using the WHO weight status categories.

Health Ramifications Associated with the Early-onset, Severe Obesity of BBS

54%

Metabolic syndrome*

~16%*

Type 2 diabetes mellitus*

67%

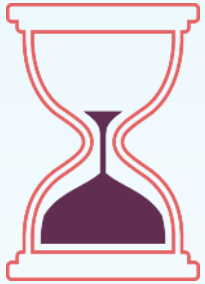
Hypertension
(systolic >135 mm Hg or diastolic >85 mm Hg)*

~17%**

Moderate to severe sleep apnea

* Mujahid S et al. *J Clin Endocrinol Metab*. 2018;103(5):1834-1841; ** Dormegny et al. , Nature and Science of Sleep 2021:13 1913–1919 1913

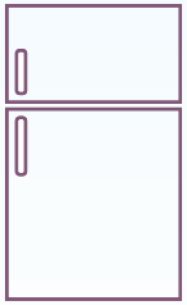
Hyperphagia is a Key Characteristic of BBS



Taking a longer time to feel full while eating

Feeling hungry again right after a meal

Thinking about food constantly



Food-seeking behavior (sneaking or stealing food)

Challenges with Hyperphagia in BBS Start Early

Hyperphagic behaviors start in early childhood[1]

91%

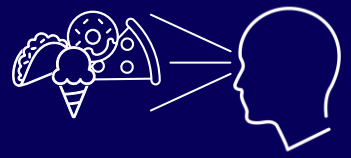
of caregivers report an increased interest in food before the age of 5 years

Hyperphagia

- Often has an early onset in patients, typically by age 5 years[2]
- Patients living with BBS have significantly greater hyperphagia scores overall compared with BMI-matched controls[2]

References:. **1.** Sherafat-Kazemzadeh R et al. *Pediatr Obes*. 2013;8(5):e64-e67; **2.** Sherafat-Kazemzadeh R et al. *Pediatr Obes. 2*013;8(5):e64-e67.

How Do We Assess Hyperphagia?



Behavior:
Excessive food-seeking behavior

Drive:
Preoccupation with food

Severity:
Significant distress when denied food

My experience

Robert Haws, M.D.
Bio and Disclosures

Dr. Robert Haws specializes in pediatric nephrology, providing treatment to patients who range from infants to young adults. He treats conditions that include acute and chronic kidney failure, hypertension, kidney abnormalities, kidney stones, urinary tract infections, metabolic diseases involving the kidney, renal cystic diseases, and inherited disorders. He came to Marshfield Clinic in 2004, after years of practice in Texas and Arizona. Because he feels that children shouldn't have to miss an entire day of school to see him, Dr. Haws also provides outreach services at Marshfield Clinic Health System centers in Chippewa Falls, Eau Claire, Minocqua, Stevens Point, Wausau, Weston, and Wisconsin Rapids. Dr. Haws earned his medical degree at the University of Utah School of Medicine, Salt Lake City. He completed his internship and residency at Wright State University Affiliated Hospitals, Dayton, Ohio. He completed a fellowship in pediatric nephrology at the University of Texas Southwestern Medical Center, Dallas.

Disclosures

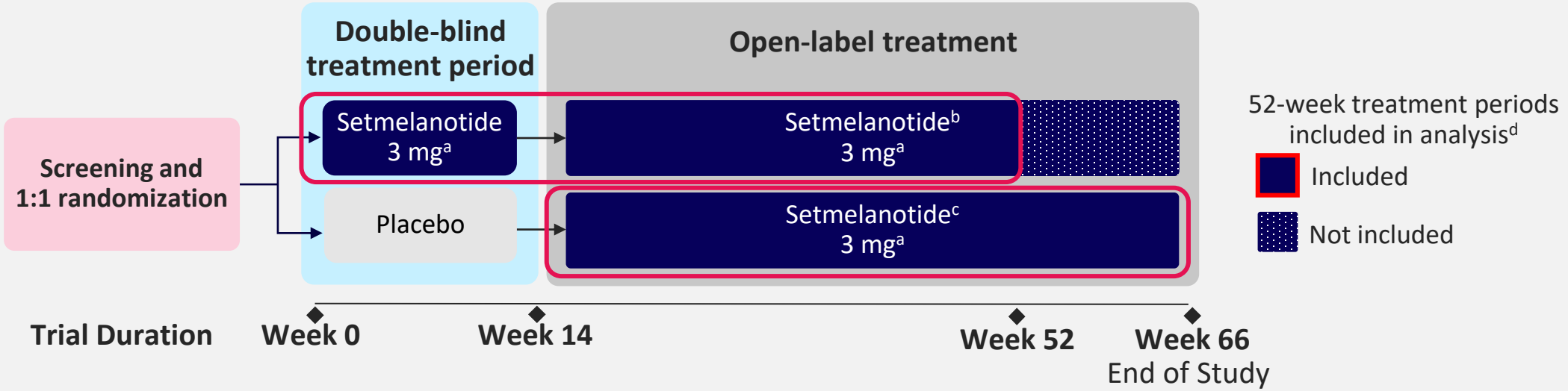
Dr. Haws was compensated by Rhythm Pharmaceuticals for the time and expense associated with today's presentation. He has also been compensated by Rhythm Pharmaceuticals for the time and expense associated with conducting setmelanotide trials in individuals with rare genetic diseases of obesity, consulting on study design, research opportunities and guidance on health concerns in BBS and other rare genetic obesity disorders, presenting poster and oral presentations at medical meetings, medical writing, serving on DSMB medical board for setmelanotide clinical trials and lecturing to Rhythm Pharmaceuticals leaders and investors. He also serves as a consultant to Axovia Therapeutics.

Robert Haws, M.D.

Director of Clinical Research Center at the Marshfield Clinic Research Institute and Director of the Center of Excellence for Bardet-Biedl Syndrome

Phase 3 Trial Evaluated Setmelanotide in Patients With BBS or AS

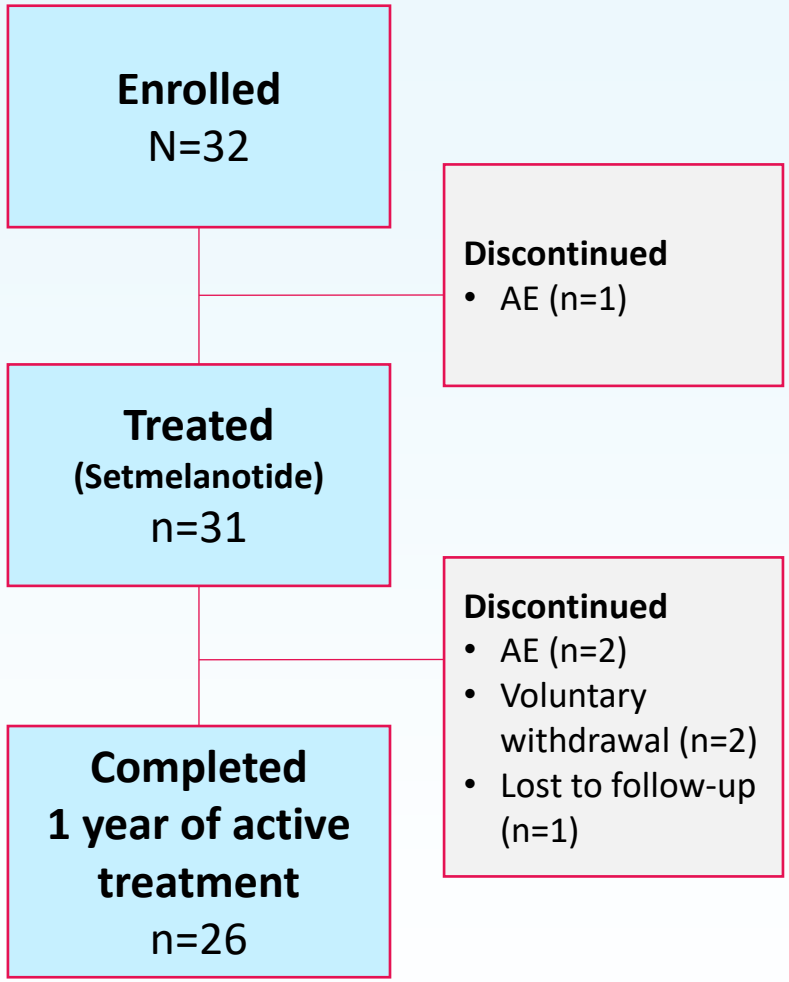
Largest and longest Phase 3 interventional study ever conducted in this patient population



No specific guidance on diet and exercise was given during the trial

[a]Dose escalation based on age up to 3.0 mg. [b]For patients who received >52 weeks of setmelanotide at the end of study, analysis was performed for 52 weeks of setmelanotide. [c]A multiple imputation model was used to impute data in patients who received <52 weeks of setmelanotide at the time of the analysis. [d]Efficacy outcomes were assessed at 52 weeks on active treatment for each study group (ie, Week 0 to 52 for the setmelanotide group and Week 14 to 66 for the group assigned to placebo during the double-blind treatment period).

Disposition and Baseline Demographics of Patients With BBS



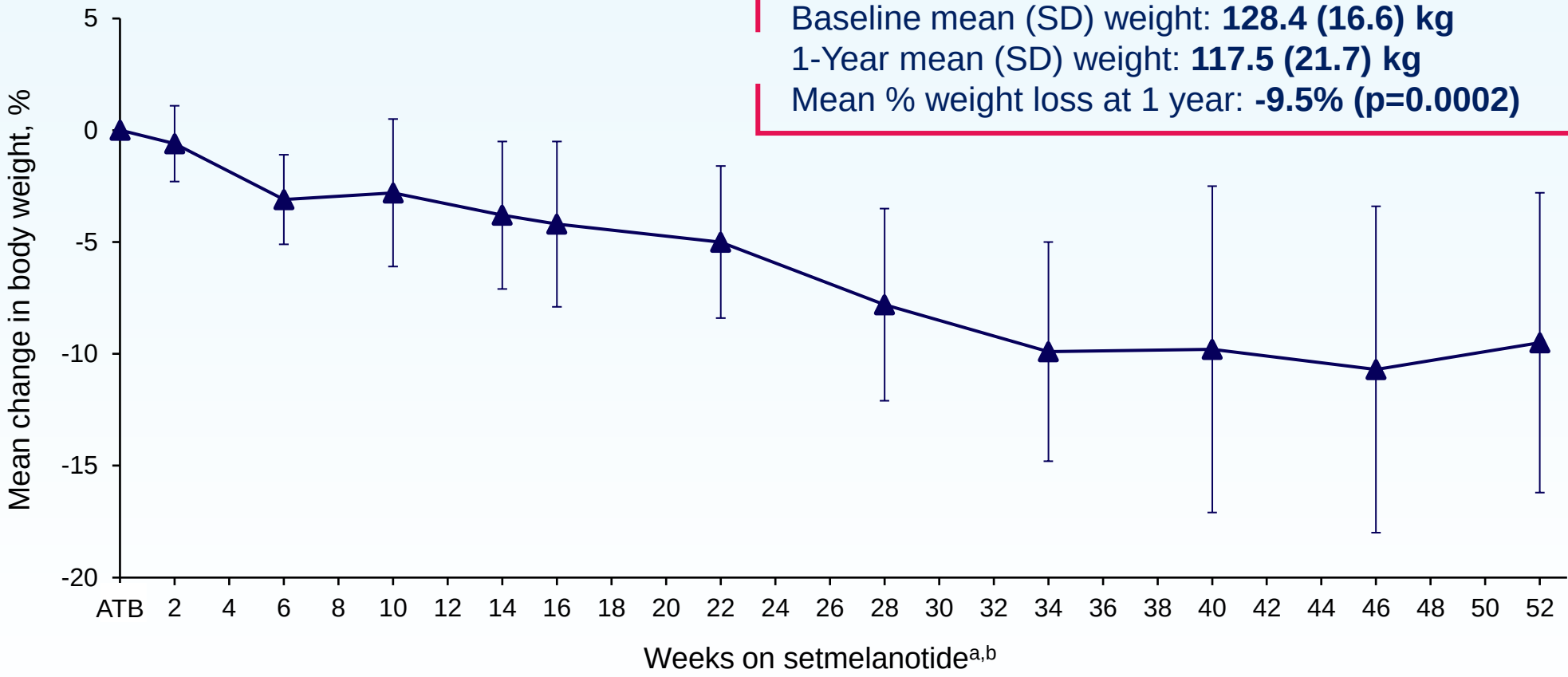
Baseline characteristic		Total (N=32)
Age, years	Mean (SD)	**20.2 (10.2)**
	Range	**7–44**
	<18 years old, n	**16**
	≥18 years old, n	**16**
Sex, n (%)	Female	**17 (53.1)**
	Male	**15 (46.9)**
Race, n (%)	White	**28 (87.5)**
	Black or African American	**1 (3.1)**
	Other	**3 (9.4)**
Ethnicity, n (%)	Hispanic or Latino	**1 (3.1)**
	Not Hispanic or Latino	**31 (96.9)**
Weight, kg	Mean (SD)	**112.3 (27.9)**
	Range	**49.3–173.8**
BMI Z <18 years old,[a]	Mean (SD) [n]	**3.7 (1.3) [16]**
BMI, kg/m^2	Mean (SD)	**41.6 (9.0)**
	Range	**24.4–61.3**

[a]At active treatment baseline.
AE, adverse event; BBS, Bardet-Biedl syndrome; SD, standard deviation.
Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021.

Setmelanotide Resulted in Clinically and Statistically Significant Reduction in Body Weight at 1 Year in Patients with BBS ≥18 Years Old

Completer Population

Baseline mean (SD) weight: **128.4 (16.6) kg**
1-Year mean (SD) weight: **117.5 (21.7) kg**
Mean % weight loss at 1 year: **-9.5% (p=0.0002)**



[a]Data shown do not include data imputed for patients who received <52 weeks of setmelanotide at the time of the analysis. [b]Populations sizes range from 7 to 15, with n=12 at 52 weeks on active treatment. Error bars are the standard deviation (SD). ATB, active treatment baseline (defined as last measurement before the first dose of setmelanotide; ie, Week 0 for setmelanotide group and Week 14 for placebo group); BBS, Bardet-Biedl syndrome.

Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021.

Setmelanotide Resulted in Clinically and Statistically Significant Reduction in Weight at 1 Year in Patients with BBS ≥18 Years Old

60%

9 of 15 patients achieved

≥5%

weight loss

46.7%

7 of 15 patients achieved

≥10%

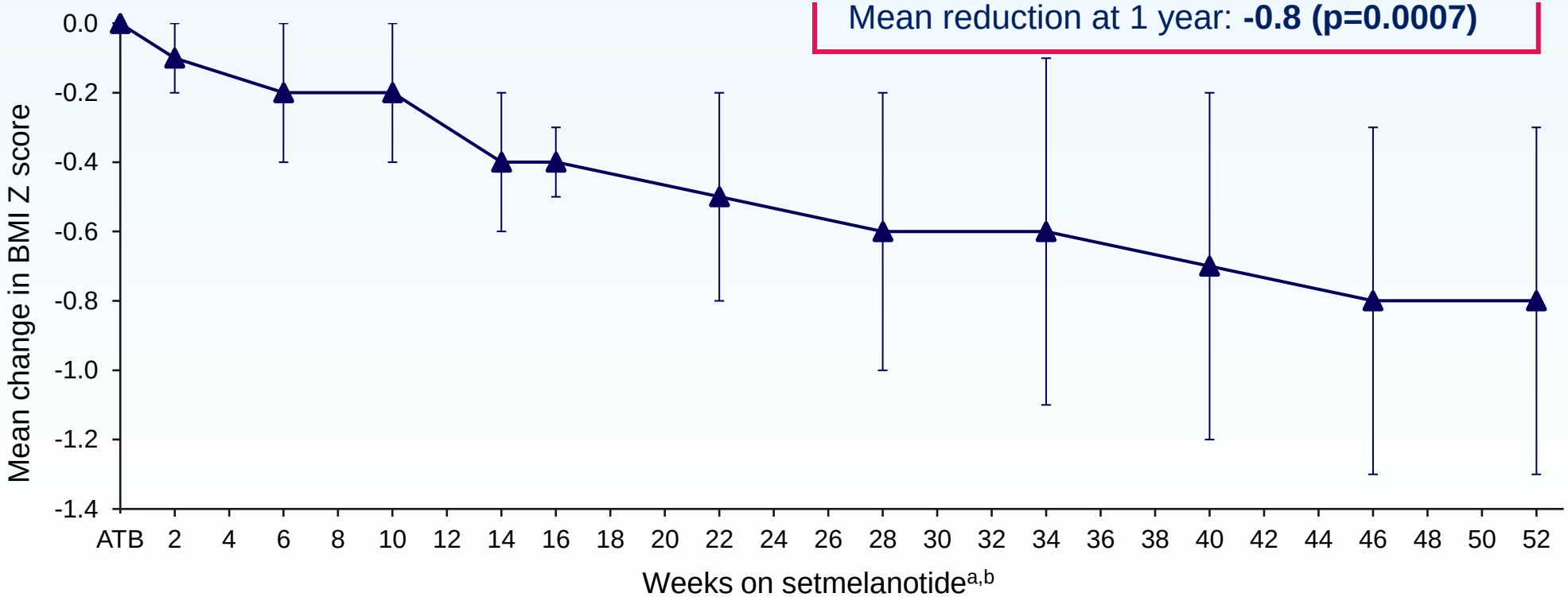
weight loss

*Data shown include data imputed for patients who received <52 weeks of setmelanotide at the time of the analysis
BBS, Bardet-Biedl syndrome.
Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021.

Setmelanotide Treatment Resulted in Statistically Significant Reduction in BMI Z Score in Patients with BBS <18 Years Old

Completer Population

Baseline mean (SD) BMI Z score: **3.7 (1.3)**
1-Year mean (SD) BMI Z score: **3.0 (1.5)**
Mean reduction at 1 year: **-0.8 (p=0.0007)**



[a]Data shown do not include data imputed for patients who received <52 weeks of setmelanotide at the time of the analysis. [b]Populations sizes range from 8 to 16, with n=14 at 52 weeks on active treatment. Error bars are the standard deviation (SD). ATB, active treatment baseline (defined as last measurement before the first dose of setmelanotide; ie, Week 0 for setmelanotide group and Week 14 for placebo group); BBS, Bardet-Biedl syndrome; BMI, body mass index.

Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021.

Vast Majority of Patients <18 Achieve Clinically Meaningful BMI Z Score Improvement of at Least ≥0.2

85.7%

12 of 14 patients achieved

≥0.2

point improvement in BMI Z score

71.4%

10 of 14 patients achieved

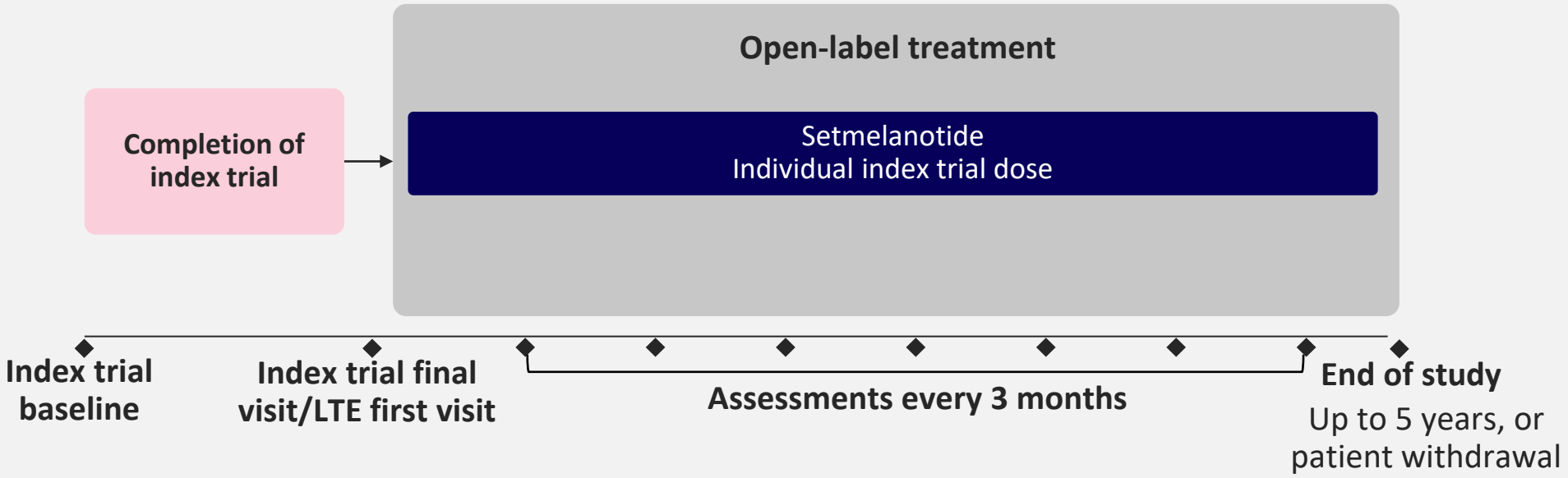
≥0.3

point improvement in BMI Z score

BBS, Bardet-Biedl syndrome; BMI, body mass index.

Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021.

Setmelanotide being Evaluated in Open Label Extension Trial



No specific guidance on diet and exercise was given during the trial

LTE, long-term extension.

Long-term Setmelanotide Treatment Resulted in Deepened, Sustained Weight Loss at 24 Months

Month 24 Efficacy Data[a]

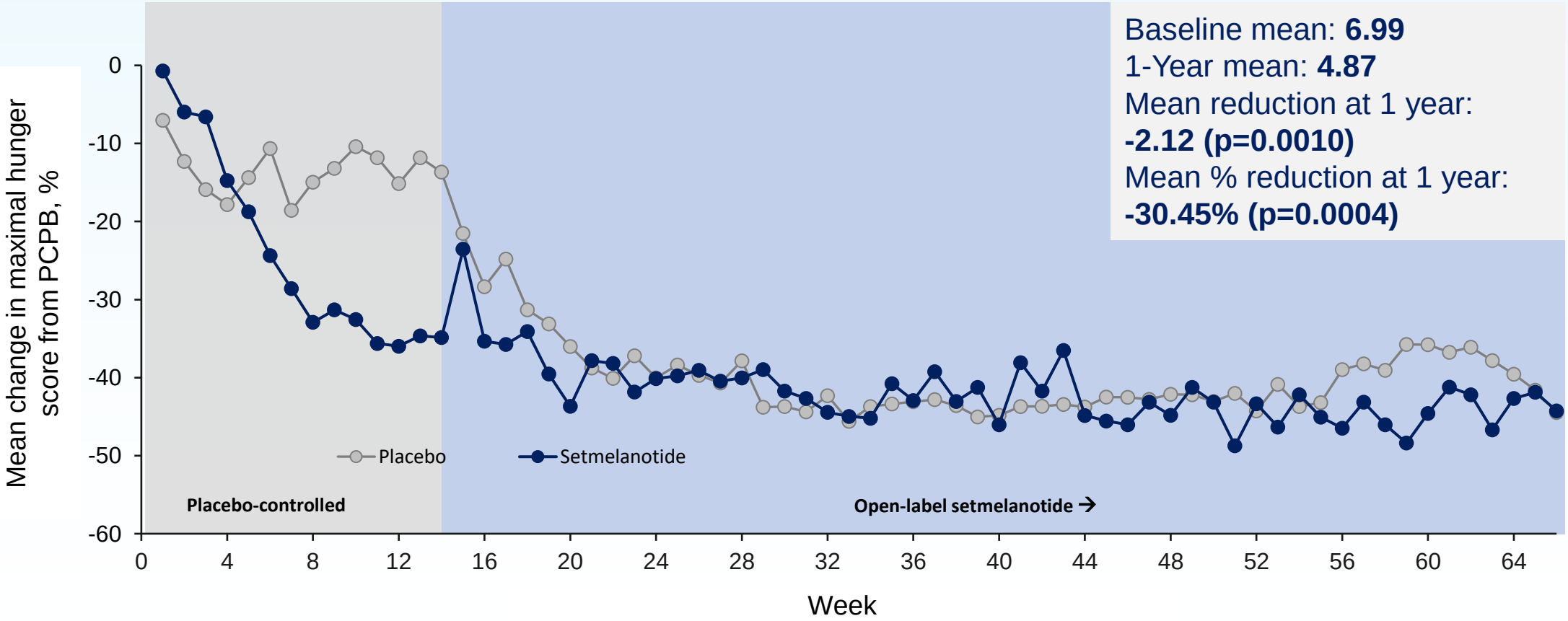
	% change in BMI all patients (n=19)	% change in body weight ≥18 years (n=6)	change in BMI Z score <18 years (n=12[b])
Mean:	**–14.3%**	**–14.9%**	**–0.72**
SD:	**11.6%**	**10.4%**	**0.54**

No new safety signals were observed during long-term setmelanotide administration
One patient discontinued due to an adverse event unrelated to setmelanotide

BMI, body mass index; a. compared with measures at index trial baseline; b. BMI Z-score could not be calculated for one 20-yr-old patient who was 17 years old at index trial baseline.

Setmelanotide Achieved Clinically Meaningful Reduction in Hunger in Adults and Children with BBS at Week 52

Data show separation in hunger reduction during placebo period followed by placebo group reaching treatment levels rapidly after crossover; all patients on placebo crossed over to treatment at week 14.



Hunger score changes in pivotal patients with BBS. Hunger scores are reported in patients ≥12 years old without cognitive impairment.

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Setmelanotide Treatment Associated with Statistically Significant Reduction in Hunger in Patients with BBS ≥12 Years Old

57.1%

of patients with BBS ≥12 years old achieved a ≥25% reduction in most hunger score after 1 year of setmelanotide (95% CI, 28.9%–82.3%; p<0.0001)

	1 year on active treatment n/N* (%)
≥1-point improvement in most hunger score	10/14 (71.4)
≥2-point improvement in most hunger score	6/14 (42.9)

* Patients without cognitive impairment; Note: Assessed using a scale where 0 = “not hungry at all” and 10 = “hungriest possible.” Scale was validated for patients 12 years and older without cognitive impairment who could self-report scores; CI, confidence interval; Haws et al. Poster presented at ObesityWeek Annual Meeting; November 5, 2021. Data on File.

Study Data Showed Safety/Tolerability in Patients with BBS was Consistent with Established Setmelanotide Data

	n (%)
Treatment-related AEs	32 (100.0)
Serious AEs	2 (6.3)
Serious treatment-related AEs[1]	1 (3.1)
AEs leading to drug discontinuation[2]	3 (9.4)
AEs leading to death	0

- Onset of treatment-related AEs was typically during the first few weeks of setmelanotide. AEs were generally mild, transient, and infrequently led to withdrawal.
- Hyperpigmentation was common and infrequently led to withdrawal. Skin darkening plateaued within the initial months of treatment.
- The tolerability profile in patients with BBS was consistent with other rare genetic diseases of obesity.

	n (%)
Treatment-emergent AEs occurring in ≥15% of patients	
Skin hyperpigmentation	18 (56.3)
Injection site erythema	16 (50.0)
Nausea	11 (34.4)
Injection site pruritus	11 (34.4)
Injection site bruising	11 (34.4)
Injection site pain	10 (31.3)
Headache	9 (28.1)
Vomiting	9 (28.1)
Injection site induration	8 (25.0)
Diarrhea	7 (21.9)

AE, adverse event; BBS, Bardet-Biedl syndrome. Safety analysis set, defined as all patients who received ≥1 dose of study drug. **1.** Anaphylaxis while on placebo. **2.** Anaphylaxis (while on placebo); hot flashes, nausea, headaches, vomiting, and abdominal pain; nausea and vomiting. Haws et al. Poster presented at ObesityWeek Annual Meeting; November 1-5, 2021.Data on File.

My Conclusions

1. Obesity and hyperphagia with BBS are serious and severe
2. Clinically meaningful impact with weight loss and hunger reduction
3. Patients report improvements in quality of life
4. Community is waiting for setmelanotide approval

Q&A

Jennifer Chien

Executive Vice President, North America

Commercial Strategy

Rhythm is Commercial Ready

Unmet need in BBS

- Hyperphagia
- Severe obesity
- Co-morbidities
- Current disease management strategies don’t work

Solution

- Address root cause
- Hunger reduction
- Weight loss
- Established safety profile

Rhythm is ready to launch in BBS

- Commercial foundation established
- Experienced commercial team in place
- Road map to patient identification

Ready to launch at PDUFA goal date of March 16

Foundation Set with IMCIVREE Commercial Availability in 2021

Success with IMCIVREE commercial availability:

HCPs and patients recognize the need for IMCIVREE →

IMCIVREE is reimbursed →

Patients remain on IMCIVREE →

Leverage learnings as starting point for BBS launch

Rhythm® PHARMACEUTICALS

Positive Feedback from Many Patients on IMCIVREE

15 year-old girl
Started IMCIVREE July 2021

-45
pounds
weight loss

-0.76
BMI Z score
improvement

- Diets, lifestyle changes: '*Nothing worked*'
- Active water polo now becoming one of the best players on team
- *'Feels fantastic'*

40 year-old woman
Started IMCIVREE October 2021

-25
pounds
weight loss

- Her mood and energy levels have improved
- *'I have a personal trainer now and I'm loving it!'*

Our Commercial Efforts are Led by a Seasoned Team, with Cumulative Experience Across >40 Launches

Sarah Ryan

Vice President of Sales and Marketing

25 YEARS EXPERIENCE

Jamie Petkunas

Vice President of Patient and Customer Services

21 YEARS EXPERIENCE

Rick Norton

Senior Director of Business Operations

26 YEARS EXPERIENCE

Rekha Greaves

Senior Director of Area Development Managers

24 YEARS EXPERIENCE

Jared Pray

Senior Director of U.S. Market Access

18 YEARS EXPERIENCE

ALDURAZYME® (LARONIDASE)

Fabrazyme® agalsidase beta

Cablivi® caplacizumab-yhdp

Tecfidera® (dimethyl fumarate) delayed-release capsules 240 mg

ELOCTATE™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein]

ALPROLIX™ [Coagulation Factor IX (Recombinant), Fc Fusion Protein]

Cerdelga® (eliglustat) capsules

Tracleer® BOSENTAN

Thyrogen® (thyrotropin alfa) for injection

DUPIXENT® (dupilumab) Injection 100mg · 200mg · 300mg

RenVela® sevelamer carbonate

Retavase® (reteplase) for injection

Lumizyme® (alglucosidase alfa)

Caprelsa® (vandetanib) Tablets

KYNAMRO® (mipomersen sodium) injection

HECTOROL® doxercalciferol injection

Diastat® AcuDial™ (diazepam rectal gel) 5 mg/mL

SYNVISC ONE® HYLAN G-F 20

Veltassa® (patiromer) for oral suspension 8.4g | 16.8g | 25.2g

Comprehensive Payer Research Conducted Ahead of Anticipated Launch

In-depth interviews and ad boards with diverse group of commercial, Medicare and Medicaid payers representing approximately

276 million

covered lives

Objectives

- Assess perception of BBS and its burden
- Evaluate product profile
- Expectations on anticipated coverage and expected usage of IMCIVREE in BBS

Market Access: Payers are Receptive to IMCIVREE for BBS

Perception of disease

- Opportunity to educate on BBS
- Extreme burden of hyperphagia differentiating from general obesity
- Recognition of early-onset of obesity and need in pediatric population

Product profile

- Positive perception of overall profile: efficacy and safety
- Understanding the value of treating hyperphagia and obesity

Payer Expectations on Coverage of IMCIVREE for BBS

Anticipated coverage

- Payers currently covering IMCIVREE anticipate covering for BBS upon approval
- Expect prior authorization
- Clear pathway via appeal for those not covering
- Genetic testing may be required by some payers

Payor Information Exchange

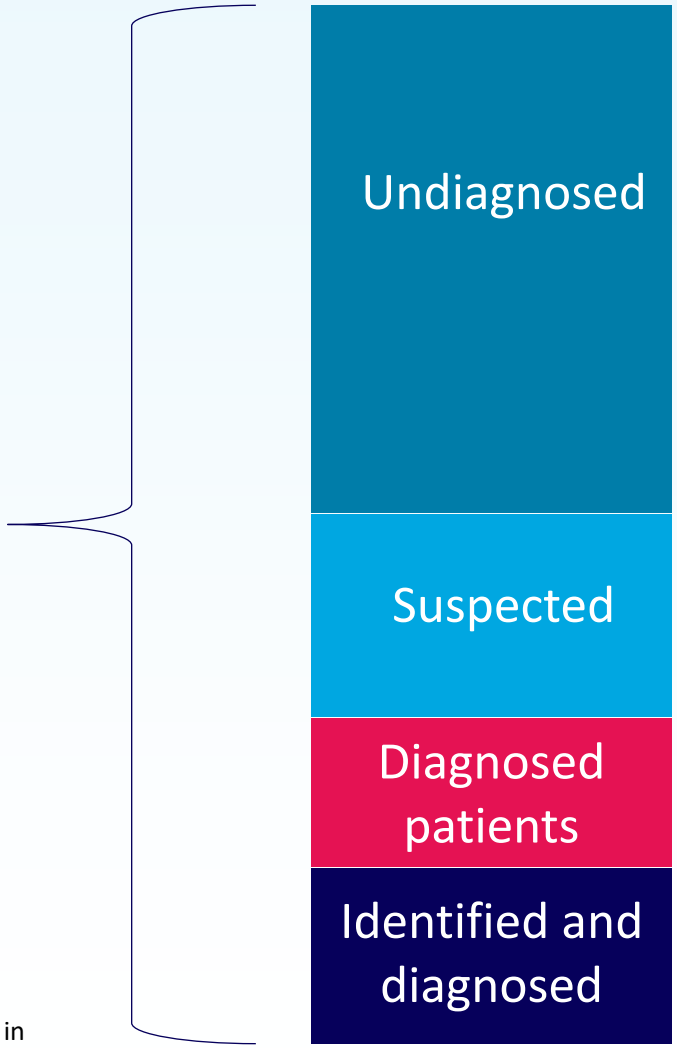
Accounts team engaging with key prioritized payers

High-touch Patient Support Services Pre-diagnosis to Ongoing Therapy

EDUCATION			ACCESS		ONGOING TREATMENT SUPPORT		COMMUNITY
							
Education Programs	Disease Education	Treatment Education	Insurance Support	Co-Pay / PAP for Uninsured	Product/ Injection Training	Adherence Program	Build Support Network

Roadmap to Identifying Patients with BBS

U.S. prevalence estimated to be
1,500 to **2,500**
patients*



>350
Identified and diagnosed patients

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

Rhythm® PHARMACEUTICALS

Rhythm is Commercial Ready

1. Foundation for BBS launch has been set with IMCIVREE commercial availability
2. Strong commercial team in place with deep rare disease and launch experience
3. Payers are receptive to IMCIVREE for BBS with positive coverage expected
4. High-touch Patient Support Services bolsters education, access, compliance and community
5. Territory Managers making solid progress with physician engagement and patient identification

Sarah Ryan

Vice President, Sales & Marketing

U.S. Commercial Launch

Market Insights Drive Launch Strategies for BBS

For physicians:
Assess understanding of MC4R pathway, obesity and hyperphagia, and IMCVIREE

For patients:
Understand their experience with obesity and hyperphagia, and IMCIVREE

Market Insights Inform Launch Focus: Disease Understanding

Health Care Providers:

- Obesity is a significant concern
- Current management options are a challenge
- Need for stronger appreciation of the impact of hyperphagia on patients
- Prefer therapy that targets root cause

Patients and Caregivers:

- Both hyperphagia and obesity viewed as significant factors on health
- Hyperphagia has extreme impact on quality of life
- Searching for treatment that can help

Market Insights Inform Launch Focus: Perceptions of IMCIVREE

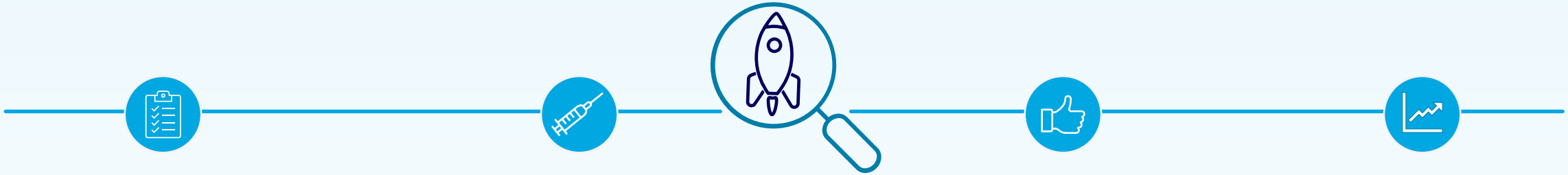
IMCIVREE for HCP:

- Most would prescribe IMCIVREE as first line
- Need for stronger appreciation of hyperphagia data
- No concerns with dosing and safety/tolerability

IMCIVREE for Patient/Caregiver:

- Positive impression of efficacy and safety of IMCVIREE
- Proactive in asking HCP about IMCIVREE
- Very positive impression of hyperphagia data

Focused on Launch Strategies



Solidify the need for treating MC4R-pathway driven hyperphagia and obesity

Establish IMCIVREE as the only appropriate treatment for hyperphagia and obesity

Cultivate a positive experience of IMCIVREE, for both patients and HCPs

Accelerate diagnosis and uncover new patients

Roadmap to Identifying Patients with BBS

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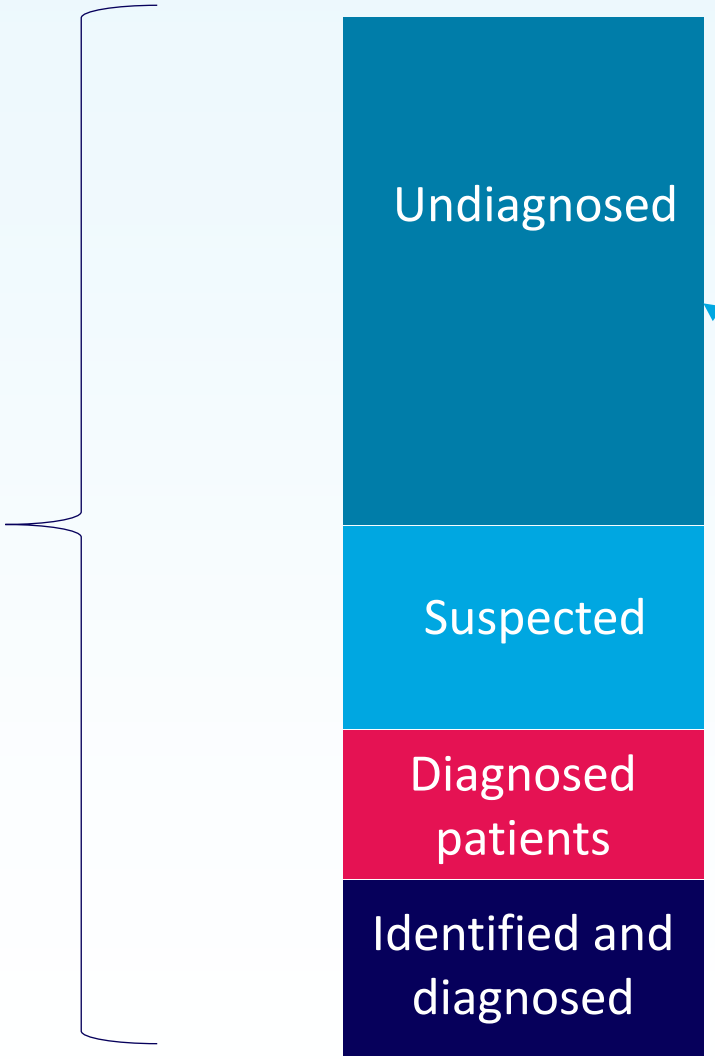

Machine Learning Leads

- ICD 10 code – BBS subcategory, algorithm using BBS symptoms
- Targeted Territory Manager outreach, prioritized by specialty
- Supplemental non-personal digital efforts, specialty focus

Roadmap to Identifying Patients with BBS

U.S. prevalence estimated to be
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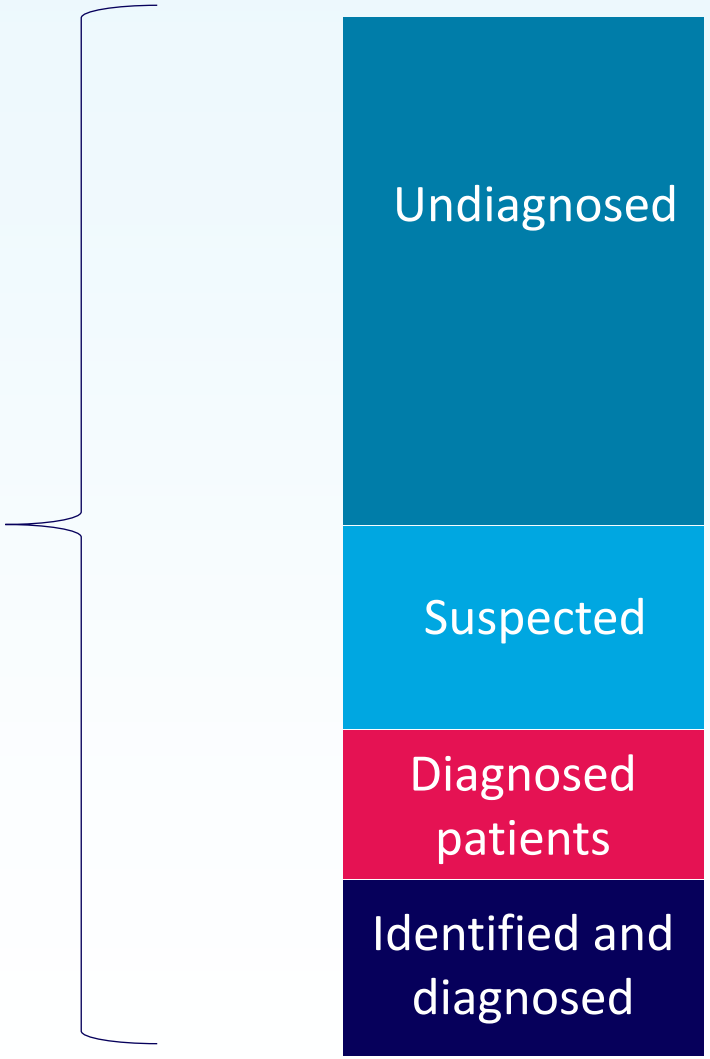
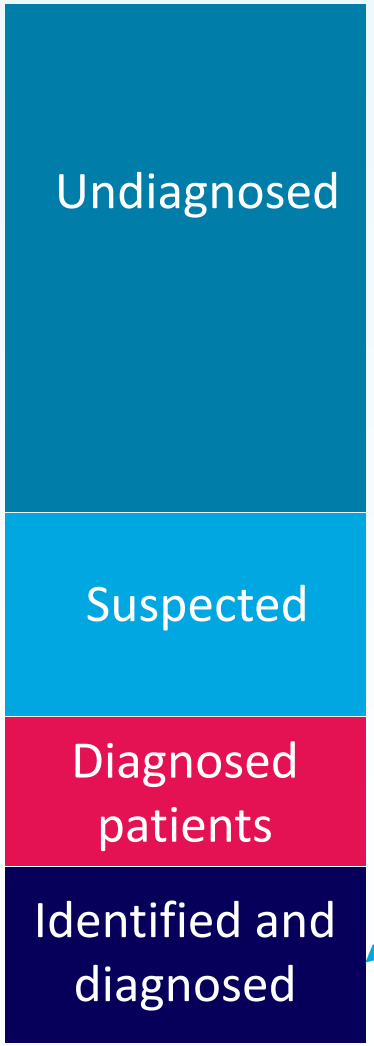


Uncovering Rare Obesity

- Suspected BBS ***or*** early onset obesity and hyperphagia
- Increased genetic testing through education efforts of Area Development Managers
- Territory Manager follow up on BBS biallelic results to educate

Roadmap to Identifying Patients with BBS

U.S. prevalence estimated to be
1,500 to **2,500**
patients



>350 Identified patients with BBS

- Identified and confirmed by field teams
- Focused Territory Manager outreach

Physicians Caring for Identified and Diagnosed Patients with BBS

>350
Identified and diagnosed patients

~150
physicians

65%
Pediatric endocrinologists or endocrinologists

Rhythm's BBS Territory Managers: Profile of Deep Experience

Early success drove field expansion from 12 to 16 Territory Managers

Howard Mannes
US Field Sales Director
West

20
Average years pharma/biotech sales experience

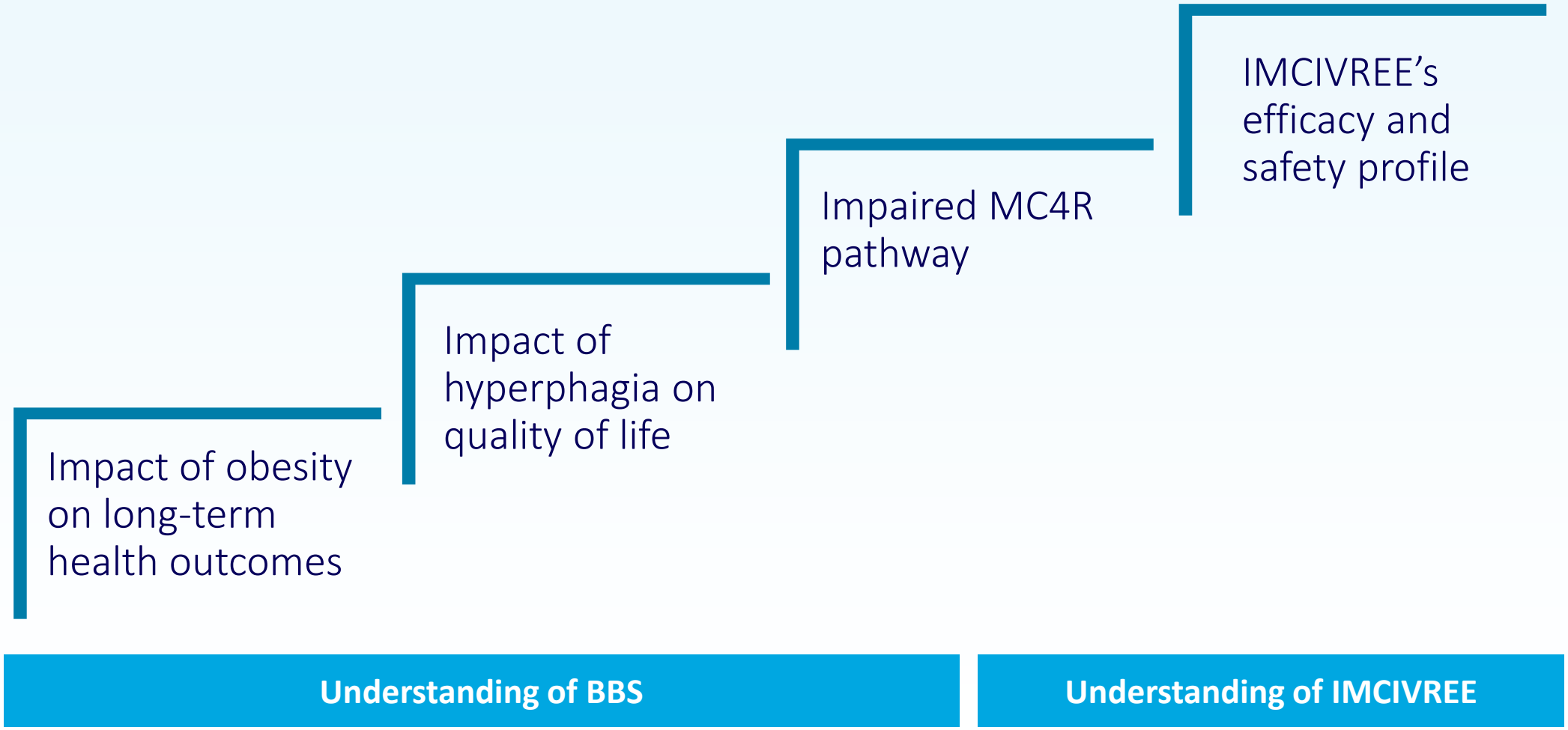
100%
launch experience

6
Average years rare disease experience

6
average number of launches

Ann Hnatishion
US Field Sales Director
East

Territory Managers to Enhance Physician Understanding of BBS and IMCIVREE

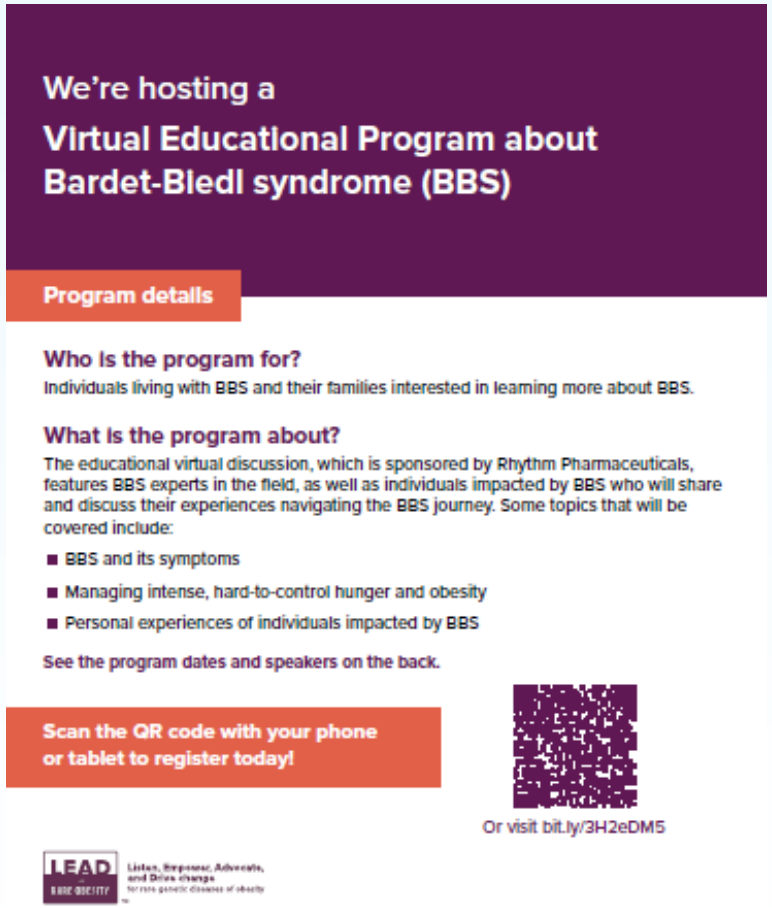


Patient Engagement Focused on Diagnosed Patients/Caregivers

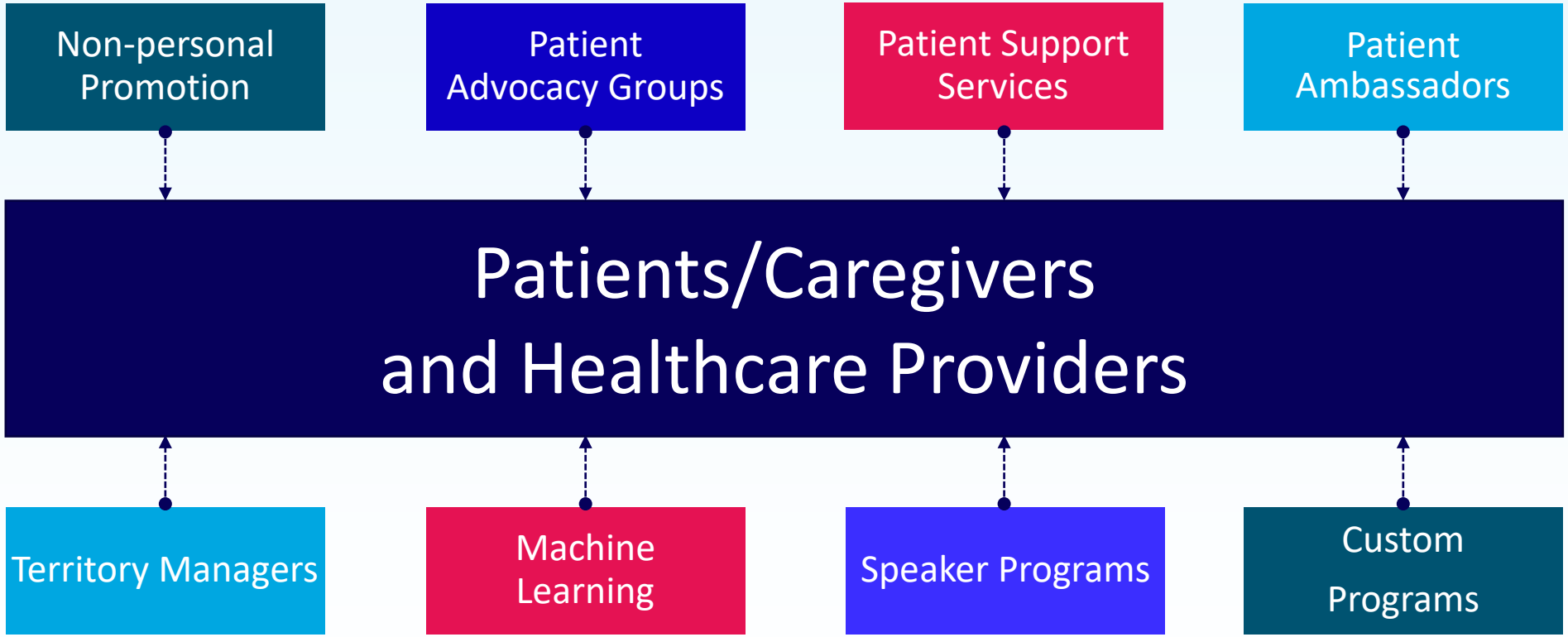
Patient Support Services

Patient Advocacy Groups

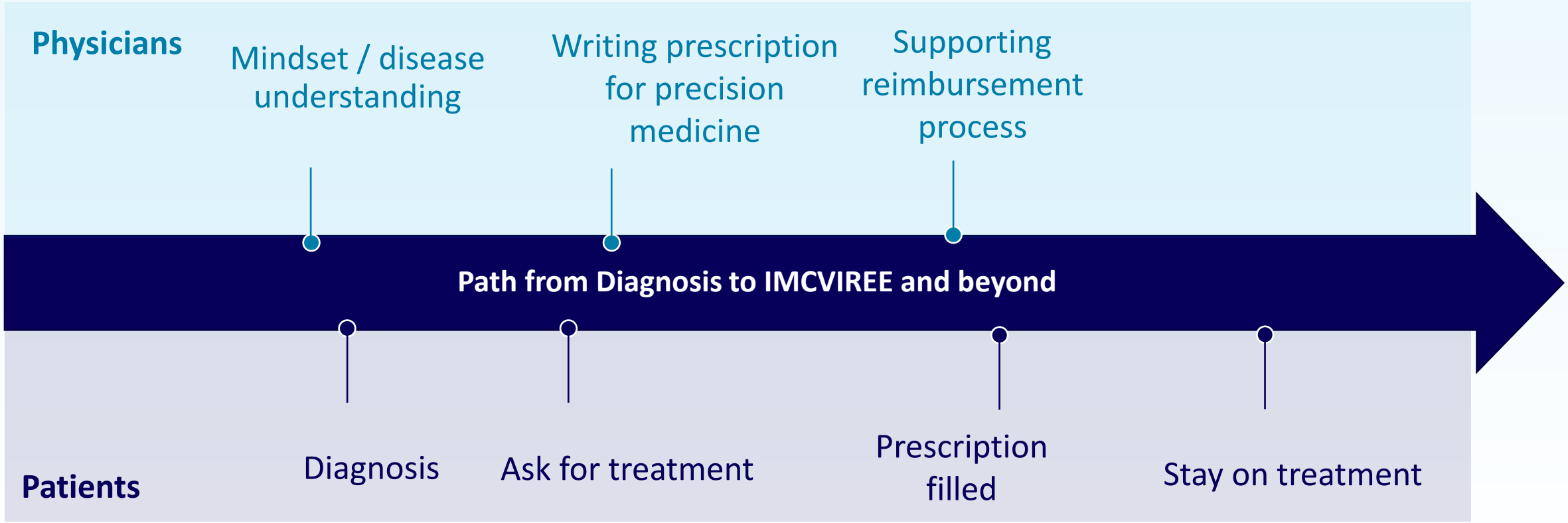
Marketing Educational Programs



Multiple Ongoing Efforts to Reach Patients/Caregivers and Health Care Providers



Launch Strategies and Organizational Focus Support the Journey to IMCIVREE



David Meeker, MD

Chairman, President, & Chief Executive Officer

Closing Thoughts

Rhythm is Commercial Ready

Unmet need in BBS

- Hyperphagia
- Severe obesity
- Co-morbidities
- Current disease management strategies don’t work

Solution

- Address root cause
- Hunger reduction
- Weight loss
- Established safety profile

Rhythm is ready to launch in BBS

- Commercial foundation established
- Experienced commercial team in place
- >350 patients already identified

Ready to launch at PDUFA goal date of March 16

Q&A

Thank you