ENDO 2023

Weight Reduction After 6 Months of Setmelanotide Treatment in Patients With Hypothalamic Obesity

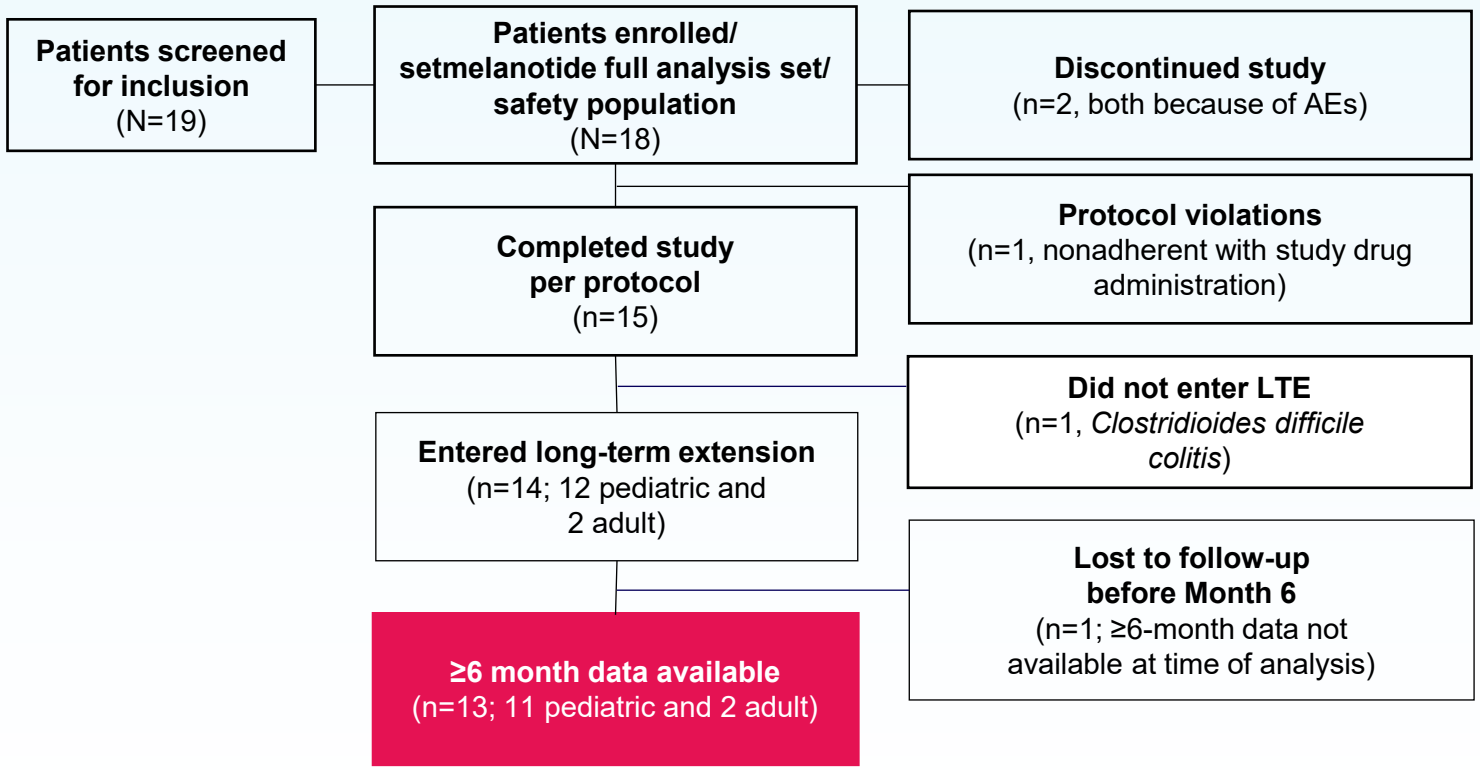
Adapted from a poster presentation delivered during The Endocrine Society Annual Meeting & Expo June 17, 2023 in Chicago

Rhythm PHARMACEUTICALS

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 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 sufficiency of our cash, cash equivalents and short-term investments to fund our operations, and strategy, prospects and plans, including regarding the commercialization of setmelanotide. 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.

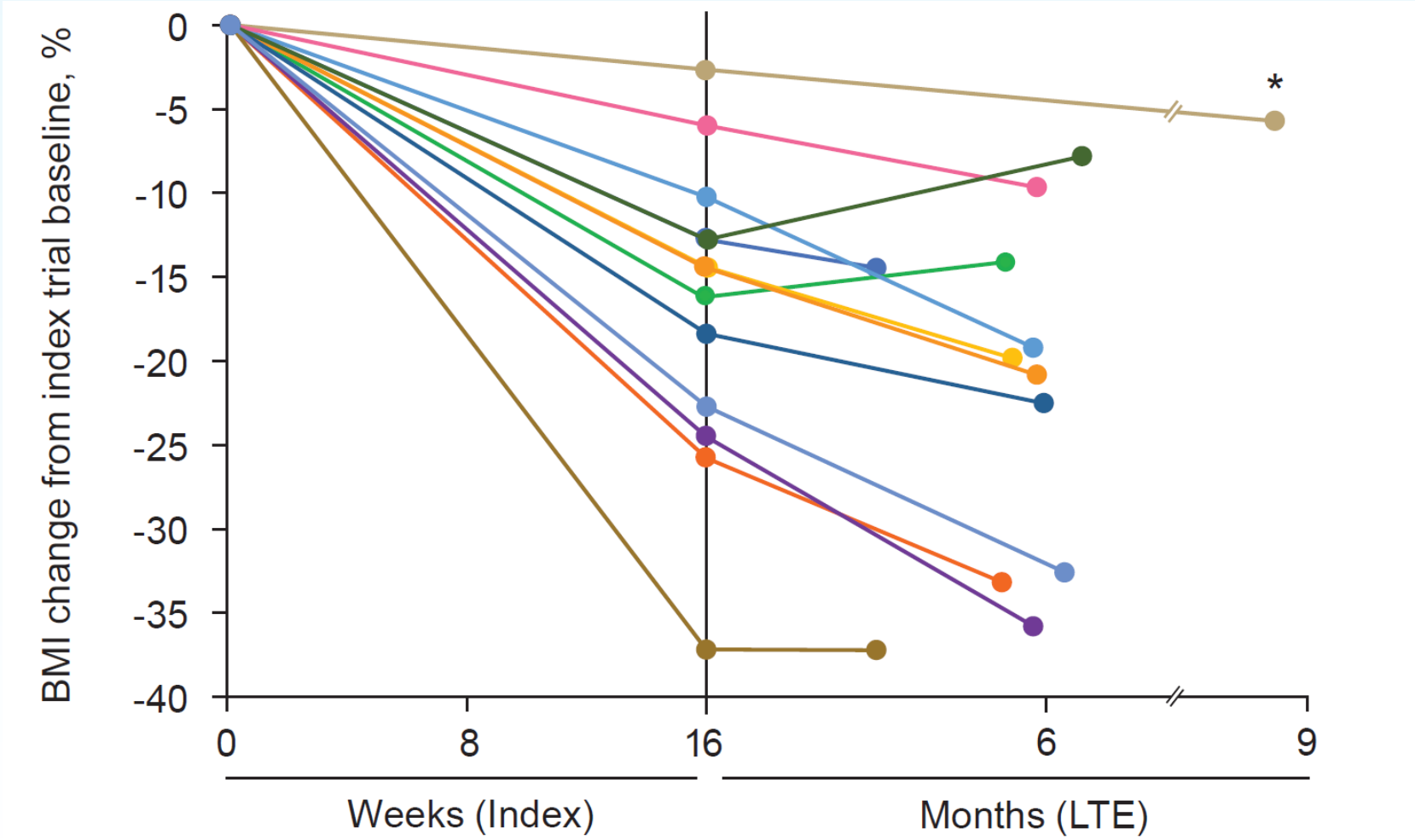
Patient Dispositions: Phase 2 to Open-label, Long-term Extension Trial



Demographics and Baseline Characteristics

	Patients, n (%)
Age	
≥18 years	2 (15.4)
<18 years	11 (84.6)
Males	9 (69.2)
Race	
White	10 (76.9)
Black or African American	2 (15.4)
Native Hawaiian or Other Pacific Islander	1 (7.7)
Ethnicity	
Not Hispanic or Latino	10 (76.9)
Hispanic or Latino	3 (23.1)
Concomitant Medications reported in ≥50% of patients	
Hydrocortisone	11 (84.6)
Levothyroxine	9 (69.2)
Somatropin	9 (69.2)
Desmopressin Acetate	7 (53.8)
Ondansetron*	7 (53.8)
Tumor type	
Craniopharyngioma	11 (84.6)
Hypothalamic hamartoma	2 (15.3)
Juvenile pilocytic astrocytoma	1 (7.7)

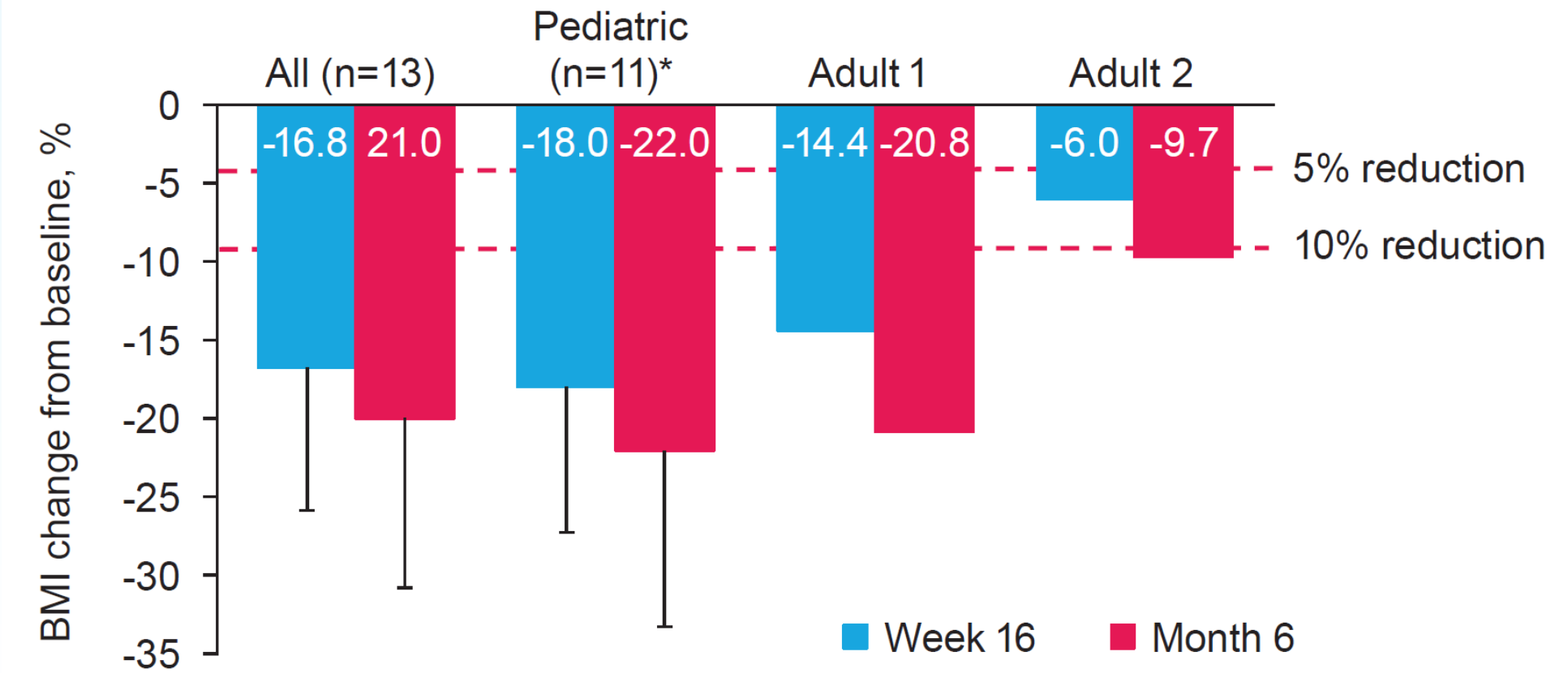
BMI Reduction Consistent and Progressive from Baseline to Week 16 and Month 6



*One patient treated for a hamartoma experienced an increase in BMI during dose escalation in the index trial. This patient's BMI has currently decreased by −5.71% (Month 9); this patient did not have a Month-6 visit. BMI, body mass index; LTE, long-term extension. Data as of Nov. 30, 2022.

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.

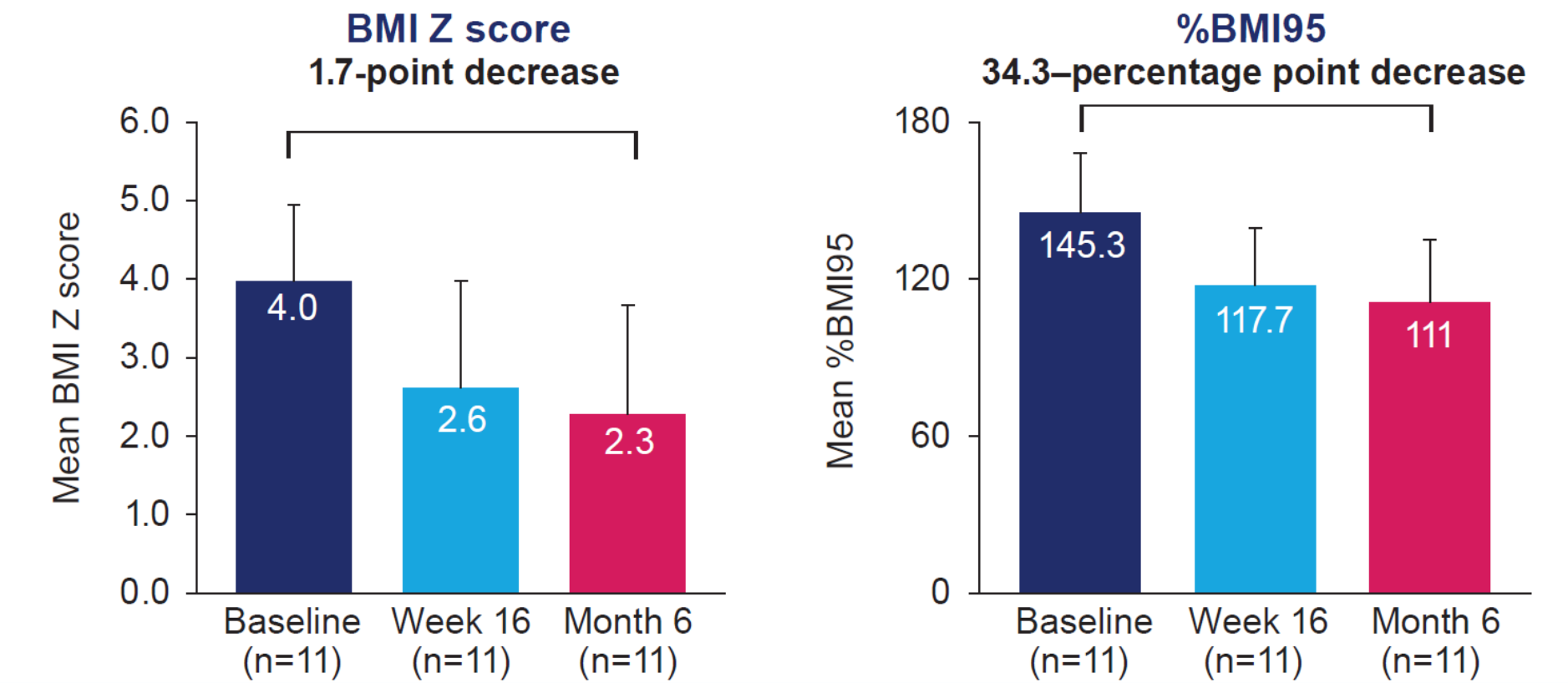
All Patients Achieved Improvement in Severity of Their Obesity

Four out of 11 patients dropped below the 95th Percentile for BMI

BMI, kg/m^2	Adults (n=2)		WHO Classification (NIH[5])	Pediatric patients (n=11)											BMI percentile[6]	
≥50	50		Obesity class III (Extreme)									190			≥140%‡	≥95th percentile
≥45 to <50						157	166						158			
≥40 to <45	40								149	144		143	142	141		
≥35 to <40		38*	Obesity class II (Severe[6])	139	124†	133	130				120				≥120% to <140%§	
≥30 to <35		34	Obesity class I	118	113			109	97						≥95% to <120%¶	
≥25 to <30			Overweight					87		91				94	≥85th to <95th percentile	
<25			Normal weight								74				≥5th to <85th percentile	

*Patient reduced dose because of tolerability in the index trial and then titrated back. †Patient had an increase in BMI during dose titration of the index trial; this patient did not have a Month-6 visit and data shown are Month-9 %BMI95. ‡Or BMI ≥40 kg/m2 (whichever is lower). §or BMI ≥35 to <40 kg/m2 (whichever is lower). ¶or BMI ≥30 to <35 kg/m2 (whichever is lower). %BMI95, percent of the BMI 95th percentile; BMI, body mass index; NIH, National Institutes of Health; SD, standard deviation; WHO, World Health Organization.

Meaningful Reductions in BMI Z Score and Percent of 95th Percentile for BMI



*One pediatric patient did not have a Month-6 visit, and Month-9 data were used for this analysis. Error bars are the standard deviation. %BMI95, percent of the BMI 95th percentile; BMI, body mass index.

Week 16 Body Composition Measures in Pediatric Patients Show Statistically Significant Reductions from Baseline