Transforming the Burden of Hyperphagia in Bardet-Biedl Syndrome: 6-Month Real-World Outcomes for the RESTORE Study

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Background

- Hyperphagia and early-onset obesity contribute to a substantial burden for patients with Bardet-Biedl syndrome (BBS), a rare ciliopathy that results in multi-organ dysfunction[1–2]
- Setmelanotide, a melanocortin-4 receptor (MC4R) agonist, has demonstrated efficacy in improving hunger and weight-related outcomes in patients with BBS by restoring disruption in the MC4R pathway[3]
- RESTORE, an ongoing, prospective longitudinal, observational study assesses the real-world effectiveness of setmelanotide in participants with BBS in United States (US) clinical settings

Objective

- To evaluate the interim real-world participant- and caregiver-reported benefits of setmelanotide on hyperphagia symptoms and impacts, as well as weight management patterns, from the RESTORE study

Methods

Study Population

- Participants aged ≥6 years and caregivers aged ≥18 years in the United States who consented into the Rhythm InTune Patient Support Program, and were prescribed but had not yet initiated setmelanotide treatment at RESTORE enrollment, were included

Data Collection

- Consenting participants completed secure online surveys at baseline (i.e., before setmelanotide initiation) and over the first year of treatment

Outcomes

- Participant demographics, including sociodemographic and clinical characteristics, were collected
- Key outcomes included hyperphagia-related signs and symptoms (i.e., Symptoms of Hyperphagia [SoH] and Impacts of Hyperphagia [IoH] questionnaires) and weight management programs and treatments
  - The SoH consists of 4 items assessing the frequency of hyperphagia symptoms over the previous 24 hours. Scores range from 0–2; higher scores indicate more frequent symptoms recognized by patients
  - The IoH consists of 6 items (2 sections of 5 items for caregiver version) assessing the extent to which hyperphagia negatively impacts a patient's life over the past 7 days. Scores range from 0–3, higher scores indicate greater negative impact of hyperphagia

Results

Participant Baseline Characteristics

- As of December 2025, a total of 22 participants were actively taking setmelanotide and completed a survey at Month 6
- The mean age (standard deviation [SD]) of participants at study enrollment was 32.8 (15.0); most were female (77.3%) (**Table 1**)
  - Additional demographic and clinical characteristics in participants who completed a baseline survey have been presented previously[4]

Clinical Characteristics

- Hyperphagia was highly prevalent (90.9%) and the most reported BBS manifestation, followed by ataxia/poor coordination (45.5%), and developmental delay (31.8%; **Table 1**)
  - Among self-reporting adult participants (n=15), 10 (66.7%) had visual impairment

Table 1: Participant Baseline Characteristics

	Study Population (N=22)*
Age (SD)	32.8 (15.0)
Sex at birth, n (%)	
Male	5 (22.7)
Female	17 (77.3)
Top BBS-related manifestations†	
Hyperphagia	20 (90.9)
Ataxia or poor coordination	10 (45.5)
Developmental delay	7 (31.8)
Common comorbidities, n (%)†	
Anxiety/depression	14 (63.6)
Seasonal allergies	10 (45.5)
Sleep apnea	10 (45.5)
Hypertension	7 (31.8)

*Of the 22 participants, 15 adults and 2 adolescents were able to self-report; †Values may not add up to 100% as participants may fall under more than one category.
BBS, Bardet-Biedl syndrome; SD, standard deviation.

Symptoms and Impacts of Hyperphagia (Participant-Reported)

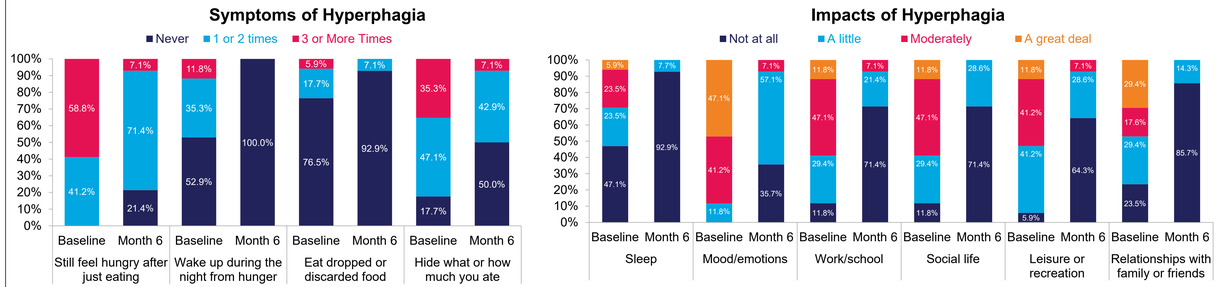
- Self-reporting participants with hyperphagia (n=17) experienced rapid and sustained reductions in hyperphagia symptoms/behaviors (SoH baseline mean: 0.9; Month 1: 0.3; Month 6: 0.4)

Results (continued)

Symptoms and Impacts of Hyperphagia (Participant-Reported, Continued)

- After one month of setmelanotide treatment, 90.0% of participants reported no "waking up during the night from hunger" and "eating dropped/discarded food," which increased to 92.9% six months after setmelanotide initiation (**Figure 1**)
- The most improved symptoms/behaviors were "feeling hungry after just eating" and "hiding what/how much you were eating"
- There were also substantial, sustained reductions in the negative impacts of hyperphagia (IoH baseline mean: 1.6; Month 1: 0.4; Month 6: 0.3 [**Figure 1**])
  - All domains were improved, with the greatest benefits in "mood/emotions," "work/school," and "social life"

Figure 1: SoH and IoH Self-Report Item Responses at Baseline and Month 6

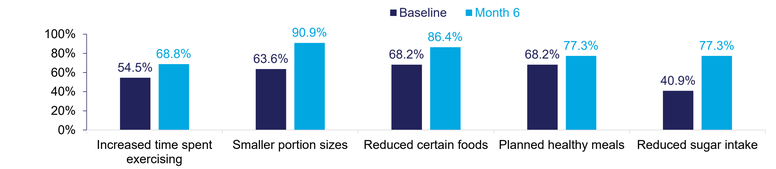


IoH, Impacts of Hyperphagia; SoH, Symptoms of Hyperphagia.

Weight Management Treatments

- There was a 25.0% reduction in the number of participants using other obesity medications* after 6 months of setmelanotide
- Participants also reported increases in salutary diet and lifestyle modifications after initiating setmelanotide (**Figure 2**)

Figure 2: Diet and Lifestyle Modifications at Baseline and Month 6



Conclusions

- **The value of early setmelanotide initiation is demonstrated in real-world practice, where patients experience rapid and durable reductions in hyperphagia, resulting in improved health-related quality of life**

*Other obesity medications included Qsymia, Contrave (naltrexone/bupropion), Saxenda (liraglutide), Xenical/Alli (orlistat), Wegovy (semaglutide), metformin, Ozempic (semaglutide), Zonegran (zonisamide), Trulicity (dulaglutide), Mounjaro (tirzepatide).

Disclosures: CH and **UGM** are employees of Rhythm Pharmaceuticals, Inc. and receive stock or stock options with Rhythm Pharmaceuticals, Inc; **BS** is a consultant for Rhythm, Novo Nordisk; speaker for Rhythm, a site PI for Emanate and collaborator on Rhythm sponsored research; **JP** receives research support from Rhythm Pharmaceuticals, Inc. as a co-investigator for the Setmelanotide Phase 2 Treatment of Obesity in Rare Genetic Disorders (ClinicalTrials.gov Identifier NCT03013543) and as a co-investigator of a study examining unmet medical needs related to obesity in people with Bardet–Biedl syndrome; **SZ**, **JL**, and **MY** are employees of Analysis Group Inc., which received funding from Rhythm Pharmaceuticals to support this research; **AMH** received grants from the Weston Family Microbiome Initiative and Canadian Institutes of Health Research, is a member of advisory boards for Rhythm Pharmaceuticals and the 2023 Novo Nordisk Pediatric Expert Obesity National advisory board and is member of clinical advisory boards for the Foundation for Prader-Willi Research USA.

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References: 1. Pomeroy J, et al. *Pediatr Obes.* 2021;16(2):e12703; **2.** Beales PL, et al. *Obes Rev.* 2025;26(7):e13915; **3.** Haqq AM, et al. *Lancet Diabetes Endocrinol.* 2022;10(12):859–868; **4.** Huber C, et al. *Value Health.* 2025;28(6):S339–S340.