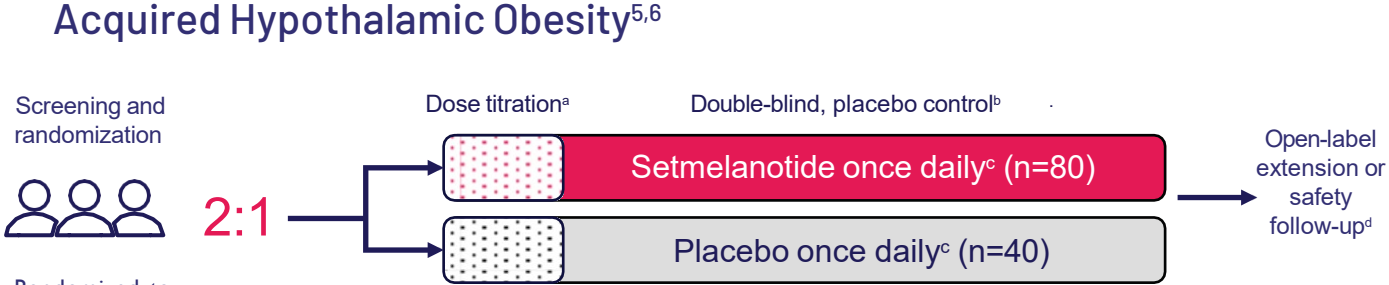
Acquired Hypothalamic Obesity

Accelerated and sustained weight gain due to decreased energy expenditure and hyperphagia observed in hypothalamic obesity are often refractory to traditional weight management strategies[1,2] Setmelanotide is an MC4R agonist being studied for its effect on weight and hunger in patients with MC4R pathway diseases[3,4]

A Phase 3, Double-Blind, Randomized, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Setmelanotide in Patients With Acquired Hypothalamic Obesity[5,6]



[a]The initial dose of 0.5 mg is to be escalated in increments of 0.5 to 1.0 mg until the patient reaches an individual therapeutic regimen based on age and weight. [b]Patients completing the trial may be eligible to participate in an open-label LTE trial. [c]Subcutaneous injection. [d]The safety follow-up visit is required only for patients prematurely discontinuing treatment or those completing the trial who do not enroll in the LTE.

Key Eligibility Criteria[5,6]

KEY INCLUSION CRITERIA

- ≥4 years of age
- Documented evidence of acquired hypothalamic obesity, defined as
  - Diagnosis of craniopharyngioma or other brain lesion affecting the hypothalamic region with treatment (ie, surgery, chemotherapy, radiation) received ≥6 months before screening
  - Documented injury to the hypothalamus ≥6 months before screening for which surgery or radiation is not indicated
- Documented weight gain associated with hypothalamic injury (before or after therapy), and
  - BMI ≥30 kg/m^2 for those aged ≥18 years
  - BMI ≥95th percentile for age and sex for those aged <18 years

KEY EXCLUSION CRITERIA

- Diagnosis of PWS or ROHHADNET syndrome
- Obesity due to genetic or syndromic conditions before hypothalamic injury
- Weight loss in the prior 3 months
  - >2% reduction in body weight for those aged ≥18 years
  - >2% reduction in BMI for those aged <18 years
- Bariatric surgery or procedure within the last 2 years
- HbA_{1c} >11.0%
- Significant dermatologic findings relating to melanoma, or a history or close family history of skin cancer or melanoma
- Severe psychiatric disorder or major depressive disorder

BMI, body mass index; GFR, glomerular filtration rate; HbA1c, glycated hemoglobin; LTE, long-term extension; PWS, Prader-Willi syndrome; ROHHADNET, rapid-onset obesity with hypoventilation, hypothalamic dysfunction, autonomic dysregulation, and neuroendocrine tumor.

US-IC1-2400037(01.01/2025)

Key Endpoints[5,6]

Approximately 120 patients enrolled across **28 sites globally**

PRIMARY ENDPOINT[a]:

- Mean percentage change in BMI

KEY SECONDARY ENDPOINTS[a]:

- Composite proportion of patients with ≥5% reduction in BMI (≥18 years of age) and BMI z-score reduction of ≥0.2 points (<18 years of age)
- Proportion of all patients with ≥5% reduction in BMI
- Mean change in weekly average of daily most hunger score in those aged ≥12 years

Safety and tolerability will be assessed by the frequency and severity of adverse events, as well as changes in ambulatory blood pressure and heart rate

[a]After 52 weeks of setmelanotide vs placebo.

Expected Trial Completion Date: April 2025[5]

- For additional trial information, including a list of eligibility criteria and endpoints, please visit https://clinicaltrials.gov/ct2/show/NCT05774756
- For questions about the trial, please contact us at clinicaltrials@rhythmtx.com

Scan to view the ClinicalTrials.gov page

References

1. Abuzzahab MJ, et al. *Horm Res Paediatr*. 2019;91(2):128-136.
2. van Iersel L, et al. *Endocr Rev*. 2019;40(1):193-235.
3. Clément K, et al. *Lancet Diabetes Endocrinol*. 2020;8(12):960-970.
4. Haqq AM, et al. *Lancet Diabetes Endocrinol*. 2022;10(12):859-868.
5. ClinicalTrials.gov identifier: NCT05774756. Accessed November 22, 2024. https://clinicaltrials.gov/ct2/show/NCT05774756
6. Roth CL, et al. Poster presented at: The Endocrine Society Annual Meeting; June 15-18, 2023; Chicago, IL. Poster FRI-065.

US-IC1-2400037(01.01/2025)