Rhythm Announces New England Journal of Medicine Publication of Setmelanotide Phase 2 Data for Treatment of POMC Deficiency Obesity

July 20, 2016 2:49 PM ET

Significant weight loss with targeted treatment for patients with rare genetic defect in critical weight regulation pathway

- View Abstract
- View Editorial

BOSTON, July 20, 2016— Rhythm, a biopharmaceutical company developing peptide therapeutics for rare genetic deficiencies that result in life-threatening metabolic disorders, today announced that the *New England Journal of Medicine* (NEJM) has published Phase 2 data on setmelanotide, the company's novel melanocortin 4 receptor (MC4R) agonist, for the treatment of pro-opiomelanocortin (POMC) deficiency obesity, a rare genetic disorder associated with severe, early-onset obesity and unrelenting hyperphagia. In January 2016, the FDA granted Breakthrough Therapy designation (BTD) to setmelanotide for the treatment of POMC deficiency obesity, the first BTD to be awarded by FDA's Division of Metabolism and Endocrinology Products.

The NEJM publication reports initial data for two patients in the Phase 2 non-randomized, open label clinical trial of setmelanotide for the treatment of POMC deficiency obesity, an ultra-orphan disease that we believe affects an estimated 100-500 people worldwide. This trial evaluated the safety and efficacy of setmelanotide administered once daily by subcutaneous injection. The NEJM presented results from this investigator-initiated, open-label study in which patients had substantial and sustainable reduction of hunger and weight:

—Both patients enrolled in the study had extreme, early-onset obesity and severe hyperphagia, along with elevated insulin levels suggestive of severe insulin resistance. Patient 1 was 21 years old with a compound heterozygous loss of function POMC gene mutation, and Patient 2 was 26 years old with a homozygous POMC mutation.

—With setmelanotide treatment, Patient 1 lost 112.4 lbs over 42 weeks, from a baseline weight of 341.7 lbs, and Patient 2 lost 45.2 lbs over 12 weeks, from a baseline weight of 336.9 lbs. Also, pre-study elevated insulin levels decreased substantially with setmelanotide treatment. Both patients continue in treatment.

—Both patients experienced substantial reductions in hunger with hunger scores from baseline scores of 9-10 (using a Likert score 0-10; 0 being no hunger and 10 being extreme hunger) to 0-1, reversing their hyperphagia.

—Resting energy expenditure normalized for lean body mass did not change dramatically during the study despite substantial weight loss. As a result, in association with the marked reduction in appetite, there was a steady and sustained weight loss in both patients that averaged between 3.75 to 4.4 lbs per week with setmelanotide treatment. This loss was mainly due to loss of body fat.

—Setmelanotide was well tolerated with no serious adverse events reported.

"These results provide further validation of the critical role of the MC4 pathway in weight regulation and the potential for setmelanotide to restore lost activity in this pathway by bypassing upstream defects of MC4R and by activating the MC4 pathway below such defects. In this way, setmelanotide may serve as replacement therapy to reestablish weight and appetite control in patients with POMC deficiency and potentially other genetic disorders associated with obesity," said Peter Kühnen, M.D., Institute for Experimental Pediatric Endocrinology, Charité Universitätsmedizin Berlin, Germany, lead investigator in the trial and lead author of the publication.

"By targeting replacement therapy for the treatment of MC4 pathway deficiencies, setmelanotide represents a new and highly promising approach to the treatment of obesity associated with POMC deficiency and potentially other genetic disorders," said Keith Gottesdiener, CEO of Rhythm. "We look forward to advancing the development program for

setmelanotide and are grateful to our investigators and the participants in our clinical trial for their dedication and commitment to this important research effort."

Rhythm is also conducting a Phase 2 clinical trial for setmelanotide in the treatment of Prader-Willi syndrome (PWS), another rare genetic disorder that causes life-threatening obesity. The company expects to soon expand setmelanotide development to include two other MC4 pathway disorders, LepR deficiency obesity, where patients have two defective leptin receptor genes, and POMC heterozygous deficiency obesity, where patients have only one normal copy of either the POMC or PCSK-1 gene. Both disorders represent areas of high unmet need with no approved or effective therapies available to patients.

About Setmelanotide

Setmelanotide is a potent, first-in-class MC4R agonist in development for the treatment of obesity caused by genetic deficiencies in the MC4 pathway, a key pathway in humans that regulates energy expenditure, homeostasis, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway result in early-onset and severe obesity. In addition to the Phase 2 trial for POMC described, a second Phase 2 setmelanotide trial is ongoing for the treatment of Prader-Willi syndrome (PWS), a rare genetic disorder that causes unrelenting hyperphagia and life-threatening obesity. Recent scientific evidence implicates defects in the MC4 pathway as the likely cause of the weight and appetite abnormalities in PWS.

About POMC Deficiency Obesity

POMC deficiency obesity is a life-threatening ultra-orphan disease, with approximately 50 patients reported to date, though we estimate that actual prevalence of this disorder could be between 100 and 500 patients worldwide. Patients with POMC deficiency have unrelenting hyperphagia that begins in infancy, and they develop severe, early-onset obesity. POMC deficiency obesity results from two different homozygous genetic defects, both upstream (which refers to the relative position of the defect earlier in the pathway) of the MC4 receptor. Currently, there is no approved treatment for the obesity and hyperphagia associated with POMC deficiency obesity.

About Rhythm (www.rhythmtx.com)

Rhythm is a biopharmaceutical company focused on developing peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Rhythm's lead peptide product candidate is setmelanotide, a first-in-class melanocortin 4 receptor (MC4R) agonist for the treatment of rare genetic disorders of obesity. Rhythm also supports The Genetic Obesity Project (www.GeneticObesity.com) which is dedicated to improving the understanding of severe obesity that is caused by specific genetic defects. The company is based in Boston, Massachusetts.