Rhythm Starts Phase 3 Clinical Trial of Setmelanotide for Rare Genetic Disorder of Obesity

May 4, 2017

BOSTON, May 4, 2017—Rhythm, a biopharmaceutical company developing peptide therapeutics for rare genetic deficiencies that result in life-threatening metabolic disorders, today announced the initiation of a Phase 3 clinical trial to evaluate the safety and efficacy of setmelanotide, the company's first-in-class melanocortin-4 receptor (MC4R) agonist, for the treatment of pro-opiomelanocortin (POMC) deficiency obesity, an ultra-rare genetic disorder associated with severe, early-onset obesity and unrelenting, abnormally increased appetite (hyperphagia).

Rhythm is developing setmelanotide for the treatment of obesity caused by genetic deficiencies in the MC4 pathway, a key biological pathway in humans that regulates weight by increasing energy expenditure and reducing appetite.

This Phase 3 registration trial is an open-label, single-arm, multinational trial to evaluate the safety and efficacy of setmelanotide in patients with POMC deficiency obesity, with setmelanotide administered once daily by subcutaneous injection for 12 months.

"In POMC deficiency obesity, setmelanotide has the potential to restore lost function in the MC4 pathway to treat the life-threatening obesity and unrelenting hunger that afflicts people with this genetic disorder," said Keith Gottesdiener, CEO of Rhythm. "We are working closely with the FDA under the Breakthrough Therapy designation and with investigators to advance setmelanotide clinical development with urgency."

About POMC Deficiency Obesity
POMC deficiency obesity is a life-threatening orphan disease for which we estimate the prevalence to be between 100 and 500 patients in the U.S. 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 of the MC4 receptor. Currently, there is no approved treatment for the obesity and hyperphagia associated with POMC deficiency obesity.

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 biological pathway in humans that regulates weight by increasing energy expenditure and reducing 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 2016, *The New England Journal of Medicine* reported results from a setmelanotide Phase 2 trial in POMC deficiency obesity that demonstrated substantial weight loss in two adult patients. At ObesityWeek 2016, investigators presented initial data for the first patient enrolled in a Phase 2, open-label clinical trial of setmelanotide for the treatment of leptin receptor (LepR) deficiency obesity. Both POMC and LepR deficiency obesity are rare genetic disorders associated with severe, early-onset obesity and unrelenting hyperphagia. The initial efficacy data with setmelanotide in these disorders demonstrate that setmelanotide has the potential to provide meaningful efficacy in genetic forms of obesity due to MC4 pathway deficiency by restoring absent LepR-POMC signaling. The company is currently evaluating setmelanotide for the treatment of the following genetic disorders of obesity: POMC deficiency obesity, LepR deficiency obesity, Prader-Willi syndrome, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.

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 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.