Rhythm Expands Phase 2 Clinical Trials of Setmelanotide to the Treatment of Bardet-Biedl Syndrome Obesity

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— Rare genetic disorder causes severe obesity and hyperphagia —

BOSTON, May 17, 2017—Rhythm today announced the expansion of the company's Phase 2 clinical trials of setmelanotide to the treatment of Bardet-Biedl syndrome (BBS) obesity. Setmelanotide is a potent, first-in-class melanocortin-4 receptor (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.

"Bardet-Biedl syndrome affects vision, kidney function, and other organs—but the obsessive appetite without relief, along with the burden of obesity, are often the most important issues for people living with this condition, including many of our patients," said Robert Haws, MD, Medical Director of Clinical Research at the Marshfield Clinic Research Foundation and an investigator for the study. "We are therefore very excited about the setmelanotide study as a potential treatment for this condition."

This initial study is an open-label, Phase 2 clinical trial of setmelanotide for the treatment of BBS obesity. The clinical trial will evaluate the safety and efficacy of setmelanotide administered once daily by subcutaneous injection in patients with BBS obesity.

"Patients with Bardet-Biedl syndrome suffer from devastating symptoms, with no approved treatment for the obesity and hyperphagia caused by this genetic disorder," said Keith Gottesdiener, CEO of Rhythm. "We are very pleased to expand the setmelanotide clinical program to Bardet-Biedl, and we are hopeful that this trial supports its potential to improve the lives of patients living with this rare genetic disorder."

About Bardet-Biedl Syndrome
Bardet-Biedl syndrome (BBS) is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in one hundred thousand in North America, which we estimate has an addressable patient population of approximately 1,500 to 2,500 patients in the United States. BBS is a monogenic disorder that causes severe obesity and hyperphagia (extreme, unrelenting hunger) as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. Recent scientific studies identify deficiencies affecting the MC4 pathway as a potential cause of the obesity and hyperphagia associated with BBS.

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 pro-opiomelanocortin (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 for genetic disorders that result in defects in the MC4 pathway that are upstream of melanocortin-4 receptor (MC4R), restoring lost function by activating the intact MC4 pathway below the genetic defect. 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. Rhythm recently initiated a Phase 3 clinical trial of setmelanotide in 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 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.