

## **Rhythm Presents Clinical Data that RM-493 Increases Energy Expenditure in Obesity Study**

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*BOSTON, June 23, 2014*—Rhythm announced today the presentation of results from a clinical trial that evaluated the effect of RM-493, the company’s novel melanocortin 4 receptor (MC4R) agonist, on resting energy expenditure in obese subjects. Analysis of the data indicates that RM-493 increased resting energy expenditure significantly in this trial. The study results were presented by Monica Skarulis, MD, an investigator at the National Institutes of Health (NIH), at the joint meeting of the International Society of Endocrinology and the Endocrine Society (ICE/ENDO 2014) on June 22nd in Chicago.

“This is the first human study to test the hypothesis that an MC4R agonist increases energy expenditure,” said Monica Skarulis, MD, investigator at the NIH. “The drug’s effect was significant with short-term treatment and has the potential to be clinically meaningful for treating obesity.”

There is compelling scientific evidence that when dieting causes weight loss, the body tries to regain the weight by decreasing energy expenditure. In effect, changes in metabolic rate can make it difficult to maintain the weight loss. Accordingly, approaches to the management of obesity that target decreasing food intake along with increasing the metabolic rate have the potential to improve treatment.

“These study results are exciting clinical support for the mechanisms underlying RM-493’s efficacy for weight loss that we have seen in preclinical studies,” said Keith Gottesdiener, MD, CEO of Rhythm. “It is well known that the MC4 receptor modulates weight through a combination of effects on food intake and energy homeostasis. But this is the first time that administration of an MC4 product candidate has demonstrated a substantive effect on energy expenditure in obese patients.”

### **Study Results**

A total of 12 obese but otherwise healthy individuals were randomized and completed both RM-493 and placebo periods in this double-blind, placebo-controlled, two-period crossover study to evaluate the effects of RM-493 on resting energy expenditure. In the oral presentation, “A Randomized, Double-Blind, Placebo-Controlled, Crossover Study to Evaluate the Effect of a Melanocortin Receptor 4 (MC4R) Agonist, RM-493, on Resting Energy Expenditure (REE) In Obese Subjects,” Dr. Skarulis presented data showing that RM-493 increased resting energy expenditure vs. placebo by 6.4%.

### **Study Design**

The trial was a randomized, double-blind, placebo-controlled, two-period crossover study in 12 obese individuals to assess the effects of RM-493 on resting energy expenditure measured in a room calorimeter. The primary outcome measure was resting energy expenditure measured in a room calorimeter on the third day of treatment with either RM-493 or placebo.

### **About RM-493**

RM-493 is a small-peptide melanocortin 4 receptor (MC4R) agonist that is in Phase 2 clinical development for the treatment of obesity, including for obesity caused by genetic deficiencies in the MC4 pathway. The MC4 receptor mediates a key pathway in humans that regulates energy homeostasis and food intake. The MC4 pathway is well validated in humans; loss-of-function mutations of MC4R are associated with obesity and have a reported prevalence of 4%-6% in severe obesity. In the population with a genetic deficiency in the MC4 pathway, RM-493 may restore MC4 function by increasing activity in the one healthy copy of MC4R.

### **About Rhythm**

Rhythm is a biotechnology company developing peptide therapeutics that address unmet needs in metabolic diseases. Rhythm is developing the ghrelin peptide agonist, relamorelin (RM-131), for the treatment of diabetic gastroparesis and other gastrointestinal functional disorders; and the MC4R peptide agonist, RM-493, for obesity and diabetes. Rhythm

investors include MPM Capital, New Enterprise Associates, Third Rock Ventures, Ipsen, and Pfizer Ventures. The company is based in Boston, Massachusetts.

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