

## **Rhythm Initiates Clinical Trial of RM-493 for Obesity Caused by Genetic Variant**

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—Personalized medicine approach to treat obesity caused by MC4R genetic deficiency—

*BOSTON, September 24, 2013*— Rhythm announced today the initiation of the first of a series of clinical trials with RM-493, the company’s novel melanocortin 4 receptor (MC4R) agonist, for the treatment of obesity in individuals with a genetic deficiency in the MC4R pathway.

“Genes with loss of function in the MC4 pathway result in severe obesity, with a prevalence that may exceed one million people in the U.S.,” said Sadaf Farooqi, PhD, FRCP, FMedSci, Wellcome Trust Senior Clinical Fellow and Professor of Metabolism and Medicine, University of Cambridge. “This RM-493 clinical trial is a new approach that targets the root cause of obesity in the MC4 heterozygote population. I am excited to be working with Rhythm on this important project.”

MC4R deficiency due to mutations in the MC4R gene has been identified as the most common monogenic cause of obesity. Up to 6% of people with a BMI >35 have MC4R deficiency, and this group has a higher predisposition than the general population for severe obesity and its complications, such as diabetes. MC4R deficiency also correlates with early-onset obesity, which lengthens exposure to the risk of obesity-associated diseases. Furthermore, MC4R deficiency may also undermine the beneficial effects of diet and exercise for weight loss, limiting treatment options for these individuals.

This first MC4R deficiency trial is a Phase 1B study designed to evaluate the effect of RM-493 on weight loss and safety in obese patients with a loss-of-function variant of the MC4R gene. Patients will be treated for up to four weeks with RM-493. This study expands on Rhythm’s ongoing Phase 2 clinical program for RM-493 for the treatment of obesity.

“RM-493 has demonstrated impressive efficacy on weight loss in both preclinical studies and early clinical trials in subjects with normal, fully functioning MC4R genes,” said Keith Gottesdiener, MD, CEO of Rhythm. “This new clinical study is a personalized medicine approach to the treatment of obesity in people with a poorly functioning MC4R gene and has the potential to restore function in this pathway and improve weight regulation. We are excited about the potential to address this significant unmet need in metabolic disease.”

### **About RM-493**

RM-493 is a small-peptide melanocortin 4 receptor (MC4R) agonist that is in clinical development for the treatment of obesity and diabetes. The MC4 receptor mediates a key pathway in humans that regulates energy homeostasis and food intake. The MC4R 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 MC4R heterozygote population, RM-493 may restore MC4R function by increasing activity in the one healthy copy of MC4R.

### **About Obesity and Diabetes**

More than 78 million U.S. adults and 12.5 million U.S. children and adolescents are obese. Obesity is also a risk factor for the development of diabetes and is likely the critical factor in the 25% increase in the prevalence of diabetes over the past 20 years. Of the 24 million people with diabetes in the U.S., two-thirds have a body mass index (BMI) exceeding 27. The World Health Organization forecasts the prevalence of both obesity and diabetes to double worldwide over the next 20 years, with substantial health and economic impact.

### **About Rhythm**

Rhythm is a biotechnology company developing peptide therapeutics that address unmet needs in metabolic diseases. Rhythm is developing the ghrelin peptide agonist, RM-131, for the treatment of diabetic gastroparesis and other GI 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.