Rivus Pharmaceuticals Announces Positive Data from Phase 2a Clinical Trial of Lead Candidate HU6, Demonstrating Fat Reduction and Weight Loss in High BMI Participants

Met primary endpoint (liver fat reduction), multiple secondary endpoints (whole body, visceral, subcutaneous fat loss)

Significant fat selective weight loss while preserving muscle mass, without changes in diet or exercise

Amplified weight and fat loss in patients with elevated HbA1c

Improvement in key markers of insulin resistance and inflammation

Well tolerated across all studied doses

HU6 leads a pipeline of first-in-class, orally administered Controlled Metabolic Accelerators (CMAs) that accelerate fat metabolism and treat the underlying cause of type 2 diabetes, HFpEF, NASH, and other cardiovascular and metabolic diseases

CHARLOTTESVILLE, Va., February 9, 2022 – Rivus Pharmaceuticals Inc., a biopharmaceutical company dedicated to improving cardio-metabolic health, today announced positive results from a Phase 2a clinical trial of HU6 in obese participants with elevated liver fat. In eight weeks, HU6 demonstrated significant reductions in liver, visceral, and total body fat while conserving skeletal muscle mass, leading to significant reductions in total body weight. Uniquely, the greatest reductions in weight and body fat were observed in patients who had high baseline HbA1c levels. Improvements were also observed in key metabolic parameters that drive the pathophysiology of type 2 diabetes, heart failure with preserved ejection fraction (HFpEF), and non-alcoholic steatohepatitis (NASH). HU6 was well tolerated across all studied doses.

"We are highly encouraged by the Phase 2a clinical data evaluating HU6 to improve cardio-metabolic health. In this a relatively short study of 8 weeks, HU6 was able to achieve meaningful results safely in a high percentage of responders. By reducing fat in the liver, and throughout the body, HU6 addresses the root cause of poor metabolic health and related diseases," said Allen Cunningham, President and CEO of Rivus Pharmaceuticals.

HU6 Phase 2a Metabolic Trial Design and Results

The phase 2a metabolic trial of HU6 was a 61-day randomized, double-blind, placebo-controlled trial designed to assess the safety and efficacy of three dose levels of HU6 (150 mg, 300mg, and 450 mg) in obese participants (body mass index 28 to 45 kg/m2) with elevated liver fat (greater than 8%). Eighty (80) participants between ages 28 and 65 were randomly assigned to one of three HU6 treatment groups or the matched placebo group, stratified and blocked for HbA1c levels of 5.7% or greater, and dosed once daily (fasting). Participants were instructed to not change behavior with regard to diet or exercise. The Phase 2a trial met primary (liver fat reduction by MRI-PDFF) and secondary (body weight and fat reduction by abdominal MRI) endpoints. Key results and observations include:

- Statistically significant ($p<0.0001$ by ANCOVA) reductions in liver fat at all three dose levels.
    - Relative reductions in liver fat were 33%, 43%, and 40% corresponding to responder rates (>30% relative reduction) of 40%, 71% and 72% at low, mid and high doses, respectively, compared to placebo relative reduction in liver fat of 2% and responder rate of 5%.
- Body weight reduction almost exclusively from loss of fat, sparing skeletal muscle mass at all dosing levels at eight weeks, without change in diet or exercise behavior.
    - Weight and fat loss showed a dose response with participants losing an average of 6 pounds ($p<0.001$, high dose vs. placebo).

- Participants with elevated HbA1c levels experienced greater weight and fat loss, losing an average of 10 pounds ($p<0.0001$, high dose vs. placebo).
- Fat loss was observed in hepatic, visceral, and subcutaneous compartments by MRI.

- Key cardiovascular and metabolic health indicators at all dosing levels including:
  - Signficant dose dependent reduction in glycated albumin, an indicator of glucose control and insulin function.
  - Significant dose dependent reduction in inflammation marker high sensitivity C-reactive protein (hsCRP), an important parameter of cardiovascular risk.
- HU6 was well-tolerated at all dose levels with excellent compliance. No Serious Adverse Events or deaths were reported. Intermittent diarrhea and transient flushing were the most commonly reported Treatment Emergent Adverse Events. The majority of these events were mild; one participant discontinued HU6 for diarrhea in the low dose arm while no participant discontinued at the high dose.

"This trial provides compelling proof of clinical concept for the efficacy and safety of mitochondrial uncoupling with HU6, our first in class CMA. HU6 pharmacology which selectively reduces fat and weight without appetite suppression is highly differentiated. Given early indications that this biology may reverse insulin resistance and systemic inflammation, we can now explore whether reducing visceral and organ fat can provide clinical benefits to patients across a host of cardiometabolic diseases," said Shaharyar Khan, Ph.D., Rivus' Chief Scientific Officer.

CMAs provide a new, measured approach to safely activating mitochondrial uncoupling, a process in the body that regulates and dissipates energy. By ferrying protons out of the mitochondrial intermembrane space, CMAs increase the oxidation of sugars and fats, while maintaining the same baseline production of adenosine triphosphate (ATP). Activating this process results in the reduction and the prevention of fat accumulation throughout the body.

In the first half of 2022, Rivus is continuing its HU6 clinical program with a Phase 2a study in heart failure with preserved ejection fracture (HFpEF) to be followed by Phase 2b studies in type 2 diabetes and non-alcoholic steatohepatitis (NASH).

About HU6
HU6 is a controlled metabolic accelerator (CMA) that provides a novel, measured approach to activating proton leak and mitochondrial uncoupling, a natural process in the body that regulates and dissipates energy. By ferrying protons out of the mitochondrial intermembrane space, CMAs cue the increased oxidation of sugars and fats, while maintaining the same baseline production of adenosine triphosphate (ATP). Activating this process results in the reduction of accumulated fat throughout the body.

About Rivus Pharmaceuticals
Rivus Pharmaceuticals, Inc., is dedicated to transforming the treatment of cardio-metabolic disease. Rivus' first-in-class small molecule therapy, HU6, is a controlled metabolic accelerator (CMA) that addresses the underlying cause of cardio-metabolic disease by harnessing the body's natural processes to improve cellular metabolism and selectively oxidize fat. Rivus' therapy presents a tremendous opportunity to empower patients on their journey to better health when facing a broad range of cardio-metabolic conditions, including type 2 diabetes, heart failure with preserved ejection fraction (HFpEF), non-alcoholic steatohepatitis (NASH), and obesity. For more information, please visit rivuspharmadev.wpengine.com.

Media Contact:

Melissa Barrett, Verge Scientific Communications
mbarrett@vergescientific.com