Rivus Pharmaceuticals Announces Completion of Enrollment in Phase 2a HuMAIN Trial of HU6

– Topline data readout from HuMAIN trial planned for mid-2024 –

– Company presenting at 2024 J.P. Morgan Healthcare Conference on January 8 at 10 a.m. PT –

CHARLOTTESVILLE, VA, and SAN FRANCISCO, CA January 5, 2024 – Rivus Pharmaceuticals Inc., a clinical-stage biopharmaceutical company dedicated to improving cardiometabolic health, today announced the completion of enrollment in its Phase 2a HuMAIN trial of HU6, an investigational controlled metabolic accelerator (CMA), in patients with the obese phenotype of heart failure with preserved ejection fraction (HFpEF). Company executives will provide a corporate update with additional details during a presentation at the 42nd Annual J.P. Morgan Healthcare Conference in San Francisco on Monday, January 8.

"We have made significant progress in advancing our HU6 clinical development program, having completed enrollment in our Phase 2a HuMAIN trial in patients with obese HFpEF," said Jayson Dallas, M.D., chief executive officer, Rivus Pharmaceuticals. "A disease-modifying treatment is urgently needed for this at-risk patient population which tends to be older, obese, and less mobile, with multiple metabolic co-morbidities. By increasing metabolism and, thus, significantly reducing adiposity, a key underlying cause of HFpEF, HU6 has the potential to modify the underlying disease progression. We plan to announce topline data in mid-2024 and initiate a Phase 3 trial in 2025."

In addition to the HuMAIN trial, the company is actively enrolling subjects with obesity and Type 2 diabetes at risk of metabolic dysfunction-associated steatohepatitis (MASH) into the ongoing Phase 2b M-ACCEL trial of HU6. A topline data readout from the M-ACCEL trial is planned for early 2025.

About the Phase 2a HuMAIN Trial

The randomized, parallel-group, double-blind, placebo-controlled, dose-escalation Phase 2a HuMAIN study (ClinicalTrials.gov, NCT05284617) is evaluating the safety, tolerability, pharmacodynamics and pharmacokinetics in ascending doses of HU6 (150 mg, 300 mg, 450 mg daily) in patients with the obese phenotype of HFpEF. Sixty-five study participants (37 women and 28 men) with a body mass index (BMI) ≥30 kg/m2 were randomized and dosed 1:1 with HU6 or placebo. Approximately two thirds of the patients were dysglycemic at screening (hemoglobin A1c levels ≥5.7%) with an average BMI of 39.6 kg/m2. The primary outcome measure is weight reduction. The study is being conducted at 14 clinical sites in the United States.

About the Phase 2b M-ACCEL Trial
The randomized, double-blind, placebo-controlled, parallel-group, Phase 2b M-ACCEL trial (ClinicalTrials.gov, NCT05979779) is evaluating the safety and efficacy of three dose levels of HU6 in patients with obesity (body mass index of ≥30.0 kg/m2) and Type 2 diabetes at risk of MASH. Approximately 280 adult patients will be randomized 2:1:2:2 into one of four treatment groups (placebo, HU6 150 mg, HU6 300 mg or HU6 450 mg) and treated for six months (26 weeks). The primary endpoint is percent change from baseline in liver fat as assessed by magnetic resonance imaging liver proton density fat fraction (MRI-Liver PDFF) at six months. Secondary endpoints will evaluate the effect of HU6 on body weight, glycemic control as assessed by hemoglobin A1c, liver fibrosis and liver fat, body composition, metabolic and inflammatory parameters, and patient-reported outcomes. The M-ACCEL trial will also evaluate safety, tolerability, pharmacodynamics and pharmacokinetics. The study is being conducted at approximately 20 clinical sites in the United States.

J.P. Morgan Healthcare Conference Presentation Details
Rivus Pharmaceuticals will present in the private company track at the 42nd Annual J.P. Morgan Healthcare Conference on Monday, January 8, at 10:00 a.m. Pacific Time (1:00 p.m. Eastern Time) at the Westin St. Francis Hotel.

About Controlled Metabolic Accelerators (CMAs)
Rivus is advancing a new class of investigational medicines called controlled metabolic accelerators (CMAs) that have the potential to improve metabolic health for people with obesity and associated metabolic diseases. CMAs are oral small molecules designed to increase resting metabolic rate, which results in increased consumption of energy, primarily from fat. The loss in fat mass addresses multiple cardiometabolic conditions driven by adiposity. CMAs increase metabolism in a continuous and imperceptible manner by leveraging the natural metabolic process of mitochondrial uncoupling. Uncoupling accounts for 20-40% of resting caloric consumption. A key advantage of this mechanism for increasing energy expenditure is that the resulting weight loss is fat selective with preservation of muscle mass, in contrast to caloric restriction strategies which reduce energy input and result in a loss of fat as well as muscle mass. Initial data in humans have demonstrated that CMAs provide fat selective weight loss, improved insulin sensitivity and a significant reduction in oxidative stress and inflammation.

About HU6
HU6, the most advanced CMA in clinical development, is purposely designed to increase the body's resting metabolic rate in a controlled and physiologic manner by leveraging the natural mechanism of mitochondrial uncoupling. In a Phase 2 metabolic trial in patients with a high body mass index (BMI) and metabolic dysfunction-associated steatotic liver disease (MASLD), HU6 reduced liver fat content and body weight, preserved lean muscle mass, and significantly improved key markers of systemic inflammation and metabolism.[1] Rivus is pursuing clinical development programs for HU6 in heart failure with preserved ejection fraction (HFpEF), metabolic dysfunction associated steatohepatitis (MASH), Type 2 diabetes and chronic weight management / obesity.

About Rivus Pharmaceuticals
Rivus Pharmaceuticals, Inc., a leader in mitochondrial biology, is dedicated to improving cardiometabolic health by advancing a new class of medicines called controlled metabolic

accelerators (CMAs). Rivus' lead CMA is the investigational small molecule HU6 in development to treat obesity and associated metabolic diseases, including heart failure with preserved ejection fraction (HFpEF), metabolic dysfunction-associated steatotic liver disease (MASLD) / metabolic dysfunction-associated steatohepatitis (MASH) and Type 2 diabetes. For more information, please visit www.rivuspharma.com.

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References

1. Noureddin M, Khan S, Portell F, et al. Safety and efficacy of once-daily HU6 versus placebo in people with non-alcoholic fatty liver disease and high BMI: a randomised, double-blind, placebo-controlled phase 2a trial. *Lancet Gastroenterol Hepatol*. 2023.