



## **Rivus Pharmaceuticals Announces Expansion of HU6 Clinical Program and New Leadership Appointments**

- First patient randomized in Phase 2b M-ACCEL trial of HU6 in obese subjects with Type 2 diabetes and at risk of metabolic dysfunction-associated steatohepatitis –
  - Robert J. Schott, M.D., M.P.H., appointed chief medical officer and Ian F. Smith appointed chairman of the board –

CHARLOTTESVILLE, Va., and SAN FRANCISCO November 15, 2023 – Rivus Pharmaceuticals Inc., a clinical-stage biopharmaceutical company dedicated to improving metabolic health, today announced key clinical and corporate updates. The company randomized the first patient in the Phase 2b M-ACCEL trial of HU6, an investigational controlled metabolic accelerator (CMA), in obese subjects with Type 2 diabetes and at risk of metabolic dysfunction-associated steatohepatitis (MASH). Additionally, Rivus appointed Robert J. Schott, M.D., M.P.H., FACC, chief medical officer and appointed Ian F. Smith chairman of the board of directors.

“Our singular purpose at Rivus is to improve overall metabolic health in people with obesity and related metabolic diseases, including MASH and Type 2 diabetes. With the initiation of the Phase 2b M-ACCEL trial, for which we expect a readout in early 2025, we are continuing to build the clinical evidence for HU6, a purposefully designed investigational medicine aimed at inducing fat-specific weight loss and significant improvements in measures of metabolic health while preserving lean muscle mass,” said Jayson Dallas, M.D., chief executive officer, Rivus Pharmaceuticals. “With the appointment of seasoned and highly respected biopharma veterans Robert Schott and Ian Smith to our leadership team and board, we are establishing a top-tier team to grow the company and advance HU6, which could replace current approaches to treating obesity and metabolic dysfunction.”

### **Initiation of Phase 2b M-ACCEL Trial**

The randomized, double-blind, placebo-controlled, parallel-group, Phase 2b M-ACCEL trial is evaluating the safety and efficacy of three dose levels of HU6 in subjects with obesity (body mass index of  $\geq 30.0$  kg/m<sup>2</sup>) and Type 2 diabetes and 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, as well as patient-reported outcomes. The M-ACCEL trial will also evaluate safety, tolerability, pharmacodynamics and pharmacokinetics. The study is being conducted at approximately 16 clinical sites in the United States.

In addition to the Phase 2b M-ACCEL trial ([ClinicalTrials.gov, NCT05979779](https://clinicaltrials.gov/ct2/show/study/NCT05979779)), Rivus is currently enrolling patients with the obese phenotype of heart failure with preserved ejection fraction (HFpEF) in the Phase 2a HuMAIN study ([ClinicalTrials.gov, NCT05284617](https://clinicaltrials.gov/ct2/show/study/NCT05284617)).

### **Appointments of New Chief Medical Officer and Board Chair**

Dr. Robert Schott, Rivus' new chief medical officer, joined the company from Nutcracker Therapeutics, where he served as chief medical officer, focusing on mRNA therapeutics. Before that, he was a senior vice president and head of development at Sangamo Therapeutics, focusing on gene and cell therapies in rare diseases. Dr. Schott was at Eli Lilly for seven years, where he served as chief medical officer for Chorus, the autonomous early-phase drug development group inside of Lilly. There, he oversaw the clinical development strategy across diverse indications and platforms. Dr. Schott earned an M.D. from the University of Michigan Medical School and an M.P.H. in epidemiology from the University of Michigan School of Public Health. He completed an internal medicine residency at the University of Michigan Hospitals and a fellowship in cardiology at Massachusetts General Hospital.

"I am delighted to be joining Rivus Pharmaceuticals, where the devoted founders and their team have made rapid progress in advancing HU6 into the clinic," said Dr. Schott. "This investigational therapeutic has the potential to address a number of obesity-associated diseases through a novel but well-characterized mechanism, which could address unmet medical needs in many patients with the metabolic consequences of obesity."

Ian F. Smith, the new chairman of the board of Rivus, currently serves as a senior advisor to Bain Capital Life Sciences. He is executive chairman of the board of Solid Biosciences, a public biotechnology company; a member of the board of Foghorn Therapeutics and Stoke Therapeutics, both public biotechnology companies; and a member of the board of Alkeus Pharmaceuticals, a private biotechnology company. He was formerly director and executive chair of the board of ViaCyte, Inc., a private biotechnology company that was acquired in fall 2022. From 2001 to 2019, Mr. Smith held the positions of executive vice president and chief operating officer and chief financial officer at Vertex Pharmaceuticals, a public biotechnology company. He received a B.A. with honors in accounting and finance from Manchester Metropolitan University in the UK.

"Obesity is a public health crisis and a global epidemic and is the primary driver of metabolic diseases that exert a tremendous burden on both individuals and the U.S. healthcare system," said Mr. Smith. "I look forward to partnering with the Rivus leadership team and other board members as we pursue the company's mission to improve human metabolic health caused by obesity. Rivus has a next-generation investigational medicine based on novel science and insights into mitochondrial biology that may be differentiated beyond the current landscape of treatments."

### **About Controlled Metabolic Accelerators (CMAs)**

Rivus created and 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 that are

designed to reduce excess fat and treat a broad range of metabolic diseases by safely leveraging mitochondrial uncoupling, a natural metabolic process in which the body generates heat. Within the mitochondria, sugars and fats are broken down by biochemical processes to help regulate the body's metabolism. CMAs cue the increased oxidation of sugars and fats by metabolic processes in the mitochondria while maintaining the same baseline production of adenosine triphosphate (ATP), the body's primary source for energy production, resulting in a sustained, imperceptible increase in the resting metabolic rate throughout the day and night. Activating this process results in the reduction of accumulated fat and sugars throughout the body, while preserving, or even improving, lean muscle mass. CMAs provide a novel, measured approach to activating this natural process, resulting in weight loss, reduction of liver fat, 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.<sup>1</sup> 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 metabolic 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](http://www.rivuspharma.com).

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### **References**

1. Nouredin 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.