Molecular Genetics and Metabolism Publishes Primary Pharmacology Data Supporting HemoShear's HST5040 as a Potential Treatment for Methylmalonic Acidemia (MMA) and Propionic Acidemia (PA)

Charlottesville, Va., March 31, 2021 – HemoShear Therapeutics, Inc., a clinical stage company developing treatments for rare metabolic disorders, today announced the publication of in vitro pharmacology data in the journal *Molecular Genetics and Metabolism*, demonstrating that the oral small molecule HST5040 may be effective in treating Methylmalonic Acidemia (MMA) and Propionic Acidemia (PA). The company has initiated the HERO (HElp Reduce Organic acids) study, a Phase 2 clinical trial investigating HST5040 for the treatment of MMA and PA in patients age 2 and older.

MMA and PA are rare genetic diseases caused by deficiencies of certain metabolic enzymes that result in the buildup of toxins that can cause severe organ damage, developmental deficits, and premature death. HemoShear scientists created in vitro models of MMA and PA to accurately reflect these human disease states by applying principles of physiological blood flow to human tissue from the livers of MMA and PA patients who underwent transplant. Administration of HST5040 to the patients' liver cells led to dose-dependent reductions to normal or near-normal values in several key biomarkers associated with MMA and PA, including propionyl-coenzyme A (P-CoA), methylmalonyl-CoA (M-CoA), 2-methylcitric acid (MCA), the propionyl-carnitine to acetyl-carnitine (C3:C2) ratio, and methylmalonic acid.

"Our team's ability to utilize human disease tissue from MMA and PA patients to create cell-based models in the HemoShear *Reveal-Tx* technology has proven to be an extremely powerful approach to uncover novel pharmacology and develop the exciting new potential therapeutic HST5040 that is moving into clinical studies." said Brian Johns, Chief Scientific Officer of HemoShear. "The research showed that the administration of HST5040 reduced levels of all measurable disease biomarkers in patients' cells."

"This important pharmacology provides a compelling rationale for HST5040 to reduce toxic metabolites and restore energy metabolism in patients with MMA and PA," said Gerry Cox, MD, PhD, Chief Medical Officer at HemoShear. "HemoShear's recently initiated Phase 2 HERO study will evaluate the safety of HST5040 in patients with MMA and PA as well as its ability to impact metabolic abnormalities and improve the lives of patients and their families."

About HST5040

The FDA has granted HemoShear's HST5040 Orphan Drug, Fast Track and Rare Pediatric Disease designations for the treatment of MMA and PA. HemoShear's HERO phase 2 clinical study of HST5040 will enroll at least 12 patients aged 2 and older with MMA or PA at select children's hospitals in the United States.

HST5040 is an investigational oral small molecule therapy developed by HemoShear to correct the metabolic abnormalities associated with MMA and PA. HST5040 is designed for convenient daily administration at home as a liquid formulation taken either orally or through a gastrostomy tube.

Mechanism of Action

Coenzyme A plays a key role in metabolism and energy production. Propionyl-coenzyme A (P-CoA) and methylmalonyl-coenzyme A (M-CoA) are metabolites that all cells in the human body make when breaking down protein and fat to produce energy. Propionic and methylmalonic acidemia (PA and MMA) are caused by a deficiency in key metabolic enzymes, leading to the build-up of toxic levels of P-CoA or M-CoA and other harmful chemicals derived from them. This buildup directly harms tissues and negatively impacts energy production throughout the body. Research with HST5040 shows that this small molecule is able to reduce P-CoA and/or M-CoA and the other derived toxic chemicals to normal or near normal levels, potentially resetting the metabolic state and energy production pathways in the body. HemoShear research indicates HST5040 does this by diverting coenzyme A from P-CoA, resulting in a decrease in P-CoA levels, and consequently, decreased formation of other harmful chemicals in the body.

About HemoShear Therapeutics

HemoShear Therapeutics, Inc. is a privately held clinical stage company developing treatments for rare metabolic disorders with significant unmet patient need. HemoShear's drug discovery platform, *REVEAL-Tx™*, enables the Company's scientists to create best-in-class, biologically relevant human disease models to uncover the underlying mechanisms of disease, translate those discoveries into drug targets, and select candidates that may treat patients successfully. In addition to the Company's proprietary rare disease programs, HemoShear has exclusive partnerships to identify novel therapeutic approaches in nonalcoholic steatohepatitis (NASH) and an undisclosed rare liver disease with Takeda, and in gout with Horizon Therapeutics. For more information visit www.HemoShear.com.