Verve Therapeutics Presents New Data in Non-Human Primates Validating Gene Editing as a Treatment Approach for Coronary Heart Disease at the ISSCR 2020 Virtual Annual Meeting

June 27, 2020 3:00 PM EDT

Data Demonstrate In Vivo *Adenine Base Editing Can Turn Off Either PCSK9 or ANGPTL3 in the Liver and Substantially Lower LDL Cholesterol or Triglyceride Levels*

CAMBRIDGE, Mass. — June 27, 2020 – Verve Therapeutics, a next-generation cardiovascular company, today announced the presentation of new preclinical proof-of-concept data in non-human primates that demonstrate the successful use of base editing to turn off a gene in the liver and thereby lower blood levels of either LDL cholesterol or triglyceride-rich lipoproteins, two factors leading to coronary atherosclerosis. Verve is developing one-time gene editing medicines that safely edit the adult human genome and mimic naturally-occurring cardioprotective variants to permanently knock out cholesterol-raising genes in the liver and treat coronary heart disease. The data were presented at the International Society for Stem Cell Research (ISSCR) 2020 Virtual Annual Meeting.

In a keynote address titled, “From reading the genome for risk to rewriting it for health,” Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve Therapeutics, presented the results of recent studies utilizing adenine base editing (ABE) technology, licensed from Beam Therapeutics, in which substantial lowering of plasma LDL cholesterol or triglycerides was successfully demonstrated in non-human primates. Base editing is a gene editing technology developed to enable precise and permanent rewriting of a single DNA letter in the genome.

“At Verve, our goal is to develop medicines, given once in life, that precisely edit targeted genes in the liver to permanently reduce LDL cholesterol and triglyceride levels in adults with coronary heart disease, the leading cause of death in the U.S. and worldwide,” said Dr. Kathiresan. “These proof-of-concept data, which to the best of our knowledge represent the first successful application of the base editing technology in non-human primates, show that we can safely edit the primate genome at highly efficacious levels to significantly lower blood LDL cholesterol and triglycerides. The findings are very encouraging and add to our growing body of evidence in using both base editing and CRISPR-Cas9 *in vivo* against various gene targets. We expect to choose a lead program by year-end 2020 with the goal of initiating human clinical studies within the next three years.”

The studies were conducted in a total of 14 non-human primates and evaluated *in vivo* liver base editing to turn off proprotein convertase subtilisin/kexin type 9 (PCSK9), a gene whose protein product elevates blood LDL cholesterol or angiopoietin-like protein 3 (ANGPTL3), a gene whose protein product elevates blood triglyceride-rich lipoproteins. Verve’s proprietary drug product consisting of the ABE mRNA and an optimized guide RNA packaged in an engineered lipid nanoparticle was delivered through a single intravenous infusion. Across two separate studies, seven animals were treated with the drug product targeting the PCSK9 gene and seven additional animals with the drug product targeting the ANGPTL3 gene.

Whole liver editing, blood protein and lipid levels were measured at two weeks and compared to baseline. The program targeting PCSK9 showed an average of 67% whole liver PCSK9 editing, which translated into an 89% reduction in plasma PCSK9 protein and resulted in a 59% reduction in blood LDL cholesterol levels. The program targeting ANGPTL3 showed an average of 60% whole liver ANGPTL3 editing, which translated into a 95% reduction in plasma ANGPTL3 protein and resulted in a 64% reduction in blood triglyceride levels and 19% reduction in LDL cholesterol levels. In addition, in studies in primary human hepatocytes, clear evidence of on-target editing was observed with no evidence of off-target editing.

“These data are exciting and demonstrate our ability to turn off PCSK9 or ANGPTL3 in the liver to safely and effectively lower LDL cholesterol and triglyceride levels in non-human primate models using adenine base editing,” said Andrew Bellinger, M.D., Ph.D., chief scientific officer of Verve Therapeutics. “Very importantly, we do not find evidence of off-target editing using adenine base editing with carefully selected guide RNAs. These findings support Verve’s transformative idea to develop once-and-done gene-editing treatments for adults with coronary heart disease and we look forward to presenting additional data in the future.”

Verve has built a portfolio of key gene editing and delivery technologies through established collaborations and license agreements with industry leaders. The company is collaborating with Beam Therapeutics, from which it exclusively licensed base editing for human therapeutic applications against certain cardiovascular targets. The company has license agreements with Harvard University and the Broad Institute of MIT and Harvard for foundational CRISPR patents, including Cas9 and Cas12a (Cpf1), for human therapeutic applications against certain cardiovascular targets.

About Verve Therapeutics

Verve Therapeutics is a biotechnology company created with a singular focus: to protect the world from heart disease. The company brings together human genetics analysis and gene editing – two of the biggest breakthroughs in 21st century biomedicine – to develop transformative therapies for coronary heart disease. Verve is developing medicines, administered once in life, to safely edit the genome of adults to permanently lower LDL cholesterol and triglyceride levels and thereby treat coronary heart disease. Founded by world-leading experts in cardiovascular medicine, human genetics and gene editing, Verve is backed by a top-tier syndicate of investors, including GV (formerly Google Ventures), ARCH Venture Partners, F-Prime Capital, Biomatics Capital, Wellington Management, Casdin Capital, and Partners Innovation Fund. Verve is headquartered in Cambridge, Massachusetts. For more information, visit **www.VerveTx.com**.

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