Imagine if there was a single-course treatment that safely and durably lowered blood LDL cholesterol. Such a medicine could have the potential to treat and ultimately prevent atherosclerotic cardiovascular disease.

Sekar Kathiresan, M.D.
Co-founder and chief executive officer

DEAR SHAREHOLDERS

Verve is taking the first steps on a very important mission to build the preeminent company developing gene editing medicines to protect the world from cardiovascular disease. Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of death worldwide. Current treatment to lower blood low-density lipoprotein cholesterol (LDL-C) relies on chronic care requiring rigorous patient adherence, regular health care access, and extensive health care infrastructure. This chronic care model is fragile and as such, cumulative exposure to LDL-C for many patients with ASCVD remains insufficiently controlled, highlighting a large unmet medical need.

Verve is taking this challenge head on. We are pioneering a new approach to the care of cardiovascular disease with single-course gene editing medicines. We are developing a pipeline of once-and-done in vivo liver gene editing treatments that leverage multiple breakthroughs of 21st century biomedicine—human genetic analysis, gene editing, messenger RNA (mRNA) -based therapies and lipid nanoparticle (LNP) delivery.

2021 was momentous year for Verve. Some highlights from the year include:

- Completed Series B financing in January followed by a successful initial public offering in June.
- Reported in the journal Nature a first proof-of-concept for efficacy of in vivo liver base editing in non-human primates (NHPs).
- Selected VERVE-101 as our lead program. VERVE-101 uses base editing technology and is designed to precisely edit a single base pair in the PCSK9 gene sequence in order to permanently turn off the gene and thereby, reduce blood LDL-C. Verve plans to investigate VERVE-101 initially as a treatment for heterozygous familial hypercholesterolemia (HeFH), a potentially fatal genetic heart disease characterized by very high blood LDL-C and ASCVD.
- Reported data from IND-enabling studies which demonstrated VERVE-101 to be potent and durable in NHPs. A single intravenous infusion of VERVE-101 led to ~90% lower blood PCSK9 protein levels and ~60% lower blood LDL-C.
- Developed a proprietary delivery system, a GalNAc-LNP, to enable potent delivery of gene editing medicines to the liver.
- Applied the GalNAc-LNP delivery system to develop a second program targeting the ANGPTL3 gene. Verve's ANGPTL3 base editor led to potent reductions in blood ANGPTL3 protein levels and LDL-C in a novel NHP model of homozygous familial hypercholesterolemia, a rare genetic subtype of ASCVD.
- Strengthened Verve's management team with the addition of Allison Dorval as our chief financial officer, and added accomplished members to our board of directors, including Sheila Mikhail, J.D., M.B.A., chief executive officer and co-founder of Asklepios BioPharmaceutical, Inc. (AskBio), a subsidiary of Bayer AG, and Michael F. MacLean, chief financial officer and chief business officer of Avidity Biosciences, Inc.

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These accomplishments set the stage for 2022 to be a transformative year for Verve as we plan to transition from a discovery company to a clinical company. To accomplish this, we are implementing a global regulatory strategy and plan to treat the first HeFH patient with VERVE-101 in the second half of 2022. Notably, if we achieve this timing, VERVE-101 could be the first in vivo base editing product candidate to move into human clinical trials.

In addition, Verve is on track to select a development candidate for our ANGPTL3 program and initiate IND-enabling studies in the second half of 2022. We plan to develop our GalNAc-LNP delivery system as a leading technology for in vivo liver delivery of gene editors. Lastly, we plan to expand beyond the VERVE-101 and ANGPTL3 programs to develop a suite of single-course gene editing medicines that address root causes of disease.

At the heart of these accomplishments, and the key to our future success, are the employees at Verve. I am extremely proud of the dedicated team of scientists and management professionals who are moving Verve forward. The drive and expertise of our employees are second to none, and we are motivated to solve the world's number one health issue. We are blazing a new path, and I'm continually impressed by our team's innovative spirit and courage.

We are just at the beginning of this significant journey to change the way heart disease is treated. Verve was founded in 2018 with a mission to transform the care of cardiovascular disease and move it from chronic care to single course gene editing medicines. In 2022, we are poised to treat our first patients with VERVE-101, a new class of in vivo liver base editing medicines. With our well-defined strategy and commitment to execution, Verve is successfully translating our know-how and expertise, both in gene editing technology and cardiovascular care, to create value for our various stakeholders.

We would like to thank you, our shareholders, for your dedication and support, and we look forward to sharing our progress with you in the coming years.

Sincerely,

Sekar Kathiresan, M.D.
Co-founder and chief executive officer

verve THERAPEUTICS