

AVANT Immunotherapeutics, Inc.

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AVANT Immunotherapeutics has used the SBIR program to **advance a revolutionary vaccine, designed to prevent or treat atherosclerosis**, into clinical trials. This vaccine has the potential to enhance the management of this disease, and reduce the cost of such treatment.

Atherosclerosis is a progressive condition leading to arterial blockage and reduced blood flow. Clinical manifestations of the disease include many forms of cardiovascular disease, the number one cause of death in the United States, including heart attack, stroke, and peripheral vascular disease. Atherosclerosis can also contribute to other conditions such as hypertension and chronic kidney failure. While a high level of low-density lipoprotein (LDL, "bad cholesterol") is a key risk factor for developing atherosclerosis, a high level of high-density lipoprotein (HDL, "good cholesterol") has been shown to be protective. Some individuals with atherogenic cholesterol levels will be given one of the daily cholesterol-lowering drugs called statins. While these drugs do provide some reduction in the risk of developing or advancing atherosclerosis, their use is limited due to the high annual cost for lifetime treatment and compliance problems. In addition, while these drugs lower LDL they only marginally raise HDL.

Understanding that there was a large unmet need in the management of atherosclerosis, scientists at AVANT undertook a program to combat the disease by modifying the relative levels of cholesterol carried by LDL and HDL in the blood. A molecule, called Cholesteryl Ester Transfer Protein, or CETP, mediates the movement of cholesterol from HDL to LDL. It was reasoned if this protein was inhibited less atherogenic cholesterol levels might be achieved, and in particular HDL levels might be raised. A novel strategy proposed by AVANT scientists was to make a vaccine that would result in the inhibition of CETP. This vaccine approach, since it might only need to be administered once every several months, would have a significantly reduced cost, compared to once-a-day pills, and would likely have fewer compliance problems. Further, with a reduced cost of treatment, patients that were not considered to be at sufficient risk to warrant the cost of a statin prescription, may be eligible to be given this vaccine. This ability to justify early intervention alone might result in a significantly decreased or delayed incidence of clinical atherosclerosis in the United States.

AVANT Immunotherapeutics applied for, and received, SBIR funds to help finance experiments demonstrating the feasibility of this vaccine concept. Following the success of those early experiments, significant additional work was done with this vaccine, both in research and development, and it has now entered into Phase I clinical trials. If clinical trials are successful, this

vaccine has the potential to greatly enhance the clinical management of atherosclerosis.

National Institutes of Health Awards

Peptide Vaccine to Prevent/Treat Atherosclerosis

(HL 59122)