



Immunization to Ameliorate Atherosclerotic Cardiovascular Diseases



Key Points:

- Products to slow, stop, reverse, and prevent atherosclerotic cardiovascular diseases, including heart attack and stroke.
- Exclusive, royalty free, worldwide license to an extensive intellectual property estate (5 issued patents, 20+ patent applications) for active immunization and companion diagnostics covering multiple disease states.
- Experienced management team with a record of success in developing and commercializing pharmaceuticals, biologics, and medical devices.
- Investigational New Drug Application (IND) submitted in March 2010.
- Privately held company with sufficient capital to fund development through Phase I

The Company: CardioVax, LLC is developing immune modulating pharmaceuticals to slow, stop, reverse, and prevent atherosclerotic cardiovascular diseases, including heart attacks and strokes. CardioVax holds an exclusive, royalty-free, fully paid-up, worldwide license to technologies in the field of active immunization discovered through collaborations between Professor Jan Nilsson, Lund University Hospital Malmö (LUHM), Malmö, Sweden, and Professor Prediman K. Shah, Cedars-Sinai Medical Center (CSMC), Los Angeles, CA.

The Unmet Medical Need: Even though there are many therapeutic options to treat atherosclerosis, the societal burden imposed by atherosclerotic cardiovascular disease remains unacceptably high. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in both men and women in the US. More than 80 million adult Americans have some form of CVD. CVD is noted as the underlying cause for over 35% of all deaths in the US and it costs the US economy in excess of \$400 billion annually. There remains a pressing need for new, innovative treatments to supplement current treatments. CardioVax' lead product, CVX-210-H, is one such treatment. CVX-210-H is the first immune modulating treatment for atherosclerotic cardiovascular disease which directly targets the underlying cause of the disease.

Rationale: In the past few years, considerable evidence has accumulated in favor of the paradigm that atherosclerosis is a chronic disease in which inflammatory and immune responses contribute to the initiation, progression, and destabilization of atherosclerotic lesions. The innate and adaptive immune responses have both been shown to modulate atherosclerosis. Like many other biologic systems, the activation of the immune system has two juxtaposed roles in atherosclerosis, with evidence of both athero-promoting and athero-protecting effects.

Mechanism of Action		
Th1	→	Th2/Treg
Pro-Inflammatory	→	Anti-Inflammatory
Athero-Promoting	→	Athero-Protecting

Professors Nilsson and Shah identified an athero-protective immune response against epitopes in oxidized low-density lipoprotein (oxLDL). They prepared a vaccine comprised of specific immunogenic peptide fragments of apolipoprotein B-100 conjugated to a carrier molecule and formulated with an adjuvant. CardioVax' lead product (CVX-210-H) has demonstrated 60% or greater reduction in atherosclerotic lesions in treated animals compared to controls.

Product Candidates: CVX-210-H is comprised of 20 amino acid peptide fragments of human apoB-100 (amino acid residues 3136-3155) conjugated to recombinant human serum albumin (Recombunin®) and formulated with aluminum hydroxide colloid gel (Alhydrogel®). Other product candidates are being evaluated in early development programs.

The Market: The global cardiovascular pharmaceutical market is forecasted to be \$120 billion in 2010. There are an estimated 38 million American adults who, according to ATP III and Framingham criteria, are in the highest risk category (10 year risk > 20%) for heart attack. The first commercial application of CVX-210-H will be to treat the underlying cause of atherosclerotic cardiovascular diseases in this group of patients. The proposed course of treatment is a series of four injections administered as an initial inoculation followed by three boosters on an every three week time schedule. A subsequent course of treatment may be warranted at some time, possibly 5 years, thereafter. If even 1% of the 38 million high risk individuals received a single course of treatment per year, then more than 1.5 million doses would be administered annually.



More importantly, we believe that the most significant public health benefit of our vaccine will be to prevent atherosclerotic cardiovascular diseases from ever progressing to the point of becoming clinically apparent. Should this goal be attained, then the total addressable market for the vaccine expands to include all American adults, roughly 240 million in 2009.

Competitive Landscape: Cholesterol homeostasis is a complex physiologic process involving a number of different biochemical steps in a number of different tissues. Therapies have been and are being developed that seek to slow or accelerate several of these biochemical reactions. However, many patients are either unable or unwilling to adhere to the optimal treatment regimen. Even in patients who are receiving the full benefit of the standard of care, additional improvements may be necessary. CardioVax' lead therapy is intended to complement many of the existing treatments, such as statins, as well as emerging treatments, such as reverse cholesterol transport agents.

At the present time, there are no known pharmaceuticals pursuing an active immunization (vaccine based) therapy or viewed as being directly competitive with CVX-210-H. There are several products that are in preclinical development that target different but related biochemical pathways.

Intellectual Property: CardioVax licensed exclusive rights to inventions made by Drs. Nilsson and Shah in the field of use of active immunization. Patents have been issued in the US, Europe (in 22 countries), and Australia. Issued US patents include:

- US 7,527,795
- US 7,528,225
- US 7,544,360
- US 7,556,811

Additional patent applications are pending in multiple countries in the Americas, Europe, and Asia.

Milestones: The IND for CVX-210-H was submitted in March 2010. First-in-human clinical studies are planned to assess safety and immune responses of CVX-210-H.

Funding: CardioVax is privately held and has raised sufficient capital to fund development through Phase 1. CardioVax will seek additional funding to optimize the lead product formulation, perform additional nonclinical safety studies, manufacture clinical supplies, conduct additional clinical studies and advance one additional product in its pipeline.

Management: CardioVax' management team includes industry experts with strong backgrounds in science, medicine, pre-clinical and clinical trials, regulations, manufacturing, marketing and strategic partnership development. Collectively, this team has been instrumental in the submission of more than twenty-five New Drug Applications, Biologic License Applications, and Premarket Authorization Applications. In addition, members of the team have nurtured dozens of companies at various stages, from founding through development and eventually to exit, either through initial public offerings or strategic acquisition.

- Oye Olukotun, MD, MPH, Chief Executive Officer
- Mark Carvlin, PhD, Chief Operating Officer
- Janice Mitrovich, Executive Director, Project Mgmt

This team is supported by a Scientific Advisory Board comprised of key opinion leaders from respected academic and corporate institutions.

Publications:

1. Hansson G and Nilsson J. Vaccination Against Atherosclerosis? Induction of Atheroprotective Immunity. *Semin Immunopathol* 2009 (On line).
2. Fredrikson G, Anand D, Hopkins D, Corder R, Alm R, Bengtsson E, Shah PK, Lahiri A, Nilsson J. Associations Between Autoantibodies Against Apolipoprotein B-100 Peptides and Vascular Complications in Patients with Type 2 Diabetes. *Diabetologia* 2009; 52:1426-1433.
3. Nilsson J, Hansson G. Autoimmunity in Atherosclerosis: A Protective Response Losing Control? *J of Intern Med* 2008; 263:464-478.
4. Fredrikson G, Björkbacka H, Söderberg I, Ljungcrantz I, Nilsson J. Treatment with apo B peptide vaccines inhibits atherosclerosis in human apo B-100 transgenic mice without inducing an increase in peptide-specific antibodies. *J of Intern Med* 2008; 264:563-570.
5. Sjögren P, Fredrikson GN, Samnegard A, Ericsson CG, Ohrvik J, Fisher R, Nilsson J, Hamsten A. High Plasma Concentrations of Autoantibodies Against Native Peptide 210 of ApoB-100 are Related to Less Coronary Atherosclerosis and Lower Risk of Myocardial Infarction. *Eur Heart J* 2008; 29:2218-2226.
6. Shah PK, Chyu KY, Fredrikson GN, Nilsson J. Immunomodulation of Atherosclerosis with a Vaccine. *Nature Clinical Practice Cardiovascular Medicine* 2005; 2(12):639-646.

A more extensive selection of publications is available at www.cardiovox.com/resources.