CEL-SCI
Empowering Immune Defenses

LEAPS COVID 19 Immunotherapy

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CEL-SCI Corporation

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NYSE American: **CVM**

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CEL-SCI Corporation

CEL-SCI Corporation **(NYSE American: CVM)** focuses on the research and development of immunotherapy products for the treatment of cancer, autoimmune and infectious diseases.

CEL-SCI's primary focus is cancer immunotherapy given right after diagnosis, before the ravages of surgery, radiation and/or chemotherapy have destroyed the immune system.

We also have a very interesting second platform technology called LEAPS that we believe may be able to contribute in the fight against COVID 19.

Why Develop LEAPS for COVID 19?

- Very promising efficacy and safety profiles in animal studies against H1N1 pandemic flu, and five other diseases. We saw both prevention and treatment in H1N1. Using the lessons learned from H1N1 we seek to repeat these promising results against COVID 19 in a transgenic mouse model.

- Immunotherapy with two key attributes: anti-viral and anti-inflammatory (reduce cytokine storm).

- You need to produce both an antibody and a T-cell response. We are seeing reports that antibody levels against COVID 19 decrease quickly. The memory for T-cell responses is much longer.

- Vaccines and some treatments under development target the spike portion of the virus which is known to mutate. To avoid/reduce the danger of mutation, LEAPS antigens are selected from a part of the virus that is less prone to mutation. This should avoid the potential loss of effectiveness that could be associated with virus mutation.

- COVID 19 is a huge problem, but what if COVID 19 becomes a virus with a much higher kill rate?

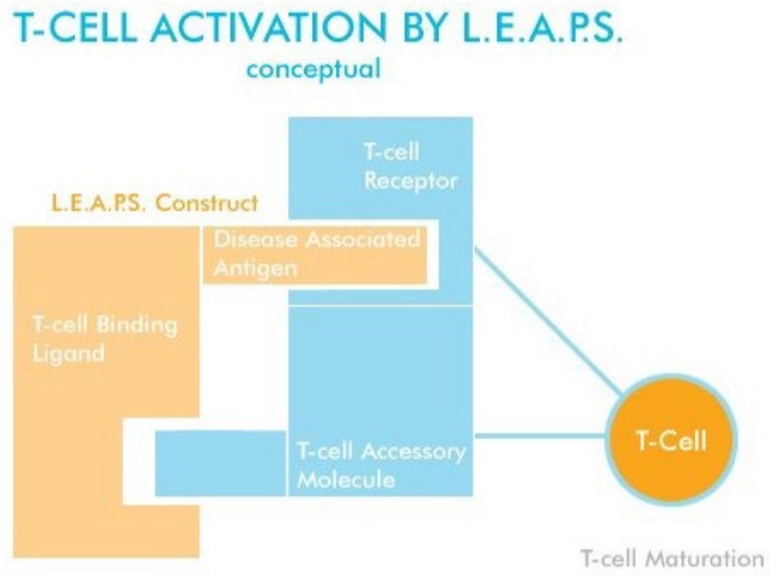
Drugs in Development

- **Multikine®** - an investigational cancer immunotherapy in a Phase 3 study under development as a potential neoadjuvant (First-Line) treatment of head and neck cancer. This study has been running for over 9 years and is now in the data lock/analysis phase. We believe that administering cancer immunotherapy BEFORE the ravages of surgery, radiation and chemotherapy has the greatest potential of helping patients.

- **L.E.A.P.S.** (Ligand Epitope Antigen Presentation System) - The LEAPS platform technology has been shown to preferentially direct immune response to a cellular (e.g., T-cell), humoral (antibody), or mixed pathway and exhibited protection in six different animal models of disease. It has the potential to be utilized in diseases for which antigenic epitope sequences have already been identified, such as in a number of infectious diseases, some cancers, autoimmune diseases, allergic asthma, and select CNS and other diseases (e.g., Alzheimer's).

LEAPS (Ligand Epitope Antigen Presentation System) Technology

- CEL-SCI's second proprietary technology platform, LEAPS, is a preclinical technology designed to stimulate the human immune system to fight bacterial, viral, and parasitic infections more effectively, as well as autoimmune conditions, allergies, transplantation rejection, and cancer.
- LEAPS is a patented, Immune- and T-cell modulation peptide delivery technology designed to stimulate antigen-specific immune responses in cells using synthetic peptides. The proprietary LEAPS peptides immunogens constructs are designed and synthesized by CEL-SCI to target specific diseases and conditions.
- Administered as a treatment/preventive vaccine, the LEAPS constructs consists of a small T- or Immune-cell binding ligand (TCBL/ICBL) linked with a small, disease-associated peptide (antigen), and is delivered directly to the patient by injection, through *in-vitro* stimulated dendritic cells, or by mucosal absorption. The LEAPS technology provide a new method to treat and prevent certain diseases by enhancing the T-cell responses to that particular antigen, acting earlier in the pathway of the specific disease than conventional vaccines.
- The ability to generate a specific immune response (cellular or humoral) is important because many diseases are often not treated and cured effectively due to the body's selection of the "inappropriate" immune response. The capability to specifically design a peptide that can reprogram an immune response may offer a more effective approach than existing vaccines and drugs in attacking an underlying disease.



LEAPS (Ligand Epitope Antigen Presentation System) Technology

The concept behind the LEAPS technology is to directly mimic cell/cell interactions on the T-cell surface using synthetic peptides. LEAPS immune therapeutic (vaccines) consist of a combination of a small peptide (referred to as a T-cell binding ligand or TCBL or Immune cell binding ligand - ICBL) that activates the immune system by targeting or binding to an antigen presenting cell, such as a dendritic cell (DC) an example of ICBL is peptide J, or to a T-cell (TCBL), with another small peptide containing a disease associated epitope. LEAPS creates a hetero-conjugate containing both a TCBL (or ICBL) and a disease specific epitope, combining adjuvant/activating and antigen/immunizing activities into one relatively small peptide construct.

When a LEAPS construct attaches to a certain immune DC or T-cell, it causes that cell to activate a particular immune response. The Company can vary the immune response depending on the type of LEAPS construct and I/TCBL used. Two I/TCBLs of particular interest for CEL-SCI are, ICBL peptides J and G (or the modified and more stable version of G, derG). Conjugates of these LEAPS peptides appear to activate different sub-sets of either DC or T-cells. LEAPS 'J' peptide is a short fragment from β2-macroglobulin (of MHC I), which elicits a Th1 response, and G is a modified fragment from MHC II β-chain, which directs a Th2 response.

When LEAPS constructs stimulates a Th1 response, first the J-LEAPS binds to the DC which secretes IL-12 and then the activated DC interacts with either Th1 or cytotoxic T-cell (Tc1). Th1 cells secrete IL-2, and interferon-γ and are associated with vigorous delayed-type hypersensitivity reactions. Th2 cells, on the other hand, synthesize and secrete IL-4, IL-5, IL-6, and IL-10 - cytokines that influence B-cell development and Tfh cells also affect antibody production switch from IgM to IgG.

Prior Results and Current Focus of LEAPS Technology

- Animal studies have demonstrated the safety and potential usefulness of specifically designed LEAPS constructs in treating rheumatoid arthritis, experimental allergic myocarditis, collagen induced arthritis (CIA), Proteoglycan induced arthritis (PGIA), Her2Neu breast cancer, HSV-1 and H1N1 Influenza A infections.

- LEAPS is currently in pre-IND studies as a rheumatoid arthritis vaccine research paid for by a U.S. government grant of $1.5 M.

Why LEAPS against COVID 19?

Prior studies (conducted in collaboration with the NIH Laboratory for Emerging Diseases) demonstrated the effectiveness of a LEAPS H1N1 construct in the treatment of Influenza A - H1N1 infected mice.
The results against H1N1 were as follows:

- Reduced mortality and morbidity (as measured by extended survival and the regaining of weight-loss following treatment) as compared to controls
- At day 4 reduced viral presence replication in lungs (by 8-48 hrs. post treatment of infected mice)
- At day 4 more favorable cytokine profile, i.e. more Th1 and lower inflammatory cytokines
- Multiple days infiltration of cytotoxic T cells into diseased tissue
- IgG2a antibody imply Th1 type response at the end of the study
- Elicited a LEAPS-specific-NP(H1N1) antigen T-cell response

We are currently working with the University of Georgia Vaccine Research Center to replicate the LEAPS results seen against H1N1 pandemic flu in ACE2 transgenic animals challenged with SARS-CoV-2.

The initial main goal of LEAPS COV19 therapy administered to COVID 19 patients early in the disease process is to circumvent the likelihood of progression to severe disease.

Summary

- Second-generation immunotherapy/vaccine technology: create better and more comprehensive immune response suitable for attacking COVID 19. Antibodies and T-cell response.
- Proven in animal tests against H1N1 pandemic flu, Herpes simplex and four other diseases.
- Able to generate protective anti-viral responses without causing an undesirable inflammatory response (cytokine storm) in the lungs or other places.
- SARS CoV-2 is known to mutate. Therefore we have directed the LEAPS immune responses against the more conserved NP regions of the SARS CoV-2 virus which are less likely to shift/drift.
- LEAPS is about reducing viral levels, upregulation of cytotoxic T cells and of Th1 cytokines (IFNγ and IL12), while suppressing inflammatory cytokines.