StemVacs Immunotherapy Platform for Breast Cancer

**StemVacs** is therefore a subcutaneously administered vaccine comprised of immune stimulatory peptides resembling cancer stem cell specific proteins.

**StemVacs** is a platform for antigen-nonspecific immune modulatory treatment that can be utilized as a monotherapy or as a combination with antigen specific modalities such as peptide or protein based vaccines.

**StemVacs** is now available as a treatment option at the Pan American Cancer Treatment Center in Tijuana, Mexico for stages 1-4 breast and prostate cancers.

**BRS-001: Cancer Stem Cell Targeted Immunotherapy**

BRS-001 is a patent-pending cellular immunotherapy developed by scientists at Therapeutic Solutions International, Inc., a San Diego Biotechnology Company, which is available at the Pan Am Cancer Treatment Center in Tijuana Mexico to treat stages 1-4 in breast cancer.

BRS-001 activates the immune system to seek and destroy cancer stem cells, based on their expression of a protein named Brother of the Regulator of Imprinted Sites (BORIS). BRS-001 is generated using white blood cells of the patient, which are grown outside of the body to create dendritic cells. The patient’s own dendritic cells are treated in vitro with peptides derived from BORIS, and subsequently are injected back into the patient in order to program the immune response to kill cells that express the protein BORIS, which are cancer stem cells.

**Without Killing of Cancer Stem Cells it is Impossible to Cure Cancer**

All tumor cells are the offspring of a single, aberrant cell, but they are not all alike. Only a few retain the capacity of the original cell to create an entire tumor. Such cancer stem cells can migrate to other tissues and become fatal metastases. To fully cure a patient’s cancer, it is crucial to find and eliminate all of these cells because any that escape can regenerate the tumor and trigger its spread through the body.

**BORIS is Essential for Cancer “To be Cancer”**

The BORIS protein functions to disable a tumor suppressor termed “CTCF”[1]. The role of CTCF is to ensure that parts of DNA that should not be activated, indeed are not activated. For example, one of the roles of CTCF is to block expression of genes that cause cancer[2]. In cancer stem cells, BORIS blocks the function of CTCF, thus allowing for propagation of cancer. It has been shown that if BORIS is blocked in cancer stem cells, the cancer stem cells no longer form tumors[3].

**BRS-001 is Selective Immunotherapy**

Dendritic cells are the most potent immune stimulatory cell of the body. Currently dendritic cell therapy is approved in the USA in the form of the drug Provenge. BRS-001 consists of dendritic cells that are treated with parts of the BORIS protein in order to stimulate killer T cell responses against any cell that expresses BORIS. Using dendritic cells to stimulate immunity offers the advantage of inducing immunological memory against the tumor. Published studies by us in collaboration with the NIH showed immunity to BORIS results in tumor killing[4],[5].

**Preclinical Proof**

The BRS-001 construct is capable of stimulating immune responses that cross over to wild-type tumors without having the potential of causing cancer. This ability to induce tumor immunity was validated across a broad variety of tissue types making the BRS-001 approach broadly applicable for numerous cancers. This was described in peer reviewed papers by Company scientists demonstrating that immunization with BRS-001 not only inhibits growth of aggressive breast cancer 4T1 cells in BALB/c mice, but also that mice immunized with BRS-001 contain high numbers of CD8+ T cells that have spontaneous cytolytic activity against breast, leukemia, and glioma cells in vitro. Company scientists have determined that vaccination with BRS-001 in the context of various immune stimulatory technologies induces a CD8 cytotoxic T cell response that recognizes tumors independent of tissue origin.
NanoStilbene: Patented Augmenter of Cancer Immunotherapy

**NanoStilbene**, a nanoparticle formulation of pterostilbene, is covered for use in cancer immunotherapy under the Company's issued U.S. Patent No.: 9,682,047 and is included as part of the Breast Cancer Protocol with StemVacs.

**NanoStilbene** is an easily absorbed nanoemulsion of nanoparticle pterostilbene in the range of 75-100nm at a concentration of 30 milligrams per milliliter. The pterostilbene placed in a nanoemulsion droplet is free from air, light, and hard environment; therefore, as a delivery system, nanoemulsion can not only improve the bioavailability of pterostilbene but also protect it from oxidation and hydrolysis, while it possesses an ability of sustained release at the same time.

Therapeutic uses of nanotechnology typically involve the delivery of small-molecule drugs, peptides, proteins, and nucleic acids. Nanoparticles have advanced pharmacological effects compared with the therapeutic entities they contain. Active intracellular delivery and improved pharmacokinetics and pharmacodynamics of drug nanoparticles depend on various factors, including their size and surface properties.

Nanoparticle therapeutics is an emerging treatment modality in cancer and other inflammatory disorders. The National Cancer Institute has recognized nanotechnology as an emerging field with the potential to revolutionize modern medicine for detection, treatment, and prevention of cancer.

**Conclusion:**

This type of immune response is usually associated with remission of tumor. Based on this mechanism of action, Therapeutic Solutions International, Inc. has decided to develop a dendritic cell BORIS-peptide pulsed candidate as the most promising method of stimulating immune responses to BORIS in cancer patients.

The Pan American Cancer Treatment Center is located a few miles south of sunny San Diego, in Tijuana, Mexico. The Pan Am facilities are state of art and offer access to cutting edge cancer immunotherapies outside of clinical trials. After we receive you in San Diego, you will travel by air conditioned transportation to our new and modern treatment center, where you will have access to cellular, small molecule, and protein therapies through accelerated means.

**References:**


**BRS-001** is patent-pending technology developed by Therapeutic Solutions International, Inc. “Exosome Mediated Innate and Adaptive Immune Stimulation for Treatment of Cancer”

Disclosed are means of stimulating innate and/or adaptive immunity to cancer by administration of exosomes. Stimulation of innate immunity involves modifying exosomes by chemical addition of innate immune stimulators, whereas stimulation of adaptive immunity involves pulsing dendritic cells generating exosomes with antigens, in some cases, pulsing with Brother of the Regulator of Imprinted Sites (BORIS) proteins, peptides, or altered peptide ligands thereof.
Additional StemVacs Platform Immunotherapeutics

The immune system's natural capacity to detect and destroy abnormal cells may prevent the development of many cancers. However, cancer cells are sometimes able to avoid detection and destruction by the immune system. Cancer cells may:

- reduce the expression of tumor antigens on their surface, making it harder for the immune system to detect them
- express proteins on their surface that induce immune cell inactivation
- induce cells in the surrounding environment (microenvironment) to release substances that suppress immune responses and promote tumor cell proliferation and survival

In the past few years, the rapidly advancing field of cancer immunology has produced several new methods of treating cancer, called immunotherapies, which increase the strength of immune responses against tumors. Immunotherapies either stimulate the activities of specific components of the immune system or counteract signals produced by cancer cells that suppress immune responses.

The overarching approach to cancer on our StemVacs platform is as follows:

- Treat innate immune suppression: Administration of oral apigenin/pterostilbene (Cancer Metabolic DeTox Product) to decrease immune suppressive toxic molecules made by tumor and tumor microenvironment.
- Treat adaptive immune suppression: Administration of MemoryMune to activate dormant memory cells recognizing the tumor. Administration of LymphoBoost to repair deficient IL-12 production.
- Stimulation of immune response to cancer stem cells (StemVacs).
- Consolidation and maintenance of immunity: Cycles of StemVacs, supported by innaMune and LymphoBoost

Cancer Metabolic DeTox: This is an orally administered agent that is derived from various herbs termed apigenin. The unique property of apigenin is that it inhibits a cancer associated metabolic pathway that degrades the amino acid tryptophan. Specifically, apigenin inhibits the enzyme indolamine 2,3 deoxygenase (IDO), which is responsible for breaking down tryptophan in the vicinity of the tumor and generating by-products such as kynurenine. It is known that immune activation is dependent on tryptophan being present in the tumor environment. The depletion of tryptophan and generation of kynurenine by tumor cells and tumor associated cells is a major cause of immune suppression in cancer. By administering Cancer Metabolic DeTox, the innate arm of the immune system has a chance to regenerate. This positions the patient for better outcome after administration of specific immune stimulating vaccines.

innaMune: Is a biological product derived from a tissue culture of blood cells derived from healthy donors. It is a combination of cytokines that maintain activity of innate immune system cells, as well as having the ability to shift M2 macrophages to M1. In one instance a composition is extracted from polyvalently activated peripheral blood mononuclear cells through dialysis. This immune modulator is useful for the treatment of cancer and alleviation of cancer associated immune depression. As an immunomodulator, innaMune acts as a costimulatory of T cell activation by modulation of cytokine production. In another application the immune modulator is concentrated for miRNA species capable of activating innate immune cells.

LymphoBoost: Is a proprietary formulation of Mifepristone, a drug approved for another indication, which we have shown to be capable of stimulating lymphocytes, particularly NK cells and T cells, both critical in maintaining anti-tumor immunity. LymphoBoost is useful for improving a treatment outcome and/or an alteration of immunity in a condition that benefits from immune stimulation. In particular, administration of sufficient doses of mifepristone or a derivative, alone, or in combination with an immunotherapeutic such as, but not limited to, an antibody, a vaccine, a cytokine, or a medicament whose therapeutic activity is associated with immune modulation.

MemoryMune: Is a product derived from a two-step culture process of donor blood cells. The product MemoryMune reawakens dormant immune memory cells. It is known that many cancer patients possess memory T cells that enter the tumor, however, once inside the tumor these cells are inactivated. MemoryMune contains a unique combination of growth factors specific for immune system cells called "cytokines."