SEEKING PARTNERS TO ACCELERATE OUR CLINICAL DEVELOPMENT PROGRAMS FOR THE NEXT GENERATION OF IMMUNOTHERAPY DRUG PRODUCTS

Contact:

Dr. Michael Har-Noy
Founder, Chief Executive Officer
Immunovative Therapies, Ltd.
Malcha Technology Park
1 Agudat Sport Hapoel Street
Jerusalem, Israel 9695101
Email: harnoy@immunovative.com
Website: www.immunovative.com

- Individualized cancer vaccine with a cost-effective, “off-the-shelf” and scalable allogeneic business model.
- Two immunotherapy products ready to advance to pivotal clinical trials.
- Gross profit margins >80% are attainable with in-house GMP facility.
- Products integrate an individualized, therapeutic cancer vaccine with a natural checkpoint blockade mechanism.
- Mechanism modelled after the most powerful anti-tumor mechanism ever discovered: the GVT effect of allogeneic transplant
- Phase I/II data demonstrate ability to debulk chemotherapy-resistant metastatic tumors.
- Potential to broaden checkpoint blockade response rates and indications of use or can be useful as monotherapy.
- Broad patent coverage

THE COMPANY

Immunovative Therapies, Ltd. (ITL) is an Israeli-based biopharmaceutical company specialized in the development and manufacturing of immunotherapy products where living immune cells are the active ingredient. ITL currently has two therapeutic cancer vaccine products, CryoVax®and AlloVax®, in clinical development. These products are derived from the company's platform Mirror Effect™ technology. The Mirror Effect™ elicits the same anti-tumor immune effect that occurs after allogeneic non-myeloablative stem cell transplant procedures ("Mini-Transplant") while eliminating the toxicity risk; the need for a HLA matched donor; and, the need for chemotherapy pre-conditioning.

ITL has state-of-the art GMP production and immunomonitoring facilities to support clinical trials. ITL also operates a wholly-owned subsidiary, Immunovative Clinical Research, Inc. (ICRI) located in Phoenix, Arizona USA. ICRI provides ITL with in-house CRO services in support of global clinical trials.

THE TECHNOLOGY PLATFORM

The "holy grail" of transplant medicine is the separation of the graft vs tumor (GVT) effect from the devastating graft vs host disease (GVHD) side effect that occurs after allogeneic, non-myeloablative stem cell transplant ("Mini-Transplant") and donor lymphocyte infusion ("DLI") procedures. The GVT effect has been described as the most powerful anti-tumor effect ever discovered due to its unique ability to debulk, and in some cases, 'sterilize' the body of chemotherapy-resistant metastatic disease.

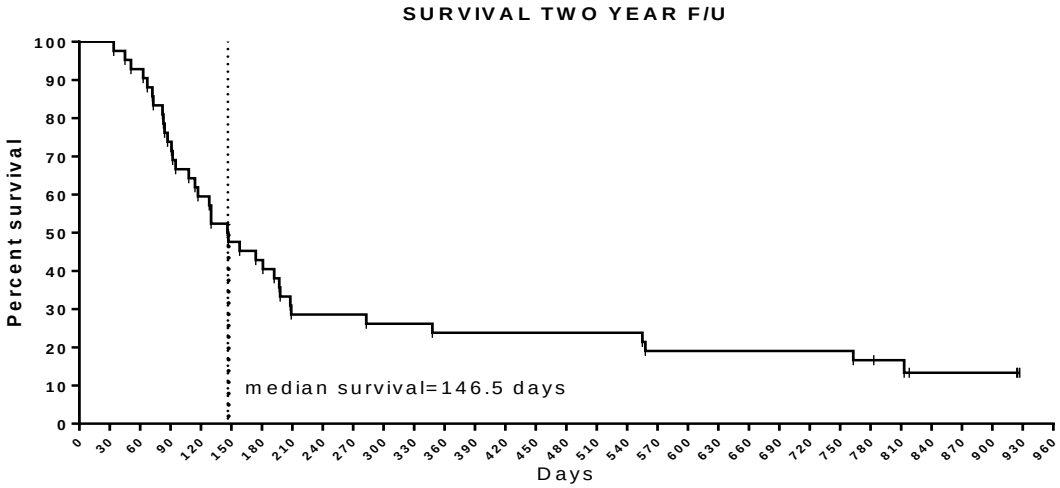
Immunovative is the first to effectively harness the powerful GVT anti-tumor effect of Mini-Transplant procedures and eliminate the related GVHD toxicity. This break-through discovery is made possible through the technology platform called the "Mirror Effect™". The Mirror Effect™ reverses the immunologic flow of events of Mini-Transplant procedures. Mini-Transplant immune effects emanate from the graft (GVT and GVHD). The Mirror Effect™ causes the effects to emanate from the host, rather than the graft. This flow reversal results in a host-mediated rejection of the graft (host vs graft or "HVG") that serves to support a host-mediated anti-tumor effect (host vs tumor or "HVT"). Significantly, however, the HVG host rejection is a non-toxic event, while the reverse flow GVHD is extremely toxic. The Mirror Effect™ thus allows the intimately related GVT/GVHD effects to remain associated, however in the reverse flow setting the beneficial effects are preserved while the detrimental effects are eliminated. The HVG effect is the 'mirror' of GVHD and the HVT effect is the 'mirror' of the GVT effect.

CLINICAL TRIAL STATUS

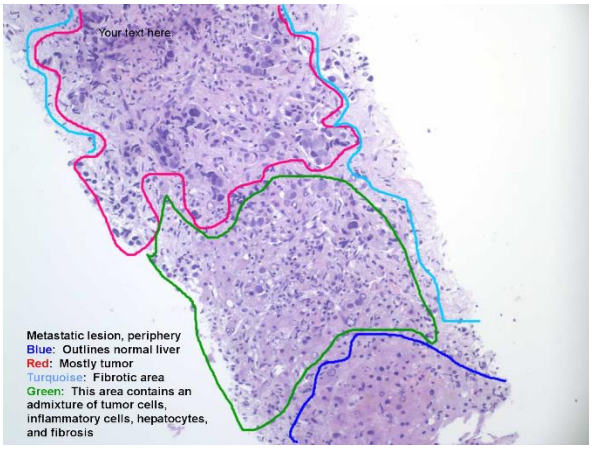
A phase I/II clinical study has been completed in 42 metastatic cancer patients with a variety of metastatic cancer indications. These subjects were heavily pre-treated, high tumor burdened, with poor performance status and a median survival expectation of 60 days. This trial demonstrated a survival tail of 11 of 42 (26%) subjects alive at one year and 9 of 42 (21%) alive at the two year follow-up. Long term survivors of 1 yr+ included metastatic breast cancer--4; colorectal/GI--3;

pancreatic adenocarcinoma--2; prostate-1 and NSCLC--1. These indications are not usually thought of as being responsive to immunotherapy. Survival correlated with the appearance of IL-12 in the plasma. 21 of 42 (50%) seroconverted to IL-12+ after immunotherapy. The survival of the IL-12 positive group was significantly greater than the IL-12 negative group. Pathological evidence of immune cell infiltration and tumor debulking, as well as radiological evidence of immune-mediated liquefaction of tumor lesions was demonstrated in the IL-12+ survivors.

Below is the survival curve demonstrating durable, long term survival in hospice patients with 60 day median survival expectation:

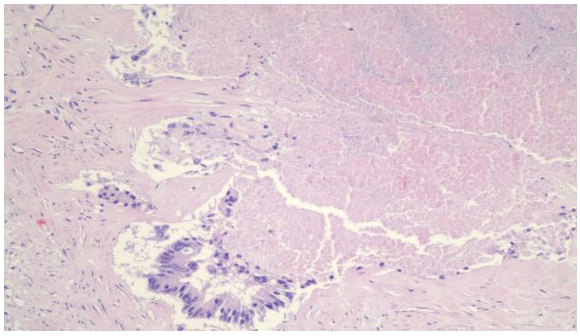


Pathology indicates massive immune cell infiltration, areas of coagulative necrosis and fibrosis:



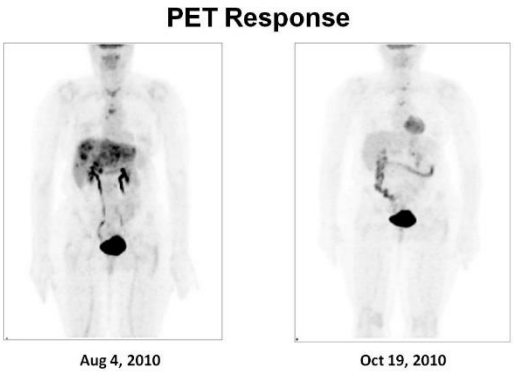
Pancreatic cancer liver metastasis

s/p immunotherapy



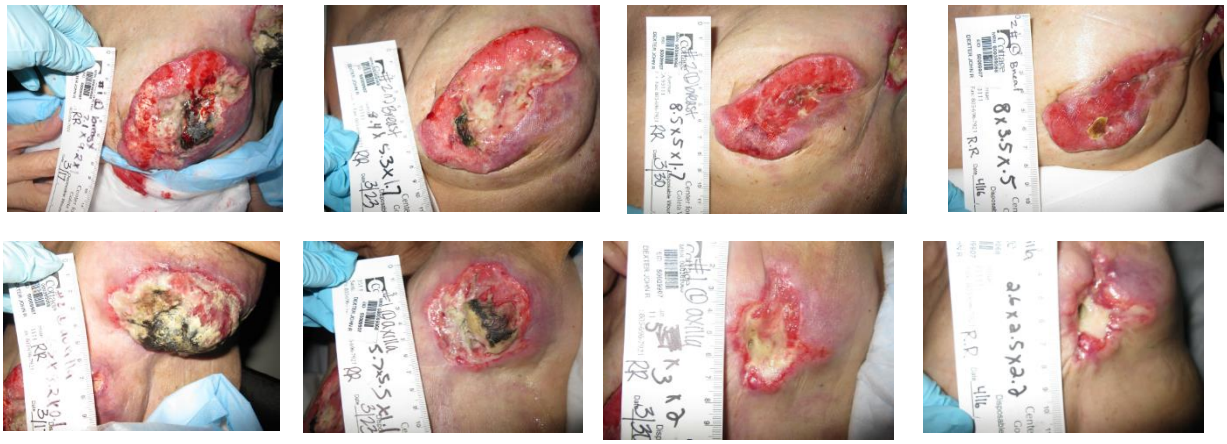
Colorectal Cancer liver metastasis

s/p immunotherapy



Radiological evidence of tumor debulking response in metastatic breast cancer s/p immunotherapy.

External breast cancer lesions on excised breast and axial lymph node after in-situ vaccination of liver metastasis:



60 days 72 days 79 days 96 days

There is currently an active IND in USA and Thailand. US FDA clearance for a Phase IIb study in third line metastatic colorectal cancer to launch at Banner/ MD Anderson (Phoenix, AZ) in April-May 2016.

Thai FDA approval for a Phase II study in hepatocellular carcinoma at the Thailand National Cancer Institute in Bangkok, Thailand to launch in March-April 2016.

Pivotal, randomized, controlled Phase II/III clinical study in third line metastatic colorectal cancer pending clearance at Thai FDA. Phase II non-inferiority study in metastatic or locally advanced head and neck cancer pending clearance at Thai FDA with expected launch in June-July 2016. Phase I/II study in HIV+ patients to replace HAART medication with immunotherapy is expected to be submitted in May-June 2016. Expected launch in August-September 2016.

Immunovative's products can be used to enhance the response rates of current immunotherapy drugs

Immune checkpoint drugs require the presence of immune effector cells within the tumor microenvironments in order to be effective. The majority of patients do not present with effector immune cells within tumor lesions. CryoVax® and AlloVax® can cause the formation of immune effector cells within the tumor lesions of patients that did not originally present with these cells. In this manner, Immunovative's products can be used to enhance response rates of current checkpoint inhibitor drugs by assuring an effective immune response within tumor lesions.

Immunovative's products can eliminate the need for checkpoint blockade drugs in some cancer indications.

For potential partners that do not have checkpoint blockade drugs under development, Immunovative's products may allow you to compete against checkpoint blockade drugs. First, Immunovative's products can provide an immunotherapy option in cancer indications where checkpoint blockade drugs are known not to be effective (e.g., colorectal cancer, pancreatic cancer, etc.). In addition, the intravenous infusion of AlloStim®, a component of the CryoVax® and AlloVax® protocols, creates an inflammatory cytokine storm. This cytokine storm naturally down-regulates the expression of multiple checkpoint molecule on tumors and antigen presenting cells, and upregulates positive co-stimulatory signals such as CD80/86. Thus, Immunovative's protocols already incorporate a natural checkpoint blockade mechanism and may not need additional blockade in order to be effective.

FIRST GENERATION CHECKPOINT BLOCKADE

Current immunotherapy products in the first generation include monoclonal antibody-based checkpoint blockade class of drugs. These drugs block negative checkpoint molecules (CTLA4 or PD-1/PD-L1) which act to suppress the killing function of tumor-specific CTL. However, for this class of drug to be effective, tumor-specific CTL must be resident in the tumor beds and be suppressed by checkpoint blockade signals. Since most patients do not have a tumor-specific CTL immune response resident within tumor beds, the response rates of these first generation immunotherapy drugs are limited. In addition, Immunovative's products are able to imprint an effective immune response that overwhelms a resident non-effective immune response to the same tumor using the Mirror Effect™ which reverses the immunological flow from being graft-mediated to being host-mediated.

Immunovative's products have potential to leap frog over current checkpoint blockade and CAR-T immunotherapy drug development programs.

Immunovative's products, which can cause the development of an effective therapeutic therapeutic cancer vaccine which incorporates a natural checkpoint blockade mechanism as a monotherapy, has the potential to disrupt the current development efforts for cancer vaccines, such as CAR-T cells with or without checkpoint blockade and combinations of checkpoint blockade drugs.

SECOND GENERATION IMMUNOTHERAPY DRUG DEVELOPMENT

Combination Checkpoint Blockade. The second generation of immunotherapy drugs aim to increase the response rates, indications and efficacy of first generation checkpoint blockade drugs. Many are pursuing combination therapies with existing CTLA4, PD-1/PD-L1 drugs as well as additional checkpoint targets, such as OX40/OX40L, HVEM/LIGHT, ICOS, GITR and CD27/CD70 or positive checkpoint targets such as CD80/86, CD40/CD40L. This approach has many practical problems. Tumors express checkpoint molecules heterogeneously with spacial and temporal variations. Thus making it difficult to design the correct combinations and timing of delivery to effectuate the most optimal response. In addition, with the healthcare industry becoming more sensitive to the cost of anti-cancer drugs, the trend towards combinations may put pressure on the margins for these drugs and lower the potential return on investment. Combination therapies are also vulnerable to a monotherapy that produces the same efficacy results.

Therapeutic Cancer Vaccines. Another active area of development for second generation immunotherapy drugs recognizes that most patients do not present with an anti-tumor immune response within the tumor beds that is actively suppressed. Most patients either present with no immune response or an immune response that fails to protect against the disease progression. To counter this reality, immunotherapy developers are seeking to develop cancer vaccines that generate effective immune responses and combine these with checkpoint blockade in order to enable immune-mediated tumor destruction. Therapeutic cancer vaccine development faces many major hurdles (see "***The Top 10 Issues that Confront Cancer Vaccine Developers***").

CAR-T cells. Chimeric antigen receptor (CAR) T-cell therapy is an approach to by-pass vaccination to produce tumor-specific CTL by genetically engineering autologous T-cells to recognize a tumor associated antigen. This approach attempts to make a T-cell work like an antibody. The approach is limited by availability of tumor associated antigens. Initial CAR-T products target tissue antigens, such as B-cell antigens. Thus the approach is initially targeted to B-cell malignancies. It is more difficult to identify antigens for solid tumor indications. In addition, the autologous business model whereby blood is removed from a patient, processed outside the body and infused back to the same patient provides no economy of scale. The commercial implications of the autologous business model brings into question whether a successful CAR-T product could ever be profitable, even if it obtained FDA marketing approval. Dendreon (DNDN) developed the first FDA approved living cell vaccine. Despite reimbursement at $93,000 for three

courses of therapy, the company was not able to reach profitability. Recent publications have suggest that CAR-T cell therapies will cost over $400,000 for a course of therapy.

UNIQUE MECHANISM OF ACTION. Integrated mechanism of action and protocol provides a method to: (1) create a tumor-specific Th1/CTL immune response customized to a patient's tumor *de-novo* and imprint this response over an existing non-protective response; (2) cause the new Th1/CTL effector cells to extravasate to tumor beds through-out the body; (3) alter the systemic and local microenvironments to dys-regulate tumor-derived suppressor circuits and reverse peripheral tolerance; and, (4) upregulate tumor immunogenicity by upregulating MHC and co-stimulatory molecules on tumors and downregulate checkpoint molecule expression.

THE PRODUCTS INTEGRATED INTO A PROTOCOL

Immunovative has two products in clinical development, CryoVax® and AlloVax®, both derived from the Mirror Effect™ technology platform. A component of both products is a drug called "AlloStim®". AlloStim® is a bioengineered, living cell, allograft derived from healthy blood donors. Blood is collected in compliance with 21 CFR 1271. Naïve CD4+ T-cells are purified from the blood and cultured in a bioreactor for 9 days without exogenous cytokines. After 9 days, the cells differentiate to an intermediary product called "T-Stim™". T-Stim™ is aliquoted into individual dose vials and stored frozen in liquid nitrogen. T-Stim™ remains stable for at least 2 years. When needed in the clinic, the T-Stim™ vials are thawed and activated with CD3/CD28-conjugated microbeads in a 4h formulation process. Over these 4 hours, T-Stim™ cells differentiate into AlloStim® . AlloStim® , with the microbeads still attached, has a memory Th1 cell phenotype with high expression of CD40L and interferon-gamma. AlloStim® also expresses Granzyme B and perforin (CTL/NK-like properties) and has antigenic and immunomodulatory properties. These properties are so unique for a living cell that they permitted AlloStim® to be patented as a composition of matter.

Formulated AlloStim®, with the microbeads remaining attached, is suspended in media for infusion and aliquoted into syringes. Formulated AlloStim® is maintained at 4^0 C in validated containers and is delivered by specialized courier to points-of-care within 24-48h. Formulated AlloStim® retains it's immunological properties for at least 72h.

The immunological properties of AlloStim® are integrated into protocols designed to elicit the same cascade of immune events that occur in Mini-Transplant procedures, without the need for a matched donor, chemotherapy conditioning or prophylaxis for the toxic effects of GVHD.

Since most metastatic cancer patients present with a failed Th2-dominated immune response, a therapeutic vaccine must not only create an effect tumor-specific Th1 immune response, but must also imprint this effective Th1 response over the existing failed Th2 response. In order to immunomodulate the Th1/Th2 balance, AlloStim® is first administered multiple times intradermally. This dosing route serves to elicit large numbers of alloantigen-specific Th1/CTL in circulation.

While intradermal injections elicit allo-specific immunity, in order to elicit host derived, tumor-specific Th1/CTL responses, AlloStim® is combined with a source of tumor antigens obtained from a patient's own tumor. Tumor antigens are derived from the internal contents of tumor cells rather than externally expressed antigens. External antigens trigger an antibody response, while the most effective anti-tumor immune response is a cellular response. CTL killer cells, the main effector cells for a cellular immune response, recognize tumor antigens in the context of MHC I molecules expressed on target cells. The tumor antigens that will be expressed on MHC I molecules are initially bound to chaperone proteins (i.e., heat shock proteins) within the tumor cells. These chaperone proteins are the basis for the design of CryoVax® and AlloVax®.

Both CryoVax® and AlloVax® are personalized, therapeutic cancer vaccines where the source of tumor antigens are chaperone proteins that reside within tumor cells. CryoVax® is an in-situ therapeutic vaccine and AlloVax® is derived externally.

For CryoVax,® the chaperone proteins residing within tumor cells are released into the tumor microenvironment using a technique called cryoablation. Cryoablation disrupts the tumor cell membrane using cycles of extreme cold followed by thaw cycles. This results in the disruption of the tumor cell membrane and the release of the internal contents of the tumor cells to the microenvironment. AlloStim® is then injected into the ablated tumor lesion to serve as an adjuvant to drive tumor-specific immunity creating an in-situ vaccine.

For AlloVax® , the internal chaperone proteins of tumor are released ex-vivo rather than in-situ. A 0.2g or greater tumor sample is the source material to make AlloVax® . The 0.2g sample requirement can be satisfied with a punch biopsy, whereas other heat shock protein-based vaccines require at least 10-fold this amount. To cause the release of chaperone proteins, tumor cells are lysed and the chaperone proteins are purified using an electrochemical gradient technique. The resulting highly purified chaperone proteins, called Chaperone Rich Cell Lysate or "CRCL", is injected together with AlloStim® intradermally. This combination creates the same effect in the skin as CryoVax® creates in a tumor lesion.

The introduction of tumor antigens to the host immune system in a cancer patient originally resulted in the formation of an ineffective, non-protective immune response and clinical disease. Vaccination is essentially the re-introduction of tumor antigens to the same immune system that originally failed to protect against the tumor formation. In order that the re-introduction of tumor antigens has a different outcome than the original interaction of the immune system with the tumor, patients are first primed to be immune to the alloantigens of AlloStim®. Priming occurs prior to the in-situ or ex-vivo vaccination step. Priming is accomplished by multiple intradermal injections of AlloStim® . This procedure creates a high titer of allo-specific Th1/CTL cells in circulation. Thus when the vaccination step occurs, the background immune response is dominated with Th1/CTL cells. This creates a different condition than occured upon the original interaction of tumor antigen with the immune system.

In patients have been previously primed to the alloantigens in AlloStim®, the presence of Allostim® in the lesion will attract allo-specific Th1/CTL memory cells to reject the AlloStim® . The presence of AlloStim® , producing Th1 cytokines and expressing high density CD40L, will influence the

maturation of dendritic cells which arrive to engulf the mixture of tumor antigens and alloantigens released at the vaccination site. This mixture of antigens is also part the mechanism that drives the powerful GVT effect of Mini-Transplant. The dendritic cells that engulf the mixed allo- and tumor-antigens mature and produce IL-12. This type of mature dendritic cell can educate T-cells resulting in high titers of circulating tumor-specific Th1/CTL.

In order for circulating allo- and tumor-specific Th1/CTL to be effective, they must leave the circulation and traffic to tumor lesions. When within tumor lesions, the microenvironment must support cellular immune function and suppress tumor-derived suppressor mechanisms. In Mini-Transplant procedures, this is occurs due to an inflammatory cytokine storm. The cytokine storm upregulates the expression of MHC and co-stimulatory molecules on tumor cells and infiltrating APC, as well activates the Th1/CTL effector cells while at the same time suppressing the function of Treg and other suppressor cells, resulting in a tumor killing response. This mechanism is duplicated in Mirror Effect™ by infusing AlloStim® intravenously.

Intravenous AlloStim® causes the tumor-specific and allo-specific Th1/CTL elicited after the priming and vaccination steps to extravasate and penetrate the tumor beds. In addition, the rejection of intravenous AlloStim® creates the same type of cytokine storm as occurs in Mini-Transplant procedures, The cytokine storm of inflammatory cytokines serves to dis-regulate systemic suppressor cells, such as Treg cells, upregulate the expression of MHC and co-stimulatory molecules on tumors and APC and either shut down or reverse local and systemic suppressor circuits.

Our Partnership Approach

Our primary aim is to build strategic partnerships to accelerate the commercialization of our immunotherapy products within territories through-out the world in cancer and infectious disease indications.

We are interested in partnering with organizations with proven marketing capability and regulatory expertise within their territory or territories of specialization. We wish to work with strategic marketing partners to conduct a pipeline of pivotal clinical trials in various disease indications each designed so that the resulting data can be utilized to support marketing applications for the selected disease indication within the target territory.

We are also interested to partner to combine our products with other compatible products where the combination would potentially enhance the efficacy of our products greater than either product alone.

Our Preferred Deal Structure

If your organization’s marketing and regulatory expertise lies in a particular territory and you are seeking to develop new immunotherapy products with broad potential in a multitude of cancer and infectious disease indications within this territory, we are interested to discuss partnership

structures with you. We are flexible in terms of deal structure and always open to new opportunities to work together.

Our preferred deal structure is to provide a partner with exclusive marketing rights within a territory for a specific indication, whereby the partner in exchange assists in the financing of the pivotal trial for the indication and in using the data in support of regulatory submissions aimed at obtaining local regulatory approval for marketing.

We manufacture our immunotherapy product as a frozen intermediate that is stable for several years. We will establish either on our own, jointly with our marketing partner, or will support our partner to establish on their own, formulation facilities within the designated territory. The formulation facilities convert the frozen intermediary product into a final formulated product packaged in a syringe. The formulated syringes can then be distributed to end-users through-out the territory. A transfer price for the frozen intermediate or the final formulated product will be negotiated with the marketing partner. The marketing partner would then have a first-right-of-refusal to exclusively develop new indications within the territory.

What we can offer marketing partners

GMP manufacturing:

We operate our own GMP manufacturing and formulation facility in Israel. The facility has two clean rooms, environmental monitoring, quality system and written SOPs, bar-code inventory tracking vein-to-vein. The facility has enough capacity to handle up to 100 patients a month to support clinical development programs.

Internal CRO

Our US subsidiary is staffed and structured to provide internal CRO services in support of our worldwide clinical development programs. These services include a quality system with written SOPs, electronic medical records, electronic CRF, AE coding and grading, regulatory compliance and report writing, and central pathology and radiology reading and analysis.

Immunological Monitoring

We have a world-class capability to support experimental immunomonitoring of our clinical subjects. In support of this we provide on-site blood and tissue processing. A complete histology laboratory is available, including paraffin embedding, slide preparation, vital staining and immunohistochemical staining supported by an image analysis system. We have cell culture capability and process serial PBMC and serum samples to monitor Th1/Th2 cell balance, cytokine and chemokine expression, phenotypic changes in immune cells as well quantitate tumor-specific and allo-specific immunity.

Clinical Collaboration Sites

We have established partnerships with the Thailand National Cancer Institute and the Center of Excellence for Cancer Treatment and Immunotherapy Research at Sukumvit Hospital. These partnerships provide us with the capability to accrue large numbers of clinical trial patients. We provide these sites with Site Management Services to assure that the clinical data obtained from the sites complies with 21 CRF 312.120 for use of the data in support of submissions to US FDA for marketing clearance.

Research Collaborations

Please contact us if you are interested in partnering to bring our next generation immunotherapy products to market in a defined territory or if you would like to research the combination of your drug or device with our products.

Since AlloStim® can upregulate the expression of Fc-gamma receptors on circulating monocytes, AlloStim® has the potential to enhance the ADCC mechanism of therapeutic IgG1 class monoclonal antibody,

Release of chaperone proteins from tumor cells combined with AlloStim® creates the novel vaccine products, CryoVax® and AlloVax®. Similarly, AlloStim® can combine with other techniques which result in the disruption of the tumor cell membrane. This includes radiotherapy, electroporation and certain types of chemotherapy.

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