



BUSINESS SUMMARY

Next Generation of Immunotherapy

Our mission is not to just bring a new immunotherapy drug to the market, but to create a new multi-billion dollar biopharmaceutical industry that will eventually replace marginally effective and highly toxic cancer treatments with highly effective and minimally toxic immunotherapy products.

Immunotherapy is the only treatment modality that has the technological capability to cure cancer. The immune system can locate and eliminate the last tumor cell, something that is not feasible for a surgeon's scalpel, radiation or chemotherapy. Without this ability, the tumors recur and spread.

There is no cure for metastatic cancer. In addition, the immune system has the special feature of memory. Once the immune system sterilizes the body of all disease, it remembers the cancer so that if the disease should return in the future, the immune system is capable of rising up and protecting against disease without any further treatment. Our goal is to fast track to FDA approval and revenues and then reinvest profits into research and development efforts that will eventually lead us to optimize our immunotherapy drugs in order to develop a cure for cancer in our lifetime.

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HIGHLIGHTS

- ❖ Immunovative has developed a new generation of immunotherapy cancer vaccine drug products where the active ingredient is patented living immune cells. No requirement to match the donor with the patient.
- ❖ Next generation immunotherapy is able to increase the efficacy, broaden the indications and replace checkpoint blockade strategies. Checkpoint blockade requires an existing effective immune response that is suppressed. Limited numbers of patients present with a suppressed response. The next generation immunotherapy creates an effective response where such a response did not exist.
- ❖ A landmark discovery solves the problem of limited efficacy that has hindered the commercial development of prior cancer vaccine immunotherapy drug products. This discovery enables, for the first time, the harnessing of the power of the immune system to debulk metastatic tumors resistant to chemotherapy with negligible toxic effects.
- ❖ Pre-clinical animal and human trials have validated the technology demonstrating anti-tumor activity in chemotherapy-resistant disease. This enables the Company to target cancer indications where no effective chemotherapy currently exists, a population previously thought not to be good candidates for immunotherapy. This provides a fast track pathway to first regulatory approval for commercialization.
- ❖ Technology for the economical, large-scale production and distribution has been developed which solves the business model problems of prior immunotherapy drugs such as Dendreon's Provenge and experimental CAR-T therapies. This technology provides high profit margins (>80%) as is usually associated with pharmaceutical products.
- ❖ The key discovery is based upon a platform technology called the "Mirror Effect™" which enables the host immune system to kill and debulk tumors in the same manner as occurs in allogeneic stem cell/bone marrow transplantation ("Mini-Transplant") but without the extremely toxic side effects and without the need for a matched tissue donor. This technology essentially reverse engineered an already proven curative immune mechanism and eliminated the toxicity.
- ❖ Broad patent coverage has been obtained on the Mirror Effect™ with allowed claims covering the product as a composition of matter, the manufacturing methods, the mechanism of action and uses. Over 20 issued patents worldwide and another 100 pending, including US, Japan, Korea and China.
- ❖ Two products currently in clinical development based on Mirror Effect™ technology: AlloStim™ and AlloVax™. These products have applications in multiple indications of cancer and infectious diseases. Metastatic colorectal cancer, advanced hepatocellular carcinoma and recurrent head and neck cancer as well as HIV/AIDS are currently in clinical development.
- ❖ AlloStim™ completed a Phase I/II, US FDA cleared, 42 patient clinical trial in patients with chemotherapy refractory metastatic cancer. Results provided radiological, pathological and immunological evidence of an immune-mediated tumor debulking that correlated with extended survival. In addition, a biomarker candidate (IL-12) was discovered which appears to predict response and extended survival.
- ❖ Ready to launch a potentially pivotal, randomized, placebo-controlled Phase II/III AlloStim™ clinical trial in third line metastatic colorectal cancer and a non-inferiority, randomized, Phase II, AlloVax™ clinical trial in recurrent or advanced Head and Neck Cancer. Both studies to be conducted at the National Cancer Institute of Thailand.

- ❖ Collaborating with MD Anderson Medical Center in USA and the National Cancer Institute of Thailand.
- ❖ Seeking \$30-45 million over next 24 months to reach the next value-added milestone: completion of potentially pivotal Phase II/III clinical trial.

❖ EXECUTIVE SUMMARY

THE COMPANY

Immunocare Therapies, Ltd. (“ICTL” or the “Company”) is a newly established Israeli corporation located in Jerusalem, Israel. ICTL was initially established as a wholly-owned subsidiary of Immunovative Therapies, Ltd., (“ITL”) an Israeli corporation founded in 2004 and located in Jerusalem, Israel. ITL was formed as a partnership between Hadassah-Hebrew University Medical Center and the Israel Office of the Chief Scientist. ITL has clean room manufacturing facilities in compliance with good manufacturing practices (GMP), quality control and immunological monitoring laboratories and research and development facilities. ITL has a wholly-owned subsidiary responsible for clinical operations located in Phoenix, AZ called Immunovative Clinical Research, Inc. (ICRI). The ICRI US subsidiary serves as an in-house clinical research organization (CRO) providing data collection and analysis, blood donor recruitment and screening, data safety monitoring board, regulatory affairs and radiology and pathology services for worldwide clinical trials.

ITL has granted ICTL the exclusive, world-wide, non-royalty-bearing rights to market and distribute current and future immunotherapy drugs and services covered by the over 100 worldwide granted and pending patents owned by ITL, including any products or services developed in the future or improvements to existing products or services. ITL currently has two immunotherapy drugs in clinical development called AlloStim™ and AlloVax™.

AlloStim™ and AlloVax™ are part of a patented new generation immunotherapy drug portfolio. This new generation immunotherapy incorporates the graft vs tumor (GVT) effect mechanism which has been described as “the most powerful anti-tumor mechanism ever discovered” and combines it with a patient-specific therapeutic vaccine technology and a natural checkpoint blockade mechanism which can disable the ability of tumors to evade immune-mediated death.

The GVT effect occurs after transplant of a new immune system from a tissue-matched normal donor into a cancer patient. This mechanism has proven to be capable of killing large amounts tumor burden and in some cases to even provide curative immunity to patients with both solid tumors and blood tumors that are resistant to chemotherapy. However, the clinical application of GVT has been severely limited due to an intimately related, highly toxic side-effect known as graft vs. host disease (GVHD). ITL has solved the problem of harnessing the beneficial GVT effect and eliminating the devastating GVHD toxicity permitting, for the first time, the wide-scale clinical use of this powerful anti-tumor mechanism.

These new generation drugs are broadly applicable to all types of cancer, as well as infectious diseases, some autoimmune diseases and diseases and symptoms associated with aging.

. AlloStim™ has completed pre-clinical and clinical Phase I/II/IIa studies demonstrating unprecedented killing of chemotherapy-refractory tumors and long-term survival in late stage metastatic cancer patients. AlloStim™ is now prepared to begin a Phase IIb randomized, controlled registration clinical trial in metastatic colorectal cancer (“Pivotal Trial”) designed to support a Biological License Application (BLA) for US FDA market approval. The Pivotal Trial is powered so as to obtain BLA approval upon showing that AlloStim™ has a median survival advantage of 2.4 months or greater compared to control treated patients. ICTL will contract with ITL and its subsidiaries for the conduct of the Pivotal Trial. While the Pivotal Trial is in progress, ICTL will focus on building the corporate infrastructure for launch of an initial public offering (IPO) and the marketing and sales infrastructure for eventual commercialization. In the commercialization phase, ITL will manufacture the drug and transfer the drug to ICTL on a cost plus 20% basis for distribution. AlloStim™ is well positioned to become the first immunotherapy drug to be approved for metastatic colorectal cancer. Virtually any drug that can meaningfully extend the life of metastatic cancer patients is likely to generate over \$1 billion in revenue per year.

THE IMMUNOTHERAPY INDUSTRY

Immunotherapy drugs are a treatment modality that seek to harness the power of the immune system to control and kill cancer. Immunotherapy is the only anti-cancer treatment with curative potential and therefore this modality is under investigation at most academic medical centers and pharmaceutical companies around the world. The promise of immunotherapy has not been shown to translate easily to the clinic, with many disappointing clinical results over the past two decades. Recently, however, immunotherapy has become mainstream with recent FDA approvals of the Provenge cancer vaccine and three Checkpoint Blockade immunotherapy drugs. These recent approvals have established immunotherapy as an emerging industry ready to explode onto the clinical and financial markets. ICTI is well positioned to take advantage of this up swell in immunotherapy support, having carved out a next generation drug that incorporates the same beneficial mechanisms of currently approved immunotherapy drugs and adds significantly to the issues that complicate the medical and business model problems related to these current drugs. Also, for those pharmaceutical companies late to the immunotherapy game, ITL has carved out broad patent protection for this next generation of immunotherapy. Science magazine has named Immunotherapy as the Technology of the Year for 2013. Goldman Sachs named cancer immunotherapy as one of the top 6 disruptive industries and projected immunotherapy to see enormous growth over the next few years. Citi Research lists immunotherapy as one of the 10 disruptive innovations of 2013. Immunotherapy is categorized as a disruptive technology platform, as it has potential to change clinical practice by rendering chemotherapy drugs obsolete and for its potential for

long-term remissions and maybe even eventually a cure of metastatic cancer. A research report titled “Immunotherapy—The Beginning of the End for Cancer” issued by analysts at U.S. bank Citigroup on May 22, 2013, predicts that the annual market for immunotherapy drugs will exceed \$35 billion and become the backbone of treatment in up to 60% of cancers over the next decade. Each recent approval of an immunotherapy drug added an average of \$8 billion in market value for the developers, including a large established pharmaceutical company. Immunotherapy has the same potential for disruptive technological change today in the medical field as the Window’s operating system had on the personal computer industry in the 1990’s. The publicity and support surrounding immunotherapy will help ICTI earn a premium market value on the public market, as well as make the company a possible joint venture/merger partner with pharmaceutical companies that are late comers and are looking to leap frog those that committed early to first generation immunotherapy technology.

CURRENT GENERATION OF IMMUNOTHERAPY TECHNOLOGY

Immunotherapy is a class of drug that uses the immune system to control or kill tumors. The two classes of immunotherapy drugs on the market today include “Checkpoint Blockade” and “Autologous Cancer Vaccine” drugs. Checkpoint Blockade drugs are monoclonal antibodies that are designed to block “check-point” molecules expressed by tumors or their counter-receptors expressed on immune cells. When these checkpoint molecules on tumors and killer cells interact it causes a signal to go to the killer cells to stand-down an immune attack. The three FDA approved drugs of this class are ipilimumab (Yervoy), nivolumab (Opdivo), (both manufactured by Bristol Myers Squib) and pembrolizumab (Keytruda) manufactured by Merck Sharpe and Dome. Checkpoint blockade works only if there are immune cells in the tumor properly educated and armed to be capable of killing the tumor. Rarely do cancer patients have this kind of resident immune response against their tumors. Mostly the immune system of cancer patients has failed to properly respond to the tumor cells. This fact limits the response rates of Checkpoint Blockade drugs. Autologous Cancer Vaccine technology, on the other hand, attempts to create a resident immune response capable of killing a patient’s own tumors through vaccination. The popularity and success of Checkpoint Blockade has generated a renewed interest in Autologous Cancer Vaccine Technology customized for each patient. This is because of the synergy between the two technologies whereby an effective cancer vaccine should increase the response rate of checkpoint blockade drugs. Provenge (Sipuleucel-T), manufactured by Dendreon (DNDN), is the first FDA approved therapeutic cancer vaccine. Many additional vaccines are in the pipeline, but many have failed late stage clinical trials. An new emerging immunotherapy technology called “CAR-T cells” has since attracted a great deal of clinical and investor interest as an alternative to vaccination as a way to elicit resident immune killer cells. This technology combines monoclonal antibody and genetic engineering techniques to customize a patient’s own immune cells with the capability to attack their own tumors. Promising early clinical results with this method and the need for customized resident immune cells to advance checkpoint blockade technology has spurred billions in investment in CAR-T cell technology. For example, Adaptimmune’s, CAR-T

platform, raised \$104 million in last September, a few months removed from signing deal with GlaxoSmithKline worth up to \$350 million. Juno, another private biotech, raised more than \$300 million in just over a year to support CAR-T development efforts, and Kite Pharma raised \$128 million in an IPO to fund CAR-T research and development. While there is a lot of investor enthusiasm in Autologous Cancer Vaccine technology, this approach is hindered with business model problems. These problems are highlighted by the recent bankruptcy filing by Dendreon. Despite reimbursement at \$93,000 a treatment course, Dendreon was unable to achieve profitable operations. The lack of profitable operations is believed to be due to the inability of a customized (autologous) business model to achieve any economy of scale. Since CAR-T cell technology has the same business model, the commercial viability of the approach is still an open question. It is not clear that money alone will solve the problem, as availability of at least \$500 million did not help Dendreon to achieve profitability.

THE TECHNOLOGY

Immunovative Therapies, Ltd. (ITL) has developed a proprietary technology platform called the “Mirror Effect™” which represents a platform for developing a new generation of immunotherapy drugs. The Mirror Effect™ has many advantages over the current generation of immunotherapy drugs: (1) provides a customized vaccination method for creating a resident immune response capable of killing a patient’s own tumors with a business model that is economically scalable; and (2) provides a natural checkpoint blockade mechanism that blocks multiple checkpoint targets on cancer cells and not normal cells, potentially increasing efficacy and reducing toxicity compared to checkpoint blockade drugs. The Mirror Effect™ technology works through the harnessing of the power of the anti-tumor immune effect that occurs after allogeneic stem cell transplant procedures, while eliminating the highly toxic and often lethal side effects that limit the wide-scale clinical application of transplant technology. The immune effect that occurs after allogeneic transplant has been called the most powerful immune effect ever discovered, as this effect is capable of killing chemotherapy-resistant tumors. The lead Mirror Effect™ drug candidate is called “AlloStim™”. The Mirror Effect™ technology and the AlloStim™ product are protected by 24 issued US patents and 4 issued foreign patents with over 100 additional patents pending worldwide.

THE PRODUCT

The active ingredient of AlloStim™ is living immune cells that have been bioengineered to express high amounts of inflammatory proteins and immunomodulatory molecules. AlloStim™ is produced from CD4+ naïve T-cells isolated from the blood of normal donors. These naïve cells are expanded and differentiated in bioreactors in a proprietary 9-day culture process to become CD4+ Th1 cells called T-Stim™. The T-Stim™ cells are aliquoted into individual dose vials and frozen in liquid nitrogen where they are stable for at least two years. When needed in the clinic, the T-Stim™ cells are thawed and activated with monoclonal

antibody-coated microbeads in a 4h culture process. This process converts the CD4+ Th1 cells into activated CD4+ Th1 memory cells which produce large amounts of inflammatory cytokines and express surface CD40L. These memory cells with the microbeads attached are called AlloStim™. The AlloStim™ cells are then formulated into syringes in the clean room and shipped in temperature controlled containers by express overnight service to clinical sites. Approximately 400 AlloStim™ doses can be produced from a single blood donor. The formulated AlloStim™ cells have a 72h shelf-life. The manufacturing process is scalable by increasing the number of input cells and by increasing the expansion of the cells. It is believed that 100-fold scale-up over current levels is a feasible milestone.

PRIOR CLINICAL DATA

AlloStim™ has been tested in a Phase I/II clinical trial under a US FDA approved Investigational New Drug (IND) application. This trial accrued 42 metastatic cancer patients that had exhausted all treatment options. These patients had high tumor burdens with an average of 22.2 metastatic lesions and had been heavily pre-treated with an average of 7 lines of chemotherapy, with 90% having had prior surgery and 45% prior radiation and poor performance status requiring assistance for daily living (ECOG=2-3). There was a 50% response rate in this patient population considered difficult for immunotherapy. Additionally, this trial provided radiological, pathological and immunological evidence of immune-mediated tumor debulking effects. Tumor debulking is unprecedented in this patient population that is refractory to chemotherapy. Remarkably, these patients that had a median life expectancy of 66 days, survived a median of 163 days with 11 of the 42 (26%) patients still alive at the two year follow-up. Multi-variant analysis found a potential biomarker, IL-12, that correlated with response and survival. AlloStim™ is now ready to launch into a pivotal trial where the data can be used to support a Biological Licensing Application (BLA) seeking permission to market the drug in USA.

THE STRATEGIC PLAN AND DEVELOPMENT TIMELINES

Proceeds from the current mezzanine round are targeted toward execution of a Phase IIb pivotal clinical trial and recruitment of an experienced pharmaceutical executive team to prepare for launch of an initial public offering (IPO). The Phase II/III pivotal trial is being prepared to launch in 6 months after the close of the mezzanine financing and is expected to be completed in 36 months after launch (42 months). The trial can be completed earlier if the drug extends life greater than 40% compared to a control group (i.e., more than 2.4 months). Within 24 months after the mezzanine financing (market conditions permitting), and prior to completion of the Pivotal Trial, an IPO is planned. The IPO will provide a possible early exit for mezzanine investors. Proceeds from the IPO will be invested in the establishment of a commercial pilot plant and build-up of marketing, sales and distribution infrastructure. Pilot production facilities are required to be operational at the time of the BLA filing. The Pivotal

Trial will launch initially in Bangkok, Thailand and will be conducted under a Thailand Investigational New Drug (IND) application in compliance with US FDA regulations that allows the data from a foreign IND to be used in support of a BLA. After launch in Thailand, additional clinical sites are planned to be initiated within 18 months, including sites in the US. The US FDA requires a 9-18 patient Phase II ‘bridge’ study be conducted for safety prior to launch of the Pivotal Study at a US site. The bridge study will launch in March 2016 and the Pivotal Trial launch in Thailand is planned for launch in June 2016. The Pivotal Trial is expected to finish accrual of subjects in month 30 after launch with final data analysis completed by month 36. The BLA is expected to be ready for submission in month 40 after launch and FDA approval is possible to be obtained at month 46 after launch or month 52 after financing (or sooner if efficacy is >40%).

THE REGULATORY STRATEGY

There is strong rationale to support the use of AlloStim™ in both solid tumor and blood tumor indications. The indication of metastatic colorectal cancer (mCRC) was selected as the first indication in which to pursue marketing approval. The subset of mCRC patients that have become refractory to chemotherapy treatments approved for first and second line treatment (FOLFOX and FOLFIRI) and have a mutation in the KRAS and/or BRAF genes (which confers resistance to third line targeted therapies) represents an unmet medical need. Addressing an unmet medical need indication is a unique opportunity and provides for numerous regulatory and commercial advantages. The regulatory strategy is integrated with the strategic plan in order to maximize valuation at IPO and support valuation growth post-IPO. Prior to IPO, AlloStim™ will be submitted for “Break-Through Product Designation” upon any early evidence of tumor debulking effects. Winning this designation is expected to propel pre-IPO valuation. In addition, the niche of KRAS/BRAF mutant mCRC patients may also qualify for orphan drug designation. After IPO, AlloStim™ will be submitted to FDA requesting Fast Track Approval status. These regulatory rulings, along with planned interim analyses of the pivotal trial data just prior to IPO and yearly thereafter, are designed to provide value-added milestones during the pre-revenue stages of development.

THE PIVOTAL TRIAL DESIGN

The design of the Phase IIb pivotal trial has been made in consultation with the US FDA to assure compliance with US regulations and to assure that the trial data (especially from foreign sites) will be accepted in support of a BLA. The Pivotal Trial will launch initially in Bangkok and at the same time a 9 patient Phase IIb ‘bridge’ study will launch in the USA. The US FDA wants additional safety data from the bridge study prior to launch of the pivotal study in the USA. After 12 months (18 months from financing) a US site is planned to open for the Pivotal Trial. The Pivotal Trial is a 450 patient, randomized, controlled, multi-site study in third line KRAS/BRAF mutant metastatic colorectal cancer. Patients will be

randomized 2:1 into a treatment group which consists of AlloStim™+cryoablation and a control group which is physician's choice+cryoablation. Physician's choice is either best supportive care or palliative chemotherapy. Historical median survival of these patients is 5-6 months. The trial is powered with a 90% certainty to detect an overall survival (OS) difference of 25% (1.25 to 1.5 months difference) between the experimental immunotherapy and physician's choice groups. Interim analyses are designed into the trial so that the trial can be stopped early for excessive efficacy or terminated for futility. The \$30-45 million mezzanine financing is projected to finance the accrual of 450 patients which provides sufficient power to detect a 40% OS advantage (2 to 2.4 months). The accrual of 450 subjects is projected to take 36 months after launch. The trial can be terminated earlier if the efficacy rate is in excess of 40%. If the efficacy rate is below 40% but predicted to reach a level above 25%, the trial will be able to continue to accrue more patients up to 950 (but this would require additional funding). As no drug has demonstrated a survival advantage for KRAS/BRAF mutant metastatic colorectal cancer after chemotherapy failure, a 25% or greater OS advantage has possibility for blockbuster (> \$1 billion annual revenue) potential of AlloStim™ in this indication. The trial design incorporates numerous exploratory end-points, such as pathology, radiology and immunology data to support correlation of the immune mechanism with any findings of OS efficacy.

THE MANUFACTURING PLAN

ITL is responsible for manufacturing AlloStim™ for both clinical trial use and for commercial production. ICTI will contract with ITL for these services. AlloStim™ is produced from immune cells purified from the blood of normal donors. Under new US FDA regulations, the donors must be examined and screened prior to acceptance. Therefore, it is not possible to simply purchase blood from a blood bank. Accordingly, ITL through its US subsidiary, Immunovative Clinical Research, Inc., has established a donor recruiting and screening center in San Diego, CA. The donors are thoroughly screened and samples of blood are tested in a US licensed testing facility to verify absence of blood-borne infectious agents. The blood is then shipped to ITL in Jerusalem under controlled conditions. In Jerusalem, the blood is processed for 9-days in clean room facilities under good manufacturing practices (GMP) to produce an intermediate product called T-Stim™. T-Stim™ is stored in liquid nitrogen and is stable for at least 18 months. Each blood donor produces an average of 400 T-Stim™ doses which is sufficient to treat approximately 10 patients. When dosing is required in the clinic, T-Stim™ is thawed and activated with monoclonal antibody coated microbeads in a 4h incubation. The cells with beads attached are then formulated and packaged into syringes. This formulation is called AlloStim™. The AlloStim™ syringes are shipped in validated refrigerated containers and shipped by overnight courier to the clinical sites. The current GMP production facilities are sufficient to support the proposed clinical trial. A new pilot plant production facility is planned for commercial operations that will incorporate automation and economies of scale. It is

believed that the current production process can be scaled to produce sufficient product for 100 patients for each blood donor. The commercial pilot plant will be financed with proceeds from the IPO. The current material, labor and shipping cost to produce a single patient treatment is approximately US\$8000. This is expected to be at least 50% lower with economy of scale or \$4000. ICTI will purchase a treatment course at cost+ 20% from ITL. or \$4800. At a sales price expected to be a minimum of \$35,000, this allows for a gross margin of at least 86%. The cryoablation procedure is already approved for treatment of colorectal cancer and provides reimbursement to the physician at \$22,000 per procedure

THE BUSINESS MODEL

The Business Model for marketing and distribution of immunotherapy drugs is a key consideration for evaluation of the commercial potential of an immunotherapy drug. Big Pharmaceutical companies prefer proven business models, such as “pill in the bottle” or “parenteral (IV) solutions”. Monoclonal antibodies are an example of a parenteral solution model and this is why monoclonal antibodies have become a popular development strategy. Monoclonal antibodies are now used for treatment of a wide array of diseases, especially cancer, autoimmune, and inflammatory diseases. One reason for the explosion of checkpoint blockade drugs is that they are based on a proven parenteral solution business model and were backed by large pharmaceutical companies. On the other hand, living cell therapies have a limited shelf-life and can not fit into a pill in a bottle or packaged for IV delivery like a monoclonal antibody drug. Thus Dendreon (DNDN), with the first cell therapy drug approval, was forced to enter the market alone without a pharmaceutical partner. DNDN used a “customized patient” business model. This meant that the blood source for manufacturing the product came from the intended patient and was sent to a manufacturing facility and returned to the same patient. Despite a \$93,000 reimbursement rate, DNDN recently had to file for Chapter 11 bankruptcy protection. The lesson learned was that without the economies of scale, the customized business model can not be profitable. However, CAR-T cell technology has the same business model as cell therapy that has recently been enthusiastically supported by the financial community due to the need created by the success of checkpoint blockade drugs. This leaves the business model problem a remaining and increasingly important issue. ICTI will use a novel business model called the “off-the-shelf” model, which has the unique feature of retaining the marketing value of a treatment customized for each individual patient, while providing for scalability and economy of scale. AlloStim™ is derived from normal blood donors and there is no requirement to match the donor to the recipient, thus the product can be used ‘off-the-shelf’ as opposed to the CAR-T and autologous cancer vaccine models that are customized for each patient. Uniquely, AlloStim™ retains the customized component by incorporating a medical procedure, cryoablation, already approved for commercial use. By combining AlloStim™ with

cryoablation, this creates an in-situ vaccine customized for each patient's tumor. The economic feasibility of the model is observed even at the clinical trial stage with costs per treatment currently only \$8000. In addition, the ability to produce an intermediate product, T-Stim™, with the capability to remain stable for at least 18 months, further provides an economical distribution model. Frozen T-Stim™ can be shipped to regional formulation centers in each country in bulk. The regional formulation centers can convert the frozen T-Stim™ into formulated AlloStim™ on a demand basis and ship the product overnight to the point-of-care. In this manner, the product can reach virtually all end-users in a territory within the 72h shelf-life of the formulated product.

RESEARCH AND DEVELOPMENT

Portions of the mezzanine proceeds will be used to support research and development efforts. ICTI conducts research and development operations under contract with ITL. These operations include immunological monitoring of patient blood and serum samples to support development of companion diagnostics and provide evidence of any correlation between immunological response and survival in support of a BLA. ITL's wholly-owned subsidiary, Immunovative Clinical Research, Inc (ICRI), provides radiological and pathological research support of the clinical trial, also through contract with ITL. Approximately US\$600,000 is budgeted for additional research to develop alternatives to single sourced items on the bill of materials and to develop lesser cost versions of materials that affect the cost-of-goods sold. In addition, ITL conducts research to automate and scale-up the manufacturing process in order to lower the product costs and increase margins for commercialization. These efforts will assist in the scale-up to commercial manufacturing operations.

THE MARKET

In 2014, about 136,830 people were diagnosed with colorectal cancer in the US, and about 51,783 people died of the disease. In the EU, the incidence in 2014 was 450,621 newly diagnosed cases with 223,268 deaths (the second leading cause of cancer deaths). For the purpose of estimating the market size, the annual death rate is assumed to represent the metastatic disease population which is the target of the Pivotal Trial. Oncology drugs with demonstrated efficacy advantages in metastatic disease have increasingly been securing reimbursement of close to (and above) \$100,000 on the basis of minimal, if any, overall survival advantage. However, many of these drugs may come under pricing pressure in future as healthcare costs continue to increase. Therefore, for purposes of discussion, a conservative price of \$35,000 was assumed in the projections. The total annual market size for metastatic colorectal in USA at this level of reimbursement is \$1.8 billion. The annual market size in the EU at this reimbursement level is \$7.8 billion. The incidence of third line KRAS/BRAF mutated metastatic colorectal cancer is estimated to be 50% of the annual death rate. This equates to approximately 137,525 patients in USA and EU combined. This should qualify

the initial target for orphan drug designation. At reimbursement rate of \$35,000, this target market in US/EU is \$4.8 billion annually. A drug with an overall survival advantage in this unmet medical need indication where there currently are no drugs approved, could reasonably reach annual sales of US\$1 billion. As the drug is approved for earlier lines of treatment, or is used off-label, these revenues could expand to over US\$2 billion annually.

BUSINESS DEVELOPMENT

Business development activities are focused on value-added projects that either increase brand awareness or market value. Activities will focus on publication of clinical data in respected scientific journals, presentations at academic research institutions and prestigious cancer congresses. In addition, plans are being made to collaborate with the American Society of Clinical Oncology (ASCO) to provide educational seminars on immunotherapy. It is expected that collaborations with prestigious cancer institutions and investigators can be established in order to conduct investigator-sponsored clinical trials in colorectal cancer, providing additional independent validation of the technology and demonstrate feasibility of the business model. These collaborations will help support acceptance of our new generation immunotherapy with the GI community and support future label expansion to earlier stage metastatic colorectal cancer and combination with other therapies. In addition, partnerships with pharmaceutical companies and distributors in territories outside the USA and EU will be pursued, such as in the territories of China, Korea, Japan, India and Brazil. These partnerships could accelerate obtaining marketing approval in these emerging markets and add significantly to the revenue projections. A professional business development team will be recruited with proceeds of the mezzanine financing to support these efforts.

BUSINESS SUMMARY

THE COMPANY

[Immunovative Therapies, Ltd.](#) (“ITL” or the “Company”) headquartered in Jerusalem, Israel is a clinical stage, private, Israeli corporation incorporated in May 2004. The Company specializes in the development and manufacturing of immunotherapy drug products that incorporate living immune cells as active ingredients for the treatment of cancer and infectious diseases. ITL envisions building an international biopharmaceutical company that will take a leadership position in the development, manufacturing and distribution of highly effective and low toxic immunotherapy drug products that have potential to eventually replace chemotherapy as primary therapy for cancer. The Company has two products in clinical development: **AlloStim™**, which contains a patented living immune cell attached to monoclonal antibody-coated microparticles designed to elicit the same tumor debulking mechanism (graft vs. tumor effect) of allogeneic stem cell/bone marrow transplant procedures (“Mini Transplants”) without the toxicity normally associated with these procedures (graft vs. host disease); and **AlloVax™**, an individualized therapeutic cancer vaccine containing purified chaperone (heat shock) proteins derived from a patient’s own tumor as a source of tumor antigen and then mixed with AlloStim™ which serves as an adjuvant to direct an immune response against the tumor antigens. AlloVax™ production has been optimized so that vaccine can be produced from as little as 0.1 gram of tumor (size of a biopsy).

AlloStim™ has completed a US FDA-cleared Phase I/II clinical trial and is *believed to be the first immunotherapy drug to demonstrate tumor debulking activity in chemotherapy-resistant metastatic cancer*. This has enabled AlloStim™ to advance to the Phase II/III development stage and provides a fast-track regulatory pathway to market approval. AlloVax™ has demonstrated significant anti-tumor activity in animal models and also in early clinical trials. AlloVax™ is now approved to advance to a randomized, Phase II clinical trial.

ITL was initially established with award of competitive grant funding from the Israel Office of the Chief Scientist through the [Misgav Venture Accelerator](#), a member of the prestigious Israeli incubator system, and through a cooperative translational research agreement with [Hadassah-Hebrew University Medical Center in Ein Karem Jerusalem](#). The Company has raised approximately \$25 million since inception from over 200 individual angel investors.

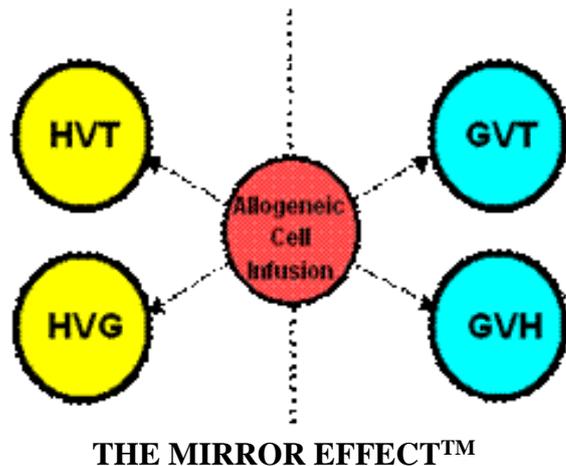
ITL has state-of-the-art clean room production facilities and quality control lab facilities that operate under good manufacturing practices (GMP) and also conducts research and development and immunological monitoring activities in well equipped laboratories located within the Malcha Technology Park in Jerusalem. Clinical research operations are conducted through a wholly-owned subsidiary, Immunovative Clinical Research, Inc. (“ICRI”), located in Carlsbad, CA USA. ICRI serves as an in-house CRO to ITL and is responsible for regulatory compliance and reporting, clinical protocol development, CRF design and for supervising worldwide clinical trials in compliance with Good Clinical Practices (GCP). In addition, ICRI supervises blood bank donor collections for product manufacturing,

coordinates centralized radiology and pathology professional reading services, and manages the Data Safety Monitoring Board (DSMB), statistical analysis professionals and randomization services. ICRI also is responsible for design and implementation of 21 CFR 11-compliant clinical databases for worldwide clinical trials.

THE TECHNOLOGY

The Company has developed a novel technology that serves as a platform to develop many immunotherapy treatments for virtually all types of cancer and infectious diseases. The technology is different than previous immunotherapy technologies that have had disappointing results in the clinic. Instead of being developed in animal models and then translated to the clinic, the Company's technology was instead reversed engineered from a human immune mechanism already proven to be capable of killing chemotherapy-resistant metastatic cancers and has been shown to be curative in many cases. The immune effect that occurs after transplant of another person's immune cells (adult stem cells) into a cancer patient has been described as the most powerful anti-tumor mechanism ever discovered. This mechanism known as the "graft vs. tumor" effect or "GVT" is the only known mechanism for killing or debulking of chemotherapy-resistant metastatic disease. However, the clinical application of the GVT effect is severely limited due to an often lethal side-effect called "graft vs. host disease" or "GVHD" which is intimately associated with the GVT mechanism. The separation of the beneficial GVT effect from the detrimental GVHD effect has been described as the "holy grail" of transplantation research.

ITL has discovered a way to elicit the beneficial GVT effect without GVHD called the "Mirror Effect™". The patented technology works by reversing the direction of the immunological effects of Mini-Transplant procedures. Instead of the transplanted immune system (the graft) mediating the immune effects of GVT and GVHD, the Mirror Effect™ provides for the host immune system to reject the graft (a host vs. graft effect or "HVT") in a manner which promotes the host immune system to attack the tumor (a host vs. tumor effect or "HVT").



The related HVG/HVT effects "mirror" the known GVT/GVHD effects of Mini-Transplant. To view a video on the Mirror Effect™ concept click [here](#).

THE PRODUCTS

Two product candidates have been developed based upon the Mirror Effect™ technology and are both in clinical development. The lead product is called AlloStim™. The active ingredient of AlloStim™ is patented, living CD4+ memory immune cells which possess both Th1 helper cell and cytolytic T lymphocyte (CTL)/ NK-like characteristics. The CD4+ cells

are attached to microbeads coated with monoclonal antibodies which activate the cells and endow them with the properties which enable them to elicit the Mirror Effect™. In solid tumors, AlloStim™ is combined with an in-situ ablation procedure (e.g., cryoablation or radiofrequency ablation) that destroys a portion of tumor releasing the specific antigens into the microenvironment. Ablation procedures are outpatient procedures that are conducted under imaging guidance with CT scan or ultrasound. AlloStim™ is then injected into the ablated tumor lesion to educate the immune system to destroy tumor lesions wherever they occur throughout the body. In hematological (blood) tumors, AlloStim™ is infused alone without ablation procedures.

AlloVax™ is an individualized cancer vaccine that is used when large target lesions are not available for ablation, such as in a situation where small disease lesions have metastasized to the lymph nodes. AlloVax™ requires only a small amount of tumor sample (0.1 grams), which is the size of a biopsy. The small amount of starting material required is a unique feature of AlloVax™. Previous tumor vaccines have required 2-5 grams of tumor as source material which limited these vaccines to patients with bulky, resectable disease. In addition, since FDA considers the harvesting of tumor to be part of the manufacturing process, surgeons are required to collect tissue under GMP. Surgeons have been reluctant to operate under GMP procedures which has been another obstacle to successful commercialization of individualized vaccines. The small sample size requirement for AlloVax™, however, permits tumor collection by biopsy which is more amenable to GMP collection. Specialized proteins called chaperone proteins or heat shock proteins are purified from the biopsy samples using a patented electrophoresis procedure. These special proteins carry the antigens that the immune system uses to identify and target the tumors for destruction. These proteins are injected together with AlloStim™ to make AlloVax™.

Both AlloStim™ and AlloVax™ have completed extensive pre-clinical testing in mice and monkeys, as well as extensive pharmacology and toxicology evaluations. Both also have active, approved Investigational New Drug (INDs) applications on file. AlloStim™ is at the final clinical testing stage of development, about to begin a Phase II/III clinical trial.

PREVIOUS CLINICAL TRIAL RESULTS (AlloStim™)

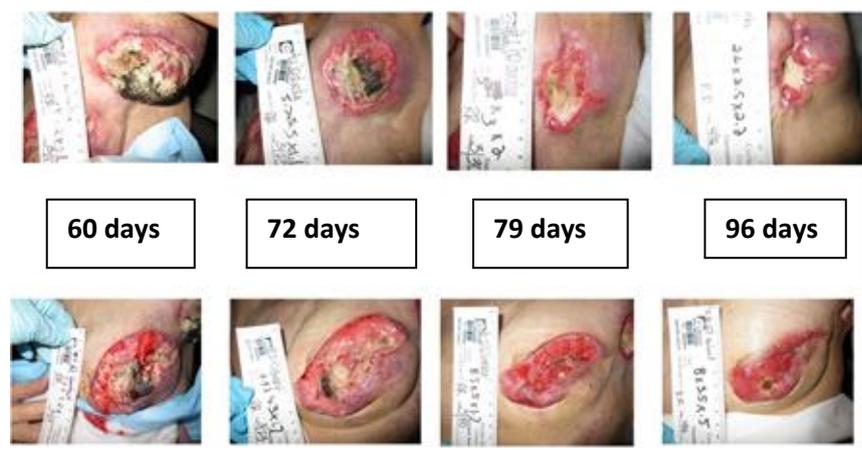
AlloStim™ was evaluated in a 42 patient, FDA-cleared, Phase I/II clinical trial. Hospice eligible subjects without any standard treatment options available were eligible for this study. Generally, subjects with metastatic (stage IV) solid tumors (non-hematological) with radiological evidence of progression within 30 days of accrual and with evidence of being refractory to at least two prior courses of chemotherapy and where no approved chemotherapy options were available were eligible to participate in the study.

These patients had high tumor burdens with an average of 21.2 metastatic lesions per patient. The most common metastatic tumor sites were lung/pleural (63% of accrued patients), liver (63%), lymph node (53%) and bone (50%). In addition, 13% of patients presented with malignant ascites, 60% with pleural effusion and/or atelectasis (lung collapse). Patients were

heavily pretreated with an average of 2.7 courses and 7 prior lines of chemotherapy. 90% had prior surgery and 40% prior radiation. Patients also had poor performance status (average: ECOG 2.7) with most patients unable to care for their daily needs and were either bedridden or in a wheel chair.

These heavily pre-treated, poor performance status and high tumor burdened patients are not considered to be good candidates for immunotherapy because their immune systems have been devastated by prior treatments. Surprisingly, 22% of these patients survived over 2 years with AlloStim™ treatment. In addition, because the drug had little to no adverse effects, these patients lived with improved qualities of life. The study also provided radiological, pathological and immunological evidence of a tumor debulking effect that correlated with survival. This is believed to be the first demonstration of an immunotherapy drug actually killing tumors and not just slowing growth. That this anti-tumor activity could be demonstrated in late stage patients without any treatment options provides an unique opportunity to advance this drug to the market.

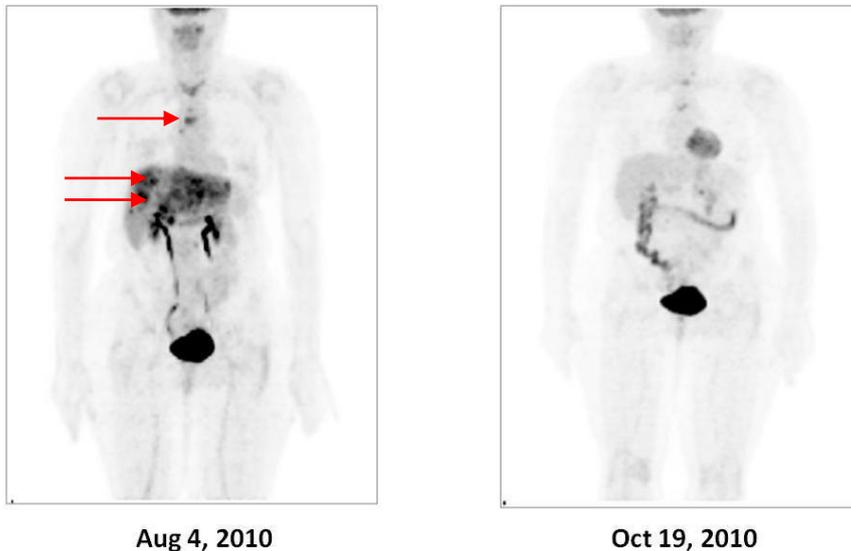
Below are photos documenting the healing metastatic tumor lesions from a 64yo woman with metastatic breast cancer. The photos show visible tumors that had recurred on the axillary lymph node (upper panel) and on the breast that had been previously resected (lower panel). As can be seen, the lesions were rapidly cleared. This patient was administered AlloStim™ combined with ablation of a tumor in the liver. While the liver lesion was the target for ablation, the distant tumors of the axillary node and breast responded. The first frame (left) was taken 60 days after AlloStim™ and shows significant tumor necrosis (death) as indicated by the black regions. Subsequent photos at 72 days, 79 days and 96 days showed eventual healing of the tumor lesions. This patient also showed significant improvement in lesions in the lungs, liver, bones and brain. The patient with a life expectancy of 60 days was alive at the last 2 year follow-up.



Below is a PET scan showing clearing of metastatic breast cancer tumors in the liver and bones after AlloStim™. The dark areas indicated by red arrows are tumors in the liver and bone. The dark area in the bladder is artifact from collection of the radioactive dye. This

patient came to the clinic in a wheel chair due to collapse of bones in the spine due metastatic growth. The patient was still alive at 2 year follow-up and was living a high quality of life, scuba diving and traveling around the world.

PET Response



HEAD AND NECK CANCER MARKET (ALLOVAX™)

Head and neck cancer includes cancers of the mouth, nose, sinuses, salivary glands, throat, and lymph nodes in the neck. The number of new cases of head and neck cancers in the United States was 40,490 in 2006, accounting for about 3% of adult malignancies. The incidence of head and neck is on the rise in the US despite a drop in cigarette smoking rates. Much of this rise is due to the increasing incidence attributable to human papillomavirus (HPV). HPV-related head and neck cancer has a high cure rate, which contributes to the stable death rates despite the increased incidence. However, up to half of patients with head and neck cancer will develop recurrence, or about 20,000 annually, and 11,700 patients die each year of this disease. There currently are no approved treatments available for recurrent head and neck cancer. At a \$50,000 patient reimbursement rate, the 20,000 annual incidence of recurrent disease equates to a \$1 billion annual US market.

The worldwide incidence of head and neck cancer exceeds half a million cases annually. African Americans are disproportionately affected by head and neck cancer, with younger ages of incidence, increased mortality, and more advanced disease at presentation. Incidence is highest in the Mediterranean countries and in the Far East. In Southeast China and Taiwan, head and neck cancer, specifically nasopharyngeal cancer is the most common cause of death in young men. The high incidence in these countries and lack of approved treatments, positions AlloVax™ for early licensing/partnering in these territories.

Palliative chemotherapy is indicated in conjunction with best supportive care for most patients with metastatic or recurrent head and neck cancer. Recurrent head and neck is a difficult problem with a poor prognosis and represents a large unmet medical need. Traditionally, surgery has been used for salvage after definitive modalities have failed. Radiation with or without chemotherapy can be used in patients who have not received radiation in the past. Patients who have been irradiated previously and have unresectable recurrent disease pose a more difficult challenge. These patients are the target market for AlloVax™. For these patients, palliative chemotherapy is the standard treatment option. However, a recent *Cancer* study suggests that postoperative reirradiation is feasible for patients who undergo surgery for recurrent or second primary head and neck cancer. A recent prospective phase 2 trial suggests that reirradiation with chemotherapy may be offered in this setting with significant but acceptable toxicities as well. However, survival rates still remain very poor. Demonstration of even minimal survival advantage demonstrated by AlloVax™ in this setting will likely provide a fast track regulatory approval pathway.

MANUFACTURING

AlloStim™ is derived from the blood of normal donors. The blood is sourced from licensed blood banks in the USA and processed in Israel in a 9-day culture process where a subset of immune cells are purified from the blood, differentiated and expanded to make an intermediate product called T-Stim™. These cells are then packaged in single dose vials and stored in frozen inventory. T-Stim™ is stable for at least 2 years in this frozen state. One unit of donor blood is currently capable of producing approximately 200 dose vials (a batch) of T-Stim™. This is expected to be capable of scaling up to over 2000 dose vials. When required for patient treatment, T-Stim™ doses are thawed and cultured with monoclonal antibody-coated microbeads for 4hr to make AlloStim™. AlloStim™ is placed in formulation media and loaded into syringes (lots). Formulated AlloStim™ is stable for 72h at 2-8°C. AlloStim™ lots are shipped by special courier service to the point-of-care within 24-48h. There is no need to match the batch donor to the patient lot recipient.

The Company operates under strict compliance with FDA-mandated Good Manufacturing Practices (GMP). The Company has state-of-the-art clean room, quality control labs and inventory control systems in Israel for the safe and economical production of AlloStim™ and AlloVax™. The facilities and documentation passed a mock-FDA inspection conducted by the Biologics Consulting Group in May 2012.

The current facility is capable of producing treatments for approximately 150 patients a year and can be increased to 300 patients a year with multiple shifts. This capacity is sufficient to support the current clinical development plans. AlloStim™ production costs are currently around \$5,000 a patient treatment. This is extremely economical at this stage of development, compared to Dendreon's Provenge, the only FDA approved cellular immunotherapy drug, which is reported to cost over \$60,000 a treatment to produce.