ONCOSEC MEDICAL Inc
Form 10-K
October 10, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended July 31, 2014

OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 000-54318

ONCOSEC MEDICAL INCORPORATED

(Exact name of registrant as specified in its charter)

Nevada	**98-0573252**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

9810 Summers Ridge Road, Suite 110

San Diego, CA 92121

(Address of Principal Executive Offices)(Zip Code)

(855) 662-6732

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, par value $0.0001 per share

(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject

to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer x
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

The aggregate market value of voting and non-voting common stock held by non-affiliates of the registrant as of January 31, 2014 totaled approximately $85,000,000 based on the closing price of $0.48. As of October 1, 2014, there were 244,631,076 shares of the Company s common stock ($0.0001 par value) outstanding.

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This Annual Report in Form 10-K contains forward-looking statements that involve risks, uncertainties and assumptions. In some cases, you can identify forward-looking statements by terminology such as may , should , expects , plans , anticipates , believes , estimates , predicts , continue or the negative of these terms or other comparable terminology. All statements made in this Annual Report on Form 10-K other than statements of historical fact could be deemed forward-looking statements.

By their nature, forward-looking statements speak only as of the date they are made, are neither statements of historical fact nor guarantees of future performance and are subject to risks, uncertainties, assumptions and changes in circumstances that are difficult to predict or quantify. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks identified in the section entitled Risk Factors in Part I, Item IA of this Annual Report, and similar discussions in our other filings with the Securities and Exchange Commission (the SEC). If such risks or uncertainties materialize or such assumptions prove incorrect, our results could differ materially from those expressed or implied by such forward-looking statements and assumptions. Risks that could cause actual results to differ from those contained in the forward-looking statements include but are not limited to risks related to: uncertainties inherent in pre-clinical studies and clinical trials; our need to raise additional capital and our ability to obtain financing; general economic and business conditions; our ability to continue as a going concern; our limited operating history; our ability to recruit and retain qualified personnel; our ability to manage future growth; our ability to develop our product candidates and to develop new product candidates; and our ability to protect our intellectual property.

You should not place undue reliance on forward-looking statements. Unless required to do so by law, we do not intend to update or revise any forward-looking statement, because of new information or future developments or otherwise.

As used in this Annual Report on Form 10-K and unless otherwise indicated, the terms the Company , we , us and our refer to OncoSec Medical Incorporated.

OncoSec Medical Incorporated has filed applications to register the following trademarks: ImmunoPulse, and NeoPulse. Other registered trademarks used in this Annual Report are the property of their respective owners.

PART I

ITEM 1. BUSINESS

The following discussion should be read in conjunction with our consolidated financial statements and the related notes and other financial information appearing elsewhere in this Annual Report on Form 10-K.

Overview

We are a hybrid device and gene therapy biotechnology company focused on designing, developing and commercializing innovative and proprietary medical approaches for the treatment of cancer where currently approved therapies are inadequate based on their efficacy or side effects. Our Company was incorporated under the laws of Nevada on February 8, 2008 under the name Netventory Solutions Inc. Initially, we provided online inventory services to small and medium sized companies. On March 1, 2011, we changed our name to OncoSec Medical Incorporated. In March 2011, we acquired certain assets related to the use of drug-medical device combination products for the treatment of various cancers from Inovio Pharmaceuticals, Inc. (Inovio). With this acquisition, we have abandoned our efforts in the online inventory services industry and are focusing our efforts in the biotechnology industry. Our goal is to improve the treatment of cancer through the development of our novel therapies.

Our Strategy

As a biotechnology company focused on discovering and developing novel oncology products, our portfolio includes biologic immunotherapy product candidates intended to treat a wide range of tumor types. Our technology includes intellectual property relating to certain delivery technologies, which we refer to as ImmunoPulse (ImmunoPulse), a therapeutic approach that is based on the use of an electroporation delivery device in combination with DNA-encoded immune targets to treat cancer. This unique therapeutic modality is based on electroporation-mediated delivery of DNA plasmids encoding immunotherapeutic proteins, which are intended to reverse the immunosuppressive microenvironment in the tumor and engender a systemic anti-tumor response. Our electroporation devices consist of an electrical pulse generator and disposable applicators, which can be adapted to treat tumors differing in histologic type, size, and location. Using ImmunoPulse, our DNA-based immunotherapy to treat cancer. Our mission is to enable people with cancer to live longer with a better quality of life than otherwise possible or available with existing therapies.

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Immunotherapy, a process which uses the patient s own immune system to treat cancer, may have advantages over surgery, radiation, and chemotherapy. But many cancers appear to have developed the ability to hide from the immune system. A treatment that can augment the immune response against tumor cells by making the cancer more visible to the immune system would likely represent a significant improvement in cancer therapy. Immune-enhancing proteins such as interleukin-2 (IL-2), interleukin-12 (IL-12), and interferon-alpha (IFN- α) have shown encouraging results in terms of efficacy but with significant target-mediated toxicity.

Our lead product candidate, an immunotherapy for metastatic melanoma, is being studied in a Phase 2 open label clinical trial. Based on the safety and efficacy of intratumoral electroporation of DNA plasmid IL-12 (pIL-12) in the Phase 1 and ongoing Phase 2 studies, we plan to pursue a Phase 2b study to evaluate the safety and efficacy of intratumoral electroporation of pIL-12 in combination with an anti-PD-1/PDL-1 therapeutic. Based on the literature and OncoSec s internal analysis of the mechanism of action of intratumoral electroporation of pIL-12, we expect that IL-12, a cytokine that has an immunomodulatory effect, may significantly improve the efficacy of anti-PD-1/PDL-1 checkpoint therapies through augmenting the immunogenicity of the tumor, thereby driving an enhanced anti-tumor immune response. In other words, we expect that electroporation of pIL will drive the production of CD8+ tumor-infiltrating lymphocytes (TILs), resulting in enhanced efficacy of anti-PD-1 checkpoint inhibitors, which are tightly correlated to the presence of a significant number of TILs. The initiation of the study is dependent on several factors including accessing a pharmacologically active anti-PD-1/PDL-1 checkpoint inhibitor (e.g. Merck s pembrolizumab, BMS s nivolimumab or Roche s MPDL3280A). Availability of these agents may be altered in the near-term based on regulatory approvals and/or partnering opportunities. Enrollment in the current Phase 2 study was recently expanded with a protocol addendum, allowing us to test the safety and efficacy of a modified dose schedule.

The safety and efficacy of intratumoral electroporation with pIL-12 is also being tested in other cancer indications, including Merkel Cell Carcinoma and Cutaneous T-Cell Lymphoma. As of date of this filing, more than 65 cancer patients have received treatment with intratumoral electroporation of pIL-12 as a monotherapy without a single drug-related severe adverse event (SAE), representing an exceptional safety profile for an oncology therapy.

Our ImmunoPulse product candidates are based on our proprietary DNA based immunotherapy technology, which is designed to stimulate the human immune system, resulting in systemic anti-tumor immune responses. Because our candidate therapeutics are plasmid constructs, we expect to benefit from a simpler, more consistent and scalable manufacturing process in comparison to therapies based on patient-derived cells or recombinant proteins.

Given that cancer deploys multiple immunosubversive mechanisms in parallel to suppress anti-tumor immune responses, we believe it is unlikely that a single immunotherapy will suffice to achieve responses in most patients in most tumor types. Therefore, OncoSec is conducting research and development on other DNA-encoded, immunologically-active molecules with an aim to produce additional immunotherapeutic drugs capable of breaking the immune system s tolerance to cancer. At OncoSec, we have the opportunity to leverage the flexibility of a DNA plasmid-based technology to rapidly pursue candidate molecules and combinations of therapeutics. We can introduce, for example, pro-inflammatory cytokines and chemokines, immune stimulatory receptors, co-stimulatory molecules, adhesion molecules, tumor suppressor genes and T-cell engagement molecules. We expect that electroporation-mediated intratumoral expression of immunologically-active molecules such as these can reverse the immunosuppressive microenvironment of the tumor and drive systemic anti-tumor immune responses while limiting systemic exposure and untoward toxicities associated with these potent immunologic effector molecules. We believe that this will become the overriding treatment goal for oncologists across all cancer therapies.

We seek to improve the treatment of cancer through the development of novel intratumoral, electroporation-based therapies. We have several clinical trials for the use of our therapies to treat different tumor types. We also continue to investigate collaboration opportunities that will enable us to identify combinations with current and emerging standard-of-care drugs, including immune-modulating checkpoint inhibitors (i.e. anti-CTLA-4 or anti-PD-1). We may seek regulatory approvals to initiate specific studies in target markets to collect clinical, reimbursement,

and pharmacoeconomic data in order to advance a commercialization strategy. Our clinical development strategy includes completing the necessary additional clinical trials in accordance with United States Food and Drug Administration (the FDA) guidelines for cancers including select, rare cancers (orphan indications) that have limited therapeutic options. Our strategy also includes expanding the applications of our technologies through strategic collaborations or evaluation of other opportunities such as in-licensing and strategic acquisitions. We may collaborate with major pharmaceutical and biotechnology companies and government agencies, providing us access to complementary technologies or greater resources. These business activities are intended to provide us with mutually beneficial opportunities to expand or advance our product pipeline and serve significant unmet medical needs. We may license our intellectual property to other companies to leverage our technologies for applications that may not be appropriate for our independent product development.

In addition, our portfolio includes an asset that utilizes electroporation delivery with a small molecule drug, which we refer to as NeoPulse. Our NeoPulse approach utilizes our electroporation technologies for the local delivery of a small molecule drug (e.g. bleomycin) to treat tumors.

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Asset Acquisition

We have acquired certain assets pursuant to our Asset Purchase Agreement with Inovio, dated March 14, 2011 (as amended, the Asset Purchase Agreement). The acquired assets include certain non-DNA vaccine technology and intellectual property relating to selective tumor ablation technologies, a therapy which uses an electroporation device to facilitate delivery of chemotherapy agents, or nucleic acids encoding cytokines, into tumors and/or surrounding tissue for the treatment and diagnosis of various cancers.

We did not assume any liabilities of Inovio except liabilities under the assigned contracts and assigned intellectual property arising after the closing date of the Asset Purchase Agreement. We agreed to pay Inovio $3,000,000 in scheduled payments beginning on the closing date as well as certain royalties in the event we commercialize our technology. We made the final payment to Inovio of $1 million on December 19, 2013. As a result, we are not subject to further scheduled payment obligations to Inovio pursuant to the Asset Purchase Agreement.

We are also party to a cross-license agreement with Inovio, which we entered into concurrently with the closing of our asset acquisition. This agreement provides for the exclusive license to Inovio of rights related to certain SECTA technology patents in the field of gene or nucleic acids, outside of those encoding cytokines, delivered by electroporation and for the non-exclusive cross-license by Inovio to us of rights related to certain non-SECTA technology patents in the our field, in exchange for specified sublicensing and other licensing fees and royalties.

University of South Florida License

On August 24, 2012, we secured an exclusive license for specific patented technology from the University of South Florida Research Foundation relating to the delivery of gene-based therapeutics via intratumoral and intramuscular electroporation. This patent directly supports our clinical development focus in solid tumor applications and specifically metastatic melanoma, Merkel cell carcinoma and cutaneous T-cell lymphoma using our ImmunoPulse therapy, and extends patent protection for the ImmunoPulse technology to the year 2024.

Electroporation Delivery

The effectiveness of many drugs and DNA-based therapeutics is dependent upon their crossing the cell membrane. In the 1970s, it was discovered that the brief application of high-intensity, pulsed electric fields to the cell resulted in a temporary and reversible increase in the permeability of the cell membrane, a mechanism known as electroporation. As a consequence, it was also demonstrated that there was a subsequent increase in the ability of both small and large molecules to move between the cell exterior and interior via the newly formed membrane pores.

The transient, reversible nature of the electrical permeabilization of cell membranes and the resulting increase in intracellular delivery of therapeutic agents is the underlying basis of our ImmunoPulse therapeutic approach. The electroporation delivery consists of an electrical pulse generator and various disposable applicators specific to the individual tumor size, type and location. While the extent of membrane permeabilization depends on various electrical, physical, chemical, and biological parameters, research with electroporation delivery has demonstrated an increase of cellular uptake of chemical molecules from 1,000- to 8,000-fold above baseline. After cessation of the electrical

pulse, the membrane pores close, trapping the molecules within the cell and allowing them to perform their function. The enhanced delivery of these agents may result in the ability to not only improve cytotoxicity and therapeutic value but also to lower the required doses, thereby providing a potentially safer treatment.

DNA Delivery With Electroporation ImmunoPulse

The greatest obstacle to making DNA-based therapeutics a reality has been the safe, efficient, and economical delivery and expression of plasmid-DNA constructs into the target cells. We are leveraging the unique ability of electroporation to enable the efficient and effective delivery of DNA-based therapeutics. The use of DNA delivery with electroporation has been validated from multiple clinical studies assessing DNA-based immunotherapies against cancers. Together with our partners and collaborators, we plan to be the leader in establishing electroporation-delivered DNA immunotherapies. We believe that electroporation should become the method of choice for plasmid-DNA delivery into cells in many clinical applications.

The immunotherapy approach of our therapy uses an electroporation system that is calibrated and designed to create favorable conditions to deliver plasmid DNA encoding immunotherapeutic cytokines into tumor cells that in turn promote anti-cancer responses. The cytokine-encoding plasmid is first injected into the selected tumor. A needle-electrode array then delivers the electrical pulses produced in the pulse generator. When DNA injection is followed by electroporation of the target tissue, transfection is significantly greater with resultant gene expression generally enhanced from 100- to 1000-fold. This electroporation-mediated enhancement of expression makes many DNA-based candidates potentially feasible without unduly compromising safety or cost.

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A Phase I clinical trial in metastatic melanoma has been completed using electroporation to deliver plasmid-DNA encoding for the IL-12 cytokine. Published data have suggested that gene transfer utilizing in vivo DNA electroporation in metastatic melanoma showed that it was safe, effective, reproducible, and titratable. In addition to regression of treated melanoma skin lesions, evidence of regression in distant untreated lesions was also observed, and in some cases a complete regression of all lesions. These findings suggest a systemic immune response to the localized treatment.

A Phase II clinical trial in metastatic melanoma has also been completed and interim data was presented at the 2014 Annual Meeting for the American Society of Clinical Oncology, where it was reported that of the 27 patients who were evaluable, an objective response rate of 33% was observed, with 11% of patients having a complete response. Regression of non-injected lesions was seen in 62% of 21 patients with evaluable lesions. Enrollment for this study is complete and analysis of final data is ongoing.

We consider these results to be significant and thus we are continuing to identify and develop new therapeutic targets that, like IL-12, can (i) be encoded into DNA, (ii) delivered intratumorally using electroporation, and (iii) have an ability to reverse the immunosuppressive mechanisms of the tumor. We plan to expand our ImmunoPulse pipeline beyond the delivery of plasmid-DNA encoding for cytokines with a focus on targeting key pathways of tumor immune subversion.

Clinical Program

We initiated three Phase 2 clinical trials to assess the safety and efficacy of our ImmunoPulse technology with DNA-encoded IL-12 in patients with melanoma**,** Merkel cell carcinoma and cutaneous T-cell lymphoma during calendar year 2012. Our lead ImmunoPulse candidate for these trials is a DNA plasmid coding for IL-12 that is delivered using our electroporation device. While the pIL-12 immunotherapy is administered locally, results from preclinical and Phase 1 clinical trials indicated that there is no evidence of a dose-related toxicity. Although Phase 1 trials are designed to study only safety and tolerability, our Phase 1 trial suggested that our ImmunoPulse produced both a local and systemic anti-tumor immune responses. All three Phase 2 clinical trials were initially physician-sponsored open label, multi-center trials. As of December 2012, all three physician-sponsored Investigational New Drug (IND) applications were transferred to us.

Phase II Melanoma Trial

Our melanoma trial, entitled Phase II trial of intratumoral pIL-12 electroporation in advanced stage cutaneous and in transit malignant melanoma, is a single dose trial treating approximately 30 patients. We are assessing objective response rate (local and distant) at six months, time to objective response (complete and partial responses), duration of distant response and overall survival. We are building on positive Phase I dose escalation trial results in 24 patients with metastatic melanoma treated with pIL-12 in combination with electroporation. That study further supported safety and tolerability and suggested a systemic objective response in more than half of the subjects; 15% of patients showed 100% clearance of distant, non-treated tumors. Based on historical data, less than 0.25% of patients would have been expected to see regression in their untreated tumors. Recent interim analysis of the Phase 2 study demonstrated an objective response rate of 33%, with 11% of patients having a complete response. Regression of non-injected lesions was seen in 62% (13/21) of patients with evaluable lesions. Enrollment for this study is complete.

Phase II Merkel Cell Carcinoma Trial

Merkel cell carcinoma is a rare but lethal skin cancer affecting about 1,500 people each year with a 33% mortality rate. Current outcomes to chemotherapy treatment have demonstrated short-lived responses with no clear impact on overall survival. Our clinical trial, entitled A Phase II study of intratumoral injection of interleukin-12 plasmid and in vivo electroporation in patients with Merkel cell carcinoma, is a single-dose, open-label trial in 15 patients. The study s endpoints are IL-12 gene expression in tumor tissue at three to four weeks post-treatment and secondary endpoints will evaluate objective response rates (both local and distant) at six months post-treatment, time to relapse or progression, and overall survival. This study will evaluate the safety and tolerability of DNA IL-12 as a treatment for Merkel cell carcinoma and aims to further validate the findings from the Phase 1 dose escalation trial carried out in 24 metastatic melanoma patients. Upon completion of this study, anticipated to be by the end of calendar 2014, management will evaluate the advancement of ImmunoPulse as monotherapy for Merkel cell carcinoma.

Phase II Cutaneous T-Cell Lymphoma

Cutaneous T-cell lymphoma, or CTCL, is a rare disease affecting approximately 3,000 people each year with current therapies requiring life-long management and treatment. Today s treatment methods delivered either locally or systemically. Many of these therapies result in systemic toxicities. Cytokine therapies have shown some therapeutic benefit, however the requirement for high dose systemic concentrations results in unwanted toxicities and eventual resistance to the therapy. In contrast, our ImmunoPulse treatment uses locally delivered low-dose pIL-12 to induce a local and systemic anti-tumor immune response.

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The planned clinical trial, entitled Phase II trial of intratumoral IL-12 plasmid electroporation in cutaneous lymphoma, is an open-label, multi-center study and is expected to enroll 34 patients. The trial s primary endpoint is to assess the objective response rate (both local and distant) at six months post-treatment, with safety and progression-free survival as secondary endpoint measures. ImmunoPulse is a potentially new treatment being evaluated for patients suffering from CTCL, who currently have few treatment options that alter the disease course in this chronic life-altering disease.

Scientific Advisory Panel

We have consulted with senior and respected oncology researchers to provide counsel as part of our scientific advisory panel for our ImmunoPulse clinical program. We expect to continue to establish relationships with scientific and medical experts in academia, as needed, to support our scientific advisory panel. The scientific advisory panel assists us on issues related to potential product applications, product development, and clinical testing.

Commercialization

We plan to continue our clinical development strategy for the ImmunoPulse program with Phase 2 and subsequent pivotal clinical trials focused on various cancers including select rare cancers that have limited, adverse or no therapeutic alternatives. We expect our current studies to validate data from previous Phase 1 and 2 clinical experience, which will be used to further develop our development strategy for this program.

Our business model for the NeoPulse program is based on a partnering and commercialization strategy that leverages previous in-depth clinical experiences, and late-stage clinical studies in the United States (Phase 3) and Europe (Phase 4). Our near-term plan will be to identify and engage potential partner(s) who are established industry leaders in the field of surgical oncology, or who are seeking to expand their portfolio into this space with the purpose of partnering the NeoPulse asset in select geographic regions, such as Europe and Asia. Once a partner is engaged, we may seek regulatory approvals to initiate specific studies in target markets to collect clinical, reimbursement, and pharmacoeconomic data in order to advance a joint commercialization strategy.

Competition

We are in a highly competitive industry. We are in competition with traditional and alternative therapies for the indications we are targeting, as well as pharmaceutical and biotechnology companies, hospitals, research organizations, individual scientists and nonprofit organizations engaged in the development of drugs and other therapies for these indications. Our competitors may succeed, and many have already succeeded, in developing competing products, obtaining FDA approval for products, or gaining patient and physician acceptance of products before us for the same markets and indications that we are targeting. Many of these companies, and large pharmaceutical companies in particular, have greater research and development, regulatory, manufacturing, marketing, financial and managerial resources, and experience than we have, and many of these companies may have products and product candidates that are in a more advanced stage of development than our product candidates. If we are not first to market for a particular indication, it may be more difficult for us or our collaborators to effectively enter markets unless we can demonstrate our products are clearly superior to existing therapies (see also Intellectual Property below).

Examples of competitive therapies include the following:

- Immunotherapy. This therapeutic approach stimulates the patient s own immune system to attack malignant tumor cells, which have managed to circumvent the body s natural immune processes that would normally recognize and destroy these cells before they are able to form growing cancerous tumors. Several methods have been employed to evoke this immune response, including monoclonal antibodies and autologous cell-based vaccines, as well as viral and non-viral targeted delivery of immunotherapeutic agents.

Yervoy® (ipilimumab), approved in 2011, is a monoclonal antibody that acts to block the CTLA-4 receptor (an immune checkpoint receptor) on T-cells. In the presence of CTLA-4 receptor it is believed tumors are able to suppress the immune system from recognizing cancerous cells, however blockade of this receptor with Yervoy® (an anti-CTLA-4 antibody) appears to allow the immune system to generate an antitumor T-cell response. Yervoy® was the first approved immunotherapy in melanoma, and current research is evaluating the use of other anti-checkpoint monoclonal antibodies. Although effective at improving overall survival, this benefit is only seen in a small population of patients that respond to the drug (~11%). Moreover, Yervoy® is known to have significant side effects which has resulted in the treatment being intolerable to some patients.

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Another monoclonal antibody approved that acts to block a checkpoint receptor, PD-1, was recently approved by the FDA. Keytruda® (pembrolizumab), was given breakthrough status by the FDA and was given market approval in August 2014 based on the impressive objective response rate data from Phase I and II clinical trials. These studies demonstrated that Keytruda®, when given to patients with unresectable metastatic melanoma, had an objective response rate of ~ 30-40%. What is more, the safety profile for this drug was markedly better than Yervoy®. With the recent approval of Keytruda®, and the pending approval of other anti-PD-1 antibodies, the use of immunotherapy to treat cancers, including melanoma, is expected to increase. However, even with the strong response data from Keytruda®, there are a significant number of patients who do not respond to anti-PD-1 antibodies (~60-70%) in melanoma. Recent research has shown that tumors with little, or no, presence of immune cells (i.e. CD8+ tumor infiltrating lymphocytes) prior to treatment with anti-PD-1 antibodies are less likely to respond, than tumors that have a high number of these cells already present in the tumor prior to treatment. The physical difference between these types of tumors clearly demarcates a population of responders versus non-responders, and it is believed that determining a method to convert the non-responder population to responders represents a significant unmet medical need. A way of addressing this medical need may be through the use of intratumoral therapies that can modify the tumor microenvironment, while combining it with anti-PD-1 antibodies or other checkpoint inhibitors antibodies.

Like Provenge®, a product developed and marketed by Dendreon Corporation, many emerging therapies continue to employ an autologous cell-based mode of delivery, which involves the harvesting of a patients own cells, growing them in a lab, incubating with a vaccine or immune stimulating agent, and re-administering the resulting product to the patient. This autologous cell-based approach has shown safety and efficacy, however the significant cost and time involved in preparing this therapeutic treatment for each individual patient has been unattractive for many patients and clinicians.

Viral vectors, such as adenoviruses and oncolytic viruses, have also been used to deliver immunotherapeutic payloads to fight against cancerous cells, either systemically or through direct injection into the tumor. Clinical trials for this therapeutic delivery method are ongoing with no approved therapies yet to be available in the clinic, however, questions still remain about efficacy of viral vectors as a delivery method, since the patient may mobilize an immune reaction against the virus itself resulting in neutralization of the virus and clearance from the body before an effectual response is elicited. Since viral vectors are occasionally created from pathogenic viruses, involving a deletion of a part of the viral genome critical for viral replication, safety has also been a concern to avoid production of new virions.

Other non-viral vector methods, including liposome-based delivery systems, are also currently being developed and employed in ongoing clinical trials. The impact of all these emerging cancer immunotherapies will ultimately be determined by their ability to improve upon the safety, efficacy, utility and cost of currently available therapies.

- Vaccination. The use of vaccination has long held interest as another potential modality that could prove beneficial in treating and limiting systemic disease. The challenge has been that many tumors do not display antigens unique to the tumor cell that the immune system can use to specifically target for selective destruction of the malignant tissue. Even though tumors over-express normal cellular products that the immune system ignores, due to a process called tolerization, the immune system is educated not to recognize self antigens early in development. As a result of the lack of immune system detection, it has proven difficult to use conventional vaccination strategies to break or overcome tolerance and generate immunity against tumor cells.

- Targeted Small Molecule Therapy. Mutations that drive signaling pathways critical to tumor growth and survival have recently been identified. One such mutation of the mitogen activated protein (MAP) kinase pathway has been shown to be important in the proliferation approximately 50% of all cutaneous melanomas. The introduction of BRAF inhibitors, which block the BRAF V600E mutation, has greatly improved the short-term prospects of some patients with these tumors, but the tumors tend to become resistant to therapy with time by activating alternative signaling pathways. Zelboraf®, approved in 2011, is a BRAF inhibitor that interrupts a key process in melanoma growth in patients with a particular melanoma mutation. Two additional drugs approved in 2013, Tafinlar® and Mekinist , are single-agent oral treatments for the

treatment of unresectable metastatic melanoma and like Zelboraf®, both of these new agents interrupt a key process in melanoma growth by inhibiting the MAP Kinase signaling pathway. Despite these therapies showing benefit to some patients by extending life beyond traditional therapeutic options, safety and tolerance to these drugs, may be a deterrent for some patients. Moreover, there appears to be a high rate of recurrence in patients who respond to these drugs, where the patient becomes refractory to the therapy and the disease often comes back quickly and aggressively.

Employees

We have assembled a senior management team with many years of experience and success in biotech/pharma operations, business and commercial development, and capital markets. In addition, we have assembled a clinical and regulatory team is experienced in developing and advancing novel therapeutic approaches through clinical testing and regulatory approvals. As of October 1, 2014, we have a total of 43 employees (of which 42 are full time). We believe that our relations with our employees are good and we have no history of work stoppages.

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We expect to hire additional staff and to engage consultants in regulatory, compliance, investor and public relations, and general administration as necessary. We also expect to engage experts in healthcare and in general business to advise us in various capacities.

Intellectual Property

Our success and ability to compete depends upon our intellectual property. We have acquired and have been issued 27 U.S. patents and have two U.S. patent applications pending. We expect to file additional patent applications. We have a total of 18 issued patents and patent applications in other jurisdictions. The bulk of our patents, including fundamental patents directed toward our proprietary technology, expire between 2014 and 2027. In addition, we have licensed intellectual property rights to use certain electroporation technology and intellectual property for delivering DNA-based cytokines as an immunotherapy.

Government Regulation

United States

In the United States, our product candidates are subject to extensive regulation by the FDA. Federal and state statutes and regulations, many of which are administered by the FDA, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA s refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves, among other things:

- completion of pre-clinical testing and formulation studies in compliance with the FDA s good laboratory practice regulations;
- submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin in the United States;
- performance of adequate human clinical trials in accordance with good clinical practices to establish the safety and efficacy of the proposed drug product for each intended use; and
- submission to the FDA of a new drug application, or NDA, which the FDA must review and approve.

The pre-clinical and clinical testing and approval process requires substantial time, effort, and financial resources, and the receipt and timing of approval, if any, is highly uncertain. The results of pre-clinical tests, together with certain manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Once an IND is in effect, the protocol for each clinical trial to be conducted under the IND must be submitted to the FDA, which may or may not allow the trial to proceed. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with good clinical practice requirements. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- *Phase 1*: The drug is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution, and excretion and, if possible, to gain an early indication of its effectiveness.

- *Phase 2*: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications, and to determine dose tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted.

- *Phase 3*: The drug is administered in large patient populations to obtain additional evidence of clinical efficacy and safety in an expanded patient population at multiple, geographically-dispersed clinical trial sites and to establish the overall risk-benefit relationship of the drug.

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- *Phase 4*: In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor s agreement to conduct additional clinical trials to further assess the drug s safety and effectiveness after NDA approval.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA requesting approval to market the product. NDAs must also contain extensive information relating to the product s pharmacology, chemistry, manufacture, controls, and proposed labeling, among other things.

Once the submission has been accepted for filing, the FDA begins an in-depth substantive review. Pursuant to the FDA s performance goals, NDA reviews are to be completed within ten months, subject to extensions by the FDA. Before approving an NDA, the FDA often inspects the facility or facilities where the product is manufactured and will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with good manufacturing practices. Additionally, the FDA will typically inspect one or more clinical sites to assure compliance with good clinical practices before approving an NDA. If the FDA determines that the NDA is not acceptable, then the FDA may outline the deficiencies in the NDA and often will request additional information or additional clinical trials. Notwithstanding the submission of any requested additional testing or information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Even if regulatory approval of a product candidate is obtained, such approval will usually impose limitations on the indicated uses for which the product may be marketed. Additionally, the FDA may require post-approval testing, such as Phase IV studies, or surveillance programs to monitor the effect of approved products, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

After FDA approval, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug/device listing, recordkeeping, periodic reporting, product sampling and distribution, manufacturing practices, labeling, advertising and promotion, and reporting of adverse experiences with the product. The FDA may withdraw its approval of a product if compliance with regulatory requirements and manufacturing standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: restrictions on the marketing or manufacturing of the product; complete withdrawal of the product from the market or product recalls; fines, warning letters or holds on post-approval clinical trials; or injunctions or the imposition of civil or criminal penalties.

International Regulation

If we pursue research and/or commercialization of our product candidates in countries other than the United States, then we would need to obtain the necessary approvals by the regulatory authorities of such foreign countries comparable to the FDA before we could commence clinical trials or marketing of our product candidates in those countries, and we would be subject to a variety of foreign regulations regarding safety and efficacy and governing, among other things, clinical trials and commercial sales and distribution of our products. The approval processes and requirements vary by country and can involve additional product testing and additional review periods, and the time may be longer or shorter than that required to obtain FDA approval.

Other Regulatory Requirements and Environmental Matters

We are or may become subject to various laws and regulations regarding laboratory practices and the experimental use of animals, as well as environmental laws and regulations governing, among other things, any use and disposal by us of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA and other government agencies have broad regulatory and enforcement powers, including, among other things, the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have a material adverse effect on us. Additionally, if we are able to successfully obtain approvals for and commercialize our product candidates, then we may become subject to various federal, state, and local laws targeting fraud, abuse, privacy, and secu