Zacks Small-Cap Research

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Grant Zeng, CFA
312-265-9466
gzeng@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

OncoSec Medical (ONCS-OTC)

ONCS: New financing boosted balance sheet, positive Phase II data of ImmunoPulse reported, on schedule to advance pipeline----- maintaining Outperform rating.

Current Recommendation	**Outperform**
Prior Recommendation	N/A
Date of Last Change	01/27/2014
Current Price (09/04/14)	$0.58
Twelve- Month Target Price	**$1.50**

OUTLOOK

ONCS is a mid-stage biotech company focused on electroporation delivery technology for cancers. Its lead candidate ImmunoPulse locally delivers a plasmid DNA encoding IL-12. Currently ImmunoPulse is in three Phase II clinical trials for melanoma, Merkel cell carcinoma, and cutaneous T-cell lymphoma respectively. Data have shown that ImmunoPulse is safe and can elicit both local and systemic immune-response.

ImmunoPulse also holds great potential in combination with checkpoint inhibitors for cancers.

We are optimistic with the technology and the prospect of OncoSec, and are positive on the company's shares.

SUMMARY DATA

52-Week High	**$0.94**
52-Week Low	**$0.24**
One-Year Return (%)	**74.58**
Beta	**1.39**
Average Daily Volume (sh)	**1,501,169**
Shares Outstanding (mil)	**244**
Market Capitalization ($mil)	**$126**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**N/A**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2014 Estimate	**N/A**
P/E using 2015 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High,**
Type of Stock	**N/A**
Industry	**Med-Biomed/Gene**
Zacks Rank in Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Oct)	Q2 (Jan)	Q3 (Apr)	Q4 (Jul)	Year (Jul)
2012					0.00 A
2013	0.00 A	0.00 A	0.00 A	0.00 A	0.00 A
2014	0.00 A	0.00 A	0.00 A	0.00 E	0.00 E
2015					0.00 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Oct)	Q2 (Jan)	Q3 (Apr)	Q4 (Jul)	Year (Jul)
2012					-$0.08 A
2013	-$0.02 A	-$0.02 A	-$0.01 A	-$0.02 A	-$0.07 A
2014	-$0.01 A	-$0.01 A	-$0.02 A	-$0.01 E	-$0.06 E
2015					-$0.04 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT'S NEW

New Financing Boosted Balance Sheet

For the nine months ended April 30, 2014, OncoSec Medical reported a net loss of $8.5 million, or $0.05 per share, compared to a net loss of $5.4 million, or $0.05 per share, for the same period last year.

There were no revenues for the nine months ended April 30, 2014 or April 30, 2013.

Research and development expenses were $3.9 million for the nine months ended April 30, 2014, compared to $2.4 million for the nine months ended April 30, 2013. This increase in research and development expenses was primarily a result of increased compensation expense, inclusive of increased salary and stock-based compensation expenses, increased clinical operation costs and costs related to the company's sponsored research agreements.

General and administrative expenses were $4.5 million for the nine months ended April 30, 2014, compared to $2.9 million for the nine months ended April 30, 2013. This increase was primarily a result of increased compensation expense, increased corporate communications and business development costs and increased legal fees associated with various corporate matters, partially offset by a decrease in travel and conference fees.

On June 6, 2014, OncoSec (ONCS) closed a registered direct offering of 22,535,212 shares of its common stock at a price of $0.71 per share and warrants to purchase up to an aggregate of 7,887,325 shares of common stock at an exercise price of $0.90 per share for a term of five years.

The gross proceeds of the offering were approximately $16 million. Net proceeds, after deducting the placement agent's fee and other estimated offering expenses payable by OncoSec, were approximately $14.9 million.

OncoSec intends to use proceeds from the offering for general corporate purposes, including clinical trial expenses and research and development expenses.

We are pleased with the new financing which not only strengthens OncoSec's cash position, but also validates the company's technology and clinical programs.

As of April 30, 2014, OncoSec held $24.3 million in cash. With the new net proceeds of $15 million, the company should have cash of $37 million at the end of July 2014, which will last through the end of fiscal 2017.

Positive Phase II Interim Data of ImmunoPulse in Melanoma Reported

On June 2, 2014, at the ASCO meeting, OncoSec announced interim data from its **Phase II** melanoma study.

OncoSec's **ImmunoPulse** locally delivers plasmid-DNA encoding **IL-12** into tumor cells.

OncoSec initiated a **Phase II** clinical trial in patients with **melanoma** in Feb 2012. The Phase II melanoma trial (**OMS-I100**) is a single dose trial treating approximately 30 patients, who are eligible to receive one **treatment cycle every 12 weeks**. The **primary endpoint** is objective response rate (local and distant) at six months. Secondary trial endpoints include time to objective response (complete and partial responses), duration of distant response and overall survival.

Data from the multicenter, open-label, single-arm study confirmed the safety of **ImmunoPulse**, which delivers the anti-tumor agent pIL-12 directly into the tumor via in-vivo electroporation (EP), with no treatment-related serious adverse events or deaths having been reported. Regression of treated and non-treated tumors suggests successful induction of systemic anti-tumor response.

As of the reporting date, **30 patients** was enrolled and received at least one cycle of treatment. At the time of this interim analysis, **28 patients** were evaluable for objective response rate (ORR) at 24-week primary time point. Best ORR was evaluated per modified RECIST1.1 criteria, and provided in Table 1 below.

Table 1: Best ORR at 24 Weeks of First Treatment (Modified RECIST)

Number of Evaluable Patients	Objective Response (%)	Complete Response (%)
28	9/28 (32%)	3/28 (11%)

In addition to best overall response, an assessment of best local response in treated lesions was conducted (Table 2). Complete response was defined as complete regression of a treated lesion. Partial response was defined as >30 percent reduction in the longest diameter of the tumor, while stable disease was defined as ≤30 percent reduction and <20 percent increase in the longest diameter of the tumor.

Table 2: Treated Lesion Best Local Response

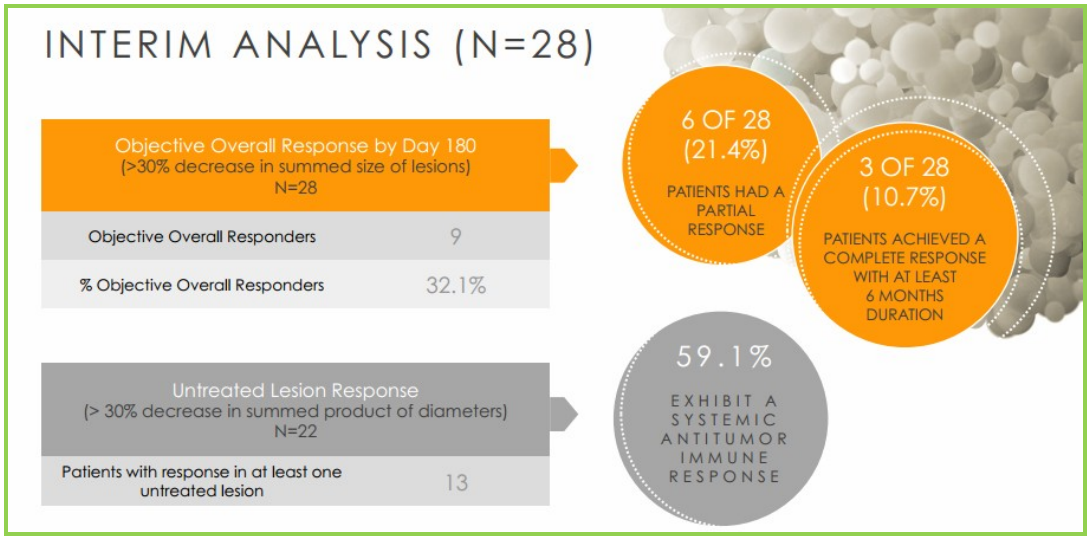
Number of Evaluable Treated Lesions	Stable Disease (%)	Partial Response (%)	Complete Response (%)
85	26/85 (31%)	7/85 (8%)	38/85 (45%)

Importantly, intratumoral treatment with IL-12 EP resulted in the development of a systemic anti-tumor effect in the majority of patients. Twenty-two of the enrolled patients presented with baseline lesions that were left untreated in order to evaluate the induction of a systemic response. Regression was documented in at least one non-injected tumor in 59 percent (13/22) of patients (Table 3). These results suggest that intratumoral therapy with IL-12 can induce systemic anti-tumor responses while avoiding the toxicities observed with systemic recombinant IL-12 therapy.

Table 3: Systemic Anti-tumor Response (Untreated lesions)

Number of Evaluable Patients	Response (at least 30% decrease) in at least 1 untreated lesion
22	13/22 (59%)

Correlative data were also presented, including gene expression in a subset of eight patients, where adequate paired pre- and post-treatment biopsy samples were available. A focused analysis of immunomodulatory cell types and pathways supported the hypothesis that IL-12 electroporation leads to induction of interferon-γ and downstream interferon-γ-inducible genes, including key modulators of antigen presentation and processing machinery and chemokines. Additional genes of interest were also up-regulated, including PD-1, PD-L1 and T cell markers, confirming the Phase I data, indicating that treatment results in T cell infiltration.



These data strengthen and expand upon previously reported Phase I results, which indicated a complete response in 16% of patients (3/19) and disease stabilization in 38% (7/19). These data were published in Journal of Clinical Oncology in 2008.

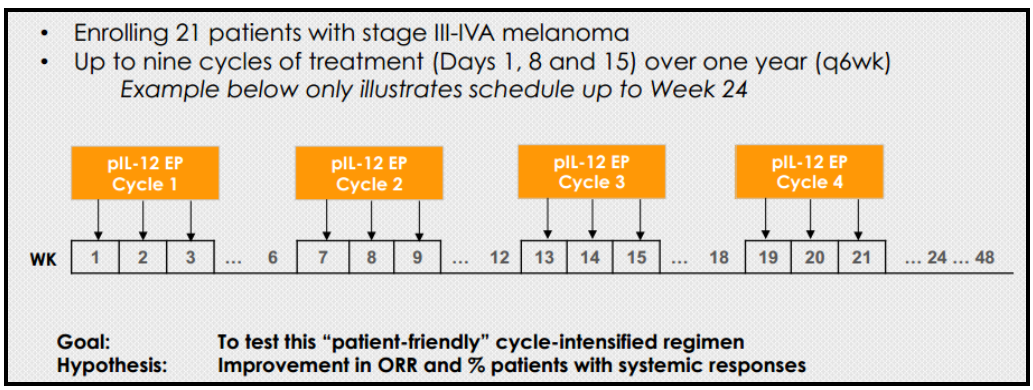
We are encouraged by the safety and efficacy data of ImmunoPulse in the Phase II study in melanoma patients. The positive Phase II data further validates results from previous Phase I study. We are especially impressed with the response rate of untreated tumors, which suggests an induction of **systemic antitumor response**, without systemic toxicity.

Systemic response is significant for two main reasons. First, it suggests that unlike most locally administered melanoma treatments, ImmunoPulse may induce antitumor response throughout the entire body, which would have clear benefits in the treatment of **metastatic disease**. Secondly, the favorable safety profile of ImmunoPulse indicates its potential to deliver systemic benefit, without the toxicities associated with many other systemic treatments.

OncoSec Plans to Evaluate Increased Dose Frequency of ImmunoPulse in Ongoing Phase II Melanoma Trial

In March 2014, OncoSec submitted a protocol addendum to the FDA and Institutional Review Board (IRB) to evaluate an **increased dose frequency** for ImmunoPulse in an expansion of its ongoing **Phase II melanoma trial**. The Company expects to enroll up to **21 patients** in this expansion.

The protocol addendum will allow for the assessment of the safety and efficacy of a **six-week treatment cycle** with ImmunoPulse in up to 21 melanoma patients. Each cycle will consist of treatments on Days 1, 8 and 15. Subjects will be eligible for an additional cycle as early as six weeks from the first treatment up to a maximum of nine treatment cycles.



There are **three goals** of the trial expansion:

- It will provide an opportunity to assess whether more frequent treatment with ImmunoPulse can provide additional clinical benefit to melanoma patients.

- The expansion is also intended to help optimize the treatment design of the Company's **Phase IIb** study in melanoma patients, which is expected to initiate in late 2014.

- Safety of this intensified dose regimen will also be assessed.

Phase IIb Study of ImmunoPulse for Metastatic Melanoma To be Initiated Soon

While OncoSec's current Phase II study in metastatic melanoma is coming to a conclusion, the company is preparing for its next phase of development and is setting up for the initiation of a **Phase IIb** metastatic melanoma study **in late 2014**. The Phase IIb study will be a randomized, controlled study, providing the company with information for a key inflection point in the development of this program.

If the Phase IIb study can confirm safety and efficacy of ImmunoPulse, **pivotal trial** could start in 2015. And we estimate approval of ImmunoPulse for the treatment of melanoma may be obtained as early as **in late 2017** if the pivotal trial data prove to be positive.

Update on the Phase II CTCL Lymphoma Study

In April, 2014, OncoSec announced that it will re-launch its **Phase II** cutaneous T-cell lymphoma (CTCL) trial under a protocol amendment.

As a reminder, in July 2012, a **Phase II** trial of ImmunoPulse was initiated at the University of California San Francisco (UCSF) under an FDA-approved investigator-sponsored Investigational New Drug application (IND) with Weiyun Ai, M.D. as principal investigator. In November 2012, this IND was transferred to OncoSec.

Following review of the protocol under OncoSec's own accord, the company determined that an amendment to the protocol should be considered in order to broaden the inclusion and exclusion criteria, implement a more patient-friendly treatment design, and expand the exploratory endpoints for the trial. In consultation with Key Opinion Leaders (KOLs), OncoSec has amended the protocol, and Institutional Review Board approval is pending.

OncoSec will expand enrollment to Stanford University. Stanford is regarded as having a large CTCL patient population and is experienced in investigating novel therapies in this disease. This Phase II clinical trial is an open label, multi-center study. 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.

In the revised protocol, all subjects will be eligible to receive up to six treatment cycles consisting of treatment days (Days 1 and 8) in a 28-day cycle. A total of up to **34 patients** will be enrolled in this study. Subjects will be followed for safety and clinical evaluation every four weeks. Quality of Life will be assessed. Survival follow-up will occur at three-month intervals over two years following the end of the study.

Yuon Kim, M.D. will serve as principal investigator for the Stanford University study.

OncoSec Presents New Data at 10th Annual PEGS

On May 5, 2014, OncoSec presented **preliminary experimental data** showing that ImmunoPulse in mice can lead to systemic anti-tumor immune responses in distant untreated lesions at the Essential Protein Engineering Summit **(PEGS)** in Boston.

In the syngeneic **B16.F10 mouse melanoma tumor model**, the left-side tumors were treated with ImmunoPulse and tumors on the right side were not treated. Forty-percent of the untreated tumors (4/10) showed brisk inflammatory infiltrate and pathologic changes of regression at day 18 or day 22 after ImmunoPulse treatment. This result demonstrated ImmunoPulse's **systemic** anti-tumor efficacy.

An IL-12-dependent TIL (tumor infiltrating lymphocyte) and interferon gamma response was confirmed in both treated and untreated tumors.

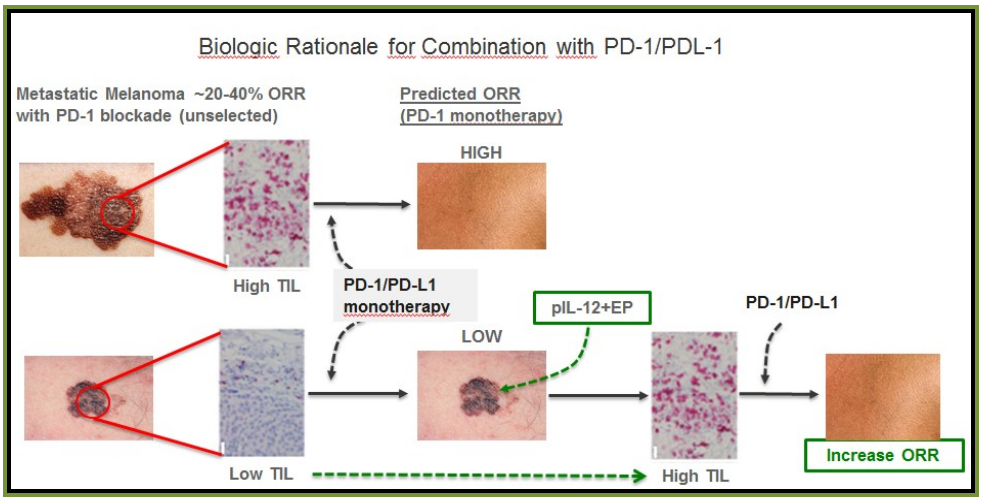
The above data are collected from an ongoing collaboration with Old Dominion University (ODU) and the Frank Reidy Research Center for Bioelectrics. Current experiments are focused on evaluating the effects of ImmunoPulse **in combination with** checkpoint inhibitors for **melanoma cancer**.

Studies have demonstrated that tumors (specifically melanoma) can be divided into a high and low TIL (tumor infiltrating lymphocyte) phenotype. Tumors with high TIL are referred to as **immunogenic**, while tumors with low TIL are referred to **non-immunogenic**. Ongoing clinical trials of PD1/PDL1 inhibitors suggest that response correlates with high TIL phenotype. Tumors with low TIL have low response rate to PD-1/PDL-1 inhibitors.

Recent melanoma studies have reported response rates in the range of 20-40% using anti-PD-1 or anti-PDL-1, and the argument is that the majority of the responders are the high-TIL population. If this is the case, then the question becomes how to make those **non-immunogenic tumors** into immunogenic tumors so that they can respond to PD-1/PDL-1 or similarly effective T cell checkpoint agents.

The therapeutic concept is that ImmunoPulse with IL-12 will convert low TIL tumors into high TIL ones, thus allowing an anti-PD1/PDL1 therapy to work in patients, who would otherwise be PD-1 unresponsive.

The potential ability of ImmunoPulse to convert the non- or weakly immune-responsive cancer into strongly immune-responsive cancer may represent a paradigm shift in cancer therapy. This area is an enormous unmet medical need and represents a huge market for OncoSec. It is estimated that about 50% to 80% cancer patients will not have TIL infiltrate at baseline or even after PD-1/PDL-1 treatment. This is where OncoSec's ImmunoPulse can get in and convert those non-immunogenic tumors into immunogenic tumors. In addition to melanoma, ImmunoPulse can virtually target any solid tumors, which represents a multi-billion dollar market for OncoSec.



There is a huge **unmet medical need** for OncoSec's ImmunoPulse in combination with checkpoint inhibitors. If we look at the melanoma indication alone, this is a disease that has the highest response rates with PD-1 inhibitor monotherapy. But still there are about 60% to 80% of patients who will not respond to PD-1 Checkpoint Inhibitors.

In **other solid tumors**, the percentage of PD-1 non-responders/non-immunogenic tumors is likely to be even greater. Thus, there is a tremendous unmet medical need, across many solid tumors.

We estimate the market for the combination therapy will be a multi-billion business.

In order to accelerate the development of the combination study, OncoSec recently hired industry veteran **Dr. Robert H. Pierce** as the Company's Chief Medical Officer (CMO). Dr. Pierce was a key member of the global development team behind Merck's anti-PD-1 program (MK-3475) before joining OncoSec. We believe the addition of Dr. Pierce will accelerate the combination development of ImmunoPulse with PD-1/PDL-1 inhibitors.

Valuation Very Attractive

We maintain our Outperform rating on OncoSec shares and reiterate our 12-month price target of $1.50.

OncoSec is an emerging biotech company focused on developing and commercializing innovative approaches for the treatment of cancers. OncoSec's key platform technology is its proprietary **electroporation delivery system** to locally deliver DNA or chemotherapeutics into tumor cells. But what makes the technology unique is that this locally delivered DNA has demonstrated systemic response for the treatment of melanoma, meaning that the technology can be used to treat **metastasis** of cancers.

OncoSec's lead candidate **ImmunoPulse** is a delivery device encoding for IL-12. ImmunoPulse is currently in three Phase II clinical trials for melanoma, Merkel cell carcinoma and cutaneous T-cell lymphoma respectively. OncoSec already reported positive data from the Phase II melanoma trial, and plans to move to Phase IIb trial for melanoma soon. We estimate pivotal trial for melanoma could start in calendar 2015, and approval of this indication could be obtained as early as in 2017.

One important application of ImmunoPulse is that it can be **combined** with **checkpoint inhibitors** such as PD-1/PDL-1 for the treatment of melanoma and other solid tumors. In this case, the combination therapy can convert non-immunogenic cancers into immunogenic cancers, which can be killed by the combination therapy.

The market for ImmunoPulse is huge even for the melanoma indication alone. If we consider other indications for solid tumors such as Merkel cell carcinoma and cutaneous T-cell lymphoma, the market is much bigger.

Based on OncoSec's fundamentals, we think its shares are undervalued at current market price. Currently, OncoSec shares are trading at about $0.58 per share, which values the company at $139 million in market capitalization based on 240 million outstanding shares. This certainly is a huge discount compared to its peers. We understand that valuing a development stage biotech company is always difficult. But if we look at similar companies in the cancer space, the value of a typical development stage biotech firm with similar fundamentals to OncoSec is usually from $50 million to $1 billion depending on how advanced the programs are and how big the markets are for its candidates. OncoSec is a mid-stage development biotech company, and is ready to move to pivotal study with its lead candidate. The market of melanoma and/or other solid tumors is huge for its lead candidate ImmunoPulse.

With the estimated approval of ImmunoPulse in 2017, we model OncoSec will become profitable in fiscal 2018 with earnings per share (EPS) of $0.03 based on ImmunoPulse sales of $50 million. Revenue could double in fiscal 2019 and EPS will grow into $0.10 per share according to our estimates. If we use the biotech industry average P/E multiple of 35 and 20% discount rate for five years, we arrive at our price

target of $1.50 per share for OncoSec, which values the Company at $360 million in market cap. This valuation is still conservative in our view considering the relatively strong fundamentals of the Company.

Recent interest in electroporation technology from big pharma could serve as a wildcard for OncoSec valuation. In September 2013, **Roche** entered into collaboration with **Inovio Pharmaceuticals** with an over $400 million investment in Inovio's electroporation technology. Also in Feb 2014, **Pfizer** entered into a collaboration agreement with **Ichor Medical Systems** to utilize Ichor's intramuscular electroporation technology. With proven clinical data, OncoSec's ImmunoPulse could be the next target for big pharma companies.

OVERVIEW

OncoSec Medical Inc. (ONCS.OTC) is an emerging **drug-medical device and therapeutic** company focused on designing, developing and commercializing innovative and proprietary medical approaches for the treatment of **solid tumors** that have unmet medical needs or where currently approved therapies are inadequate based on their efficacy or side-effects.

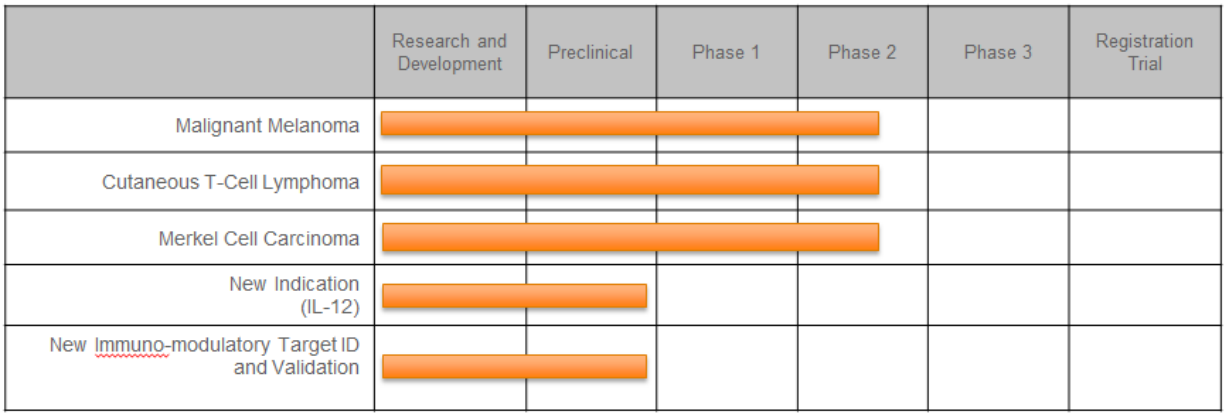
OncoSec is the survivor company after the reverse merger with **Netventory Solutions Inc**. In March 2011, OncoSec acquired from **Inovio Pharmaceuticals, Inc**. certain assets of non-DNA vaccine technology and intellectual property relating to selective **electrochemical tumor ablation**, which is related to the use of drug-medical device combination products for the treatment of various cancers.

The assets OncoSec acquired include intellectual property relating to certain **delivery technologies**, which are referred to as the OncoSec Medical System **(OMS).** OMS is a therapeutic approach which is based on the use of an **electroporation delivery device** in combination with a DNA-based cytokine to treat solid tumors.

OncoSec's lead candidate is **ImmunoPulse,** which is based on the use of electroporation to enhance the local delivery of DNA plasmids encoding interleukin-12 (IL-12). Upon uptake into cells, IL-12 will generate a local, regional and systemic immune response for the treatment of various cancers.

OMS is designed to increase the permeability of cancer cell membranes and, as a result, increases the intracellular delivery of selected therapeutic agents.

OncoSec's current focus is on ImmunoPulse approach for tumor treatment. It has built a robust pipeline based on this unique technology.



OncoSec is headquartered in San Diego, California.

INVESTMENT THESIS

The Unique, Proprietary OncoSec Medical System (OMS)

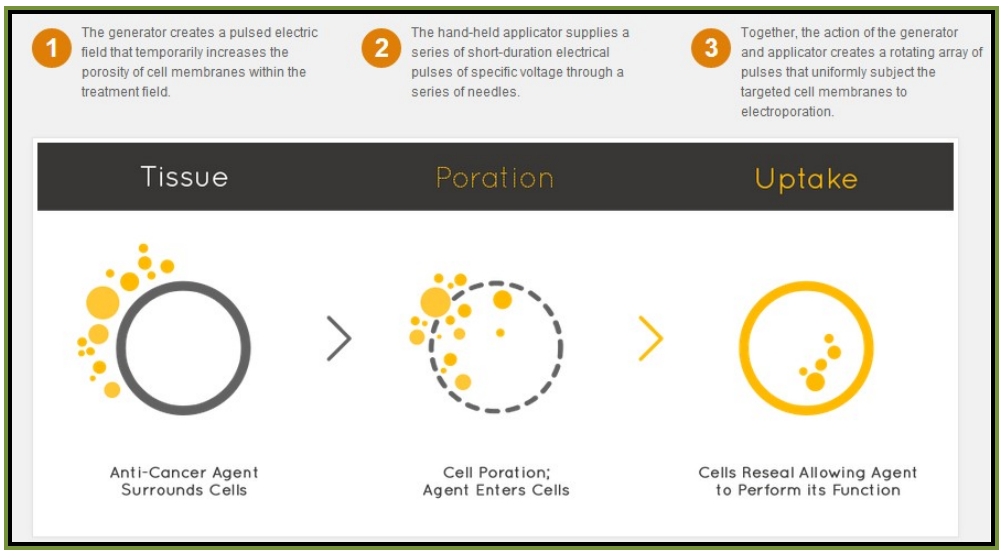
OncoSec's core technology for cancer treatment is called **the OncoSec Medical System (OMS)**. This breakthrough technology hinges on a proprietary process called **electroporation**, which uses an electrical pulse to create temporary pores in cancer cells. After the electroporation, DNA-encoded cytokines or other immunomodulatory molecules are delivered through these pores, leading to sustained expression of these molecules in the tumor, leading to lower "doses" than what would normally be delivered systemically. The result is a more potentially effective treatment with fewer side effects.

Supported by extensive research and development and a comprehensive patent portfolio, OncoSec is now a world leader in this emerging technology. This technology includes the design and manufacture of medical-grade electrical pulse generators, treatment applicators, and software that are adaptable for different clinical applications. The technology and methods of use are all patented intellectual property.

These proprietary elements, along with the company's clinical trial experience and expertise in using these technologies, have helped OncoSec to consolidate its position as the leading proponents of this promising treatment for solid tumors.

The OncoSec Medical System **(OMS)** is developed based on the following rational. Many drugs and DNA-based therapeutics must enter the target cell through its membrane in order to perform their intended function. However, the effectiveness of these medicines is limited since gaining entry into target cells through the outer membrane can be a significant challenge. 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, enabling the intracellular delivery of a variety of payloads, most notably, DNA constructs (i.e. plasmids) encoding biologically active molecules such as cytokines.

This transient and reversible **electrical permeabilization** of cell membranes and the resulting increase in intracellular delivery of immune-activating DNA plasmids is the underlying basis of OncoSec's OMS therapeutic approach. While the extent of membrane permeabilization depends on various electrical, physical, chemical, and biological parameters, research with OMS has demonstrated an increase of cellular uptake in chemical molecules from **1,000- to 8,000**-fold above baseline. 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, and thereby providing a potentially safer treatment.



DNA Delivery With Electroporation — ImmunoPulse

The lead candidate based on the electroporation delivery technology is **ImmunoPulse**, which delivers plasmid DNA encoding immunotherapeutic **cytokines (interleukin 12, IL-12)** into tumor cells that stimulate the patient's immune system to fight cancer.

The greatest obstacles to making conventional immunotherapy and DNA-based immunotherapies a reality has been the limited data supporting safe, efficient, and economical delivery and expression of plasmid-DNA constructs into the target cells. The use of OMS in this approach has been validated from multiple clinical studies assessing DNA-based immunotherapies against cancers. Together with its partners and collaborators, OncoSec plans to be the leader in establishing electroporation-delivered DNA immunotherapies. Based on existing data generated, electroporation could become the method of choice for plasmid-DNA delivery into cells in many clinical applications.

The ImmunoPulse approach utilizes an **optimized electroporation system** to deliver plasmid DNA encoding immunotherapeutic cytokines into tumor cells which in turn promote anti-cancer responses. The cytokine-encoding plasmid is first injected with a syringe/needle into the selected tumor. Using a remote control, the pulse generator is switched on and electrical pulses are generated and delivered through an attached electrical cord into the injected tissue through an electrode-needle array on the applicator. Studies have shown that 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 increase makes many DNA-based candidates potentially feasible without unduly compromising safety or cost.

A **Phase I** clinical trial in **metastatic melanoma** has been completed using ImmunoPulse to deliver plasmid-DNA encoding for the **IL-12** cytokine. The study was designed to assess both the adaptive and innate immunity responses from the targeted delivery of the IL-12 into melanoma tumor cells. The findings demonstrated not only regression of treated melanoma skin lesions, but also regression of distant untreated lesions, suggesting a **systemic immune response** to the localized treatment. Based on the positive Phase I data, OncoSec is conducting Phase II clinical trials of ImmunoPulse IL-12 for various tumors.

Advantages of OMS

Cancer is a disease of uncontrolled cell growth. The primary front line treatment of solid tumors involves surgical resection and/or radiation to eliminate or debulk tumor growth prior to initiating systemic therapy with chemotherapeutic agents. When detected early and still confined to a single location, cancer may be cured by surgery or radiation. However, neither surgery nor radiation can cure cancer that has spread throughout the body. Although chemotherapy can sometimes effectively treat cancer that has spread throughout the body, a number of non-cancerous cells, such as bone marrow cells, are also highly susceptible to chemotherapy. As a result, chemotherapy often has fairly significant side effects. In addition, it is common to see cancer return after apparently successful treatment by each of these means.

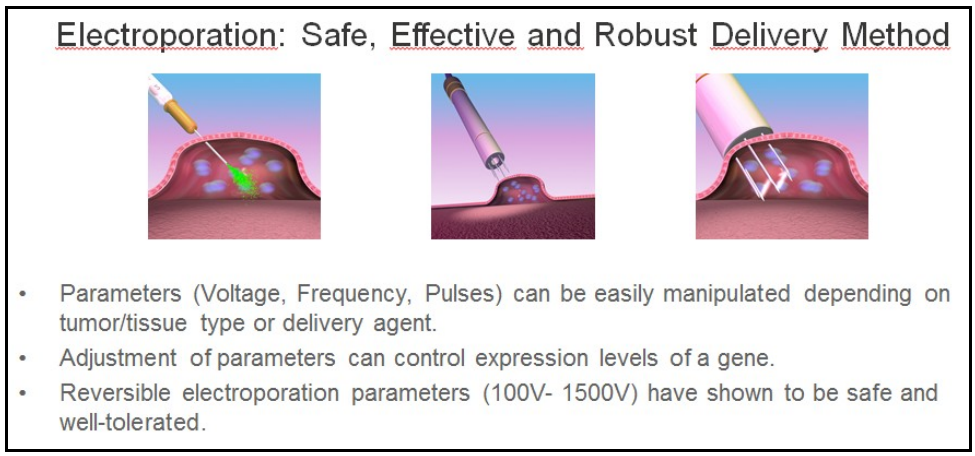
We believe that OncoSec's **ImmunoPulse** could offer a solution for cancers with an improvement in safety and quality of life for patients over conventional systemic treatments such as chemotherapy.

OncoSec's ImmunoPulse is an **immunotherapy**, which may have advantages over surgery, radiation, and chemotherapy. Immunotherapy is a process which uses the patient's own immune system to treat cancer. 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**) and interferon-alpha (**IFN- a**) have shown

encouraging results. However, these agents often require frequent doses that may result in severe side effects.

ImmunoPulse approach consists of directly injecting solid tumors with a DNA plasmid, which, upon uptake into cells, directs the production of the encoded immunostimulatory cytokine **(IL-12)** to generate a loco-regional immune response against the tumor, which can potentially induce a systemic immune response. The ease of manufacture, convenience, and ability to repeat administration may offer advantages over current modalities of therapy. In addition, cancer therapies using **non-viral DNA** delivery may offer an added margin of safety compared with viral-based delivery, as no viral particles or other potentially infectious agents are contained in the formulation.

OncoSec's electroporation technology is a safe, effective and robust tool for delivering payloads into cells. Because of this, the company is able to deliver potentially toxic payloads, like IL-12, locally into the tumor as a gene, and have it expressed in the tumor microenvironment. The beauty of electroporation is its ability to modify and manipulate the parameters and the payloads to target any indication, thus making it a well-defined, safe and effective delivery tool.



Another advantage of ImmunoPulse is that this technology has the potential for broad application. The use of electroporation to deliver immune-modulating DNA agents directly and safely into tumors provides for a robust and flexible technology that can be applied towards the treatment of numerous solid tumor indications either alone or in combination.

Potential Solid Tumor Indications	Potential immune targets
Head and Neck	Pro-inflammatory cytokines
Sarcoma	Immuno-modulatory receptors
Prostate	Cell trafficking molecules
Ovarian	
Breast	

Market Opportunity for ImmunoPulse

The initial indication for ImmunoPulse therapy will be for the treatment of **melanoma**. Melanoma is one of the most common skin cancers, with around 80,000 new diagnoses each year in the US, and leads to around 10,000 deaths each year, accounting for 75% of all deaths related to skin cancer. While survival rates have increased markedly in recent years, primarily due to early diagnosis, incidence rates have also tripled in the last 30 years from 8 cases per 100,000 persons to 24 per 100,000 according to

National Cancer Institute. The number of melanoma patients suitable for ImmunoPulse therapy outside the U.S. is approximately twice that of the U.S.

When diagnosed early almost all localized melanoma can be safely treated by surgical removal of the tumor. However in about 20% of the cases the tumor is metastatic and inoperable, and can spread to the brain, liver, bones, abdomen or lymph nodes, with far lower chances of survival. Patients with metastatic melanoma have a poor prognosis with a 5 year survival rate of 5%. Two commonly used therapeutic agents for metastatic melanoma are **dacarbazine** and **interleukin-2**. **Dacarbazine** has an objective response rate of approximately 12% with 2-3% complete response rate that are often transient. **Interleukin-2** has an objective response rate of approximately 16% with 4-6% durable complete response rate.

The US FDA recently approved a few agents for the treatment of metastatic melanoma.

In March 2011, the FDA approved **YERVOY (ipilimumab)** from **Bristol-Myers Squibb** for the treatment of unresectable or metastatic melanoma. Ipilimumab is a human cytotoxic T-lymphocyte antigen 4 (CTLA-4) antibody. CTLA-4 is expressed on activated T-cells and is a **negative regulator** of T-cell activation. Ipilimumab binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. By binding CTLA4, ipilimumab enhances T-cell activation.

In a Phase III trial of 676 patients, overall survival was longer with ipilimumab alone compared with tumor vaccine gp100. Patients treated with ipilimumab alone had a median OS of 10 months. Patients treated with gp100 had a median overall survival of 6 months. Patients who received ipilimumab plus gp100 had a median OS of 10 months. Patients treated with ipilimumab alone also had the **best overall response rate** (investigator assessed), of 10.9 percent. Patients treated with the combination of ipilimumab plus vaccine arm had an overall response rate of 5.7 percent. The patients treated with vaccine gp100 alone had an overall response rate of 1.5 percent.

Overall Survival Data for Yervoy

	YERVOY n=137	YERVOY+gp100 n=403	gp100 n=136
Hazard Ratio (vs. gp100) (95% CI)	0.66 (0.51, 0.87)	0.68 (0.55, 0.85)	
p-value	p=0.0026	p=0.0004	
Hazard Ratio (vs. YERVOY) (95% CI)		1.04 (0.83, 1.30)	
Median (months) (95% CI)	10 (8.0, 13.8)	10 (8.5, 11.5)	6 (5.5, 8.7)

In August 17, 2011, the FDA approved **vemurafenib** tablets (**ZELBORAF**, made by Hoffmann-La Roche Inc.) for the treatment of patients with unresectable or metastatic melanoma with the $BRAF^{V600E}$ mutation. ZELBORAF is a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with $BRAF^{V600E}$ mutation.

The confirmed, investigator-assessed best overall response rate was 48.4% for ZELBORAF. There were 2 complete responses (0.9%) and 104 partial responses (47.4%).

On May 29, 2013, the FDA approved **dabrafenib (Tafinlar™** capsule) and **trametinib (Mekinist** tablet), from GlaxoSmithKline, for the treatment of patients with unresectable or metastatic melanoma. Dabrafenib is approved for BRAFV600E mutation, while trametinib is approved for $BRAF^{V600E}$ or ^{V600K} mutation.

The investigator-assessed objective response rates were 52 percent for patients treated with dabrafenib, which included a **3 percent complete response rate**. The objective response rates were 22 percent for patients treated with trametinib. None of the 40 patients achieved a confirmed complete response.

The very small number of durable complete response rate makes it unlikely that many patients with metastatic melanoma will be cured utilizing any of these approaches. Also, all these drugs are associated with significant side effects and long-term use may lead to drug resistance by tumor cells.

OncoSec's **ImmunoPulse therapy** is a totally different treatment approach for melanoma. ImmunoPulse clinical-stage approach consists of directly injecting solid tumors with a DNA plasmid which, upon uptake into cells, directs the production of the encoded **IL-12** to generate a loco-regional immune response against the tumor. Both Phase I and Phase II data demonstrated not only regression of treated melanoma skin lesions, but also regression of distant untreated lesions, suggesting a **systemic immune response** to the localized treatment.

Melanoma is a huge market. Sales of **YERVOY** reached $706 million in 2012, first full year after launch. In 2013, BMS recorded $960 million in YERVOY sales. Sales of YERVOY are projected to reach $ 2 billion by 2018.

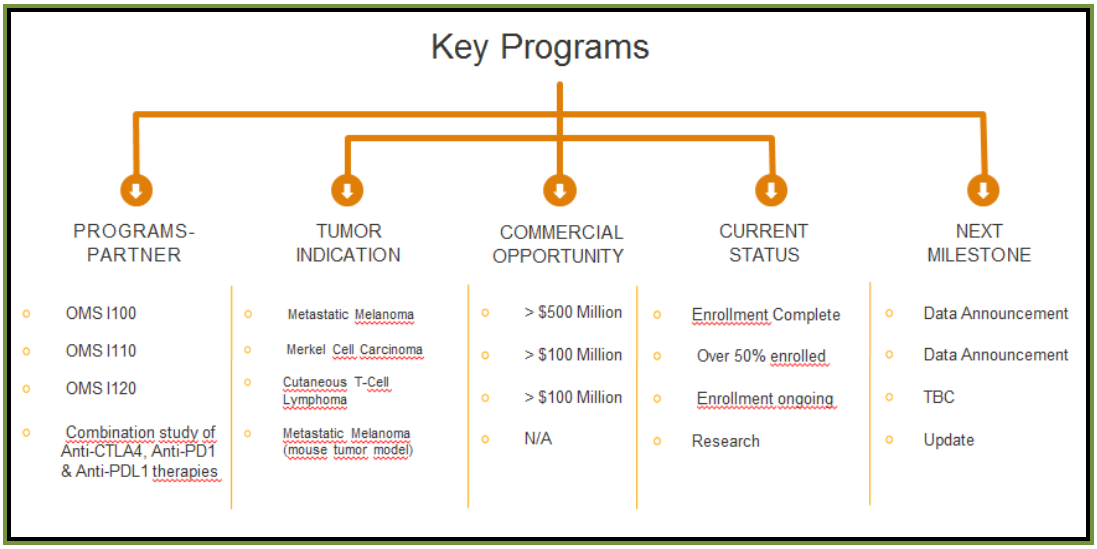
Considering the huge market for melanoma, we think **peak sales** of ImmunoPulse, alone and in combination, could reach $500 million for the indication of melanoma alone. In addition to melanoma, OncoSec also plans to develop ImmunoPulse therapy for other tumors. If ImmunoPulse therapy proves to be effective to treat additional indications, the market opportunity will be significantly larger. We see a blockbuster potential for ImmunoPulse if additional indications are approved.

ImmunoPulse for Merkel Cell Carcinoma Trial (OMS-I110)

Merkel cell carcinoma (MCC) is a rare but lethal **skin cancer** affecting about 1,500 people each year with 33% mortality rate in the US. The majority of Merkel cell carcinomas appear to be caused in part by a virus, Merkel cell polyomavirus. If this cancer metastasizes to the lymph nodes, the five-year survival rate is about 50 percent. A patient with a small tumor (less than 2 cm) that has not metastasized to the lymph nodes may have a five-year survival rate of more than 80 percent. The current treatment options for these patients are surgery, radiation and chemotherapy; however, up to half of patients suffer a recurrence. Current chemotherapy treatments have demonstrated short-lived responses with no clear impact on overall survival. Rapid advances in the biology of this disease provide a strong rationale for immunotherapy of this virus-associated cancer.

OncoSec initiated a **Phase II** trial of ImmunoPulse for Merkel cell carcinoma **(OMS-I110)** in **Feb 2012**. The trial "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 I dose escalation trial carried out in 24 metastatic melanoma patients.

In partnership with leading clinical centers, OncoSec is continuing enrollment in the Phase II study in Merkel cell carcinoma. The company expects to **complete enrollment** in this trial in **1Q14** and report additional data from the trial in **mid-2014**.



In addition to the above clinical programs, OncoSec also plans to initiate a new **Phase I study** in new solid tumor indication **in 2014**.

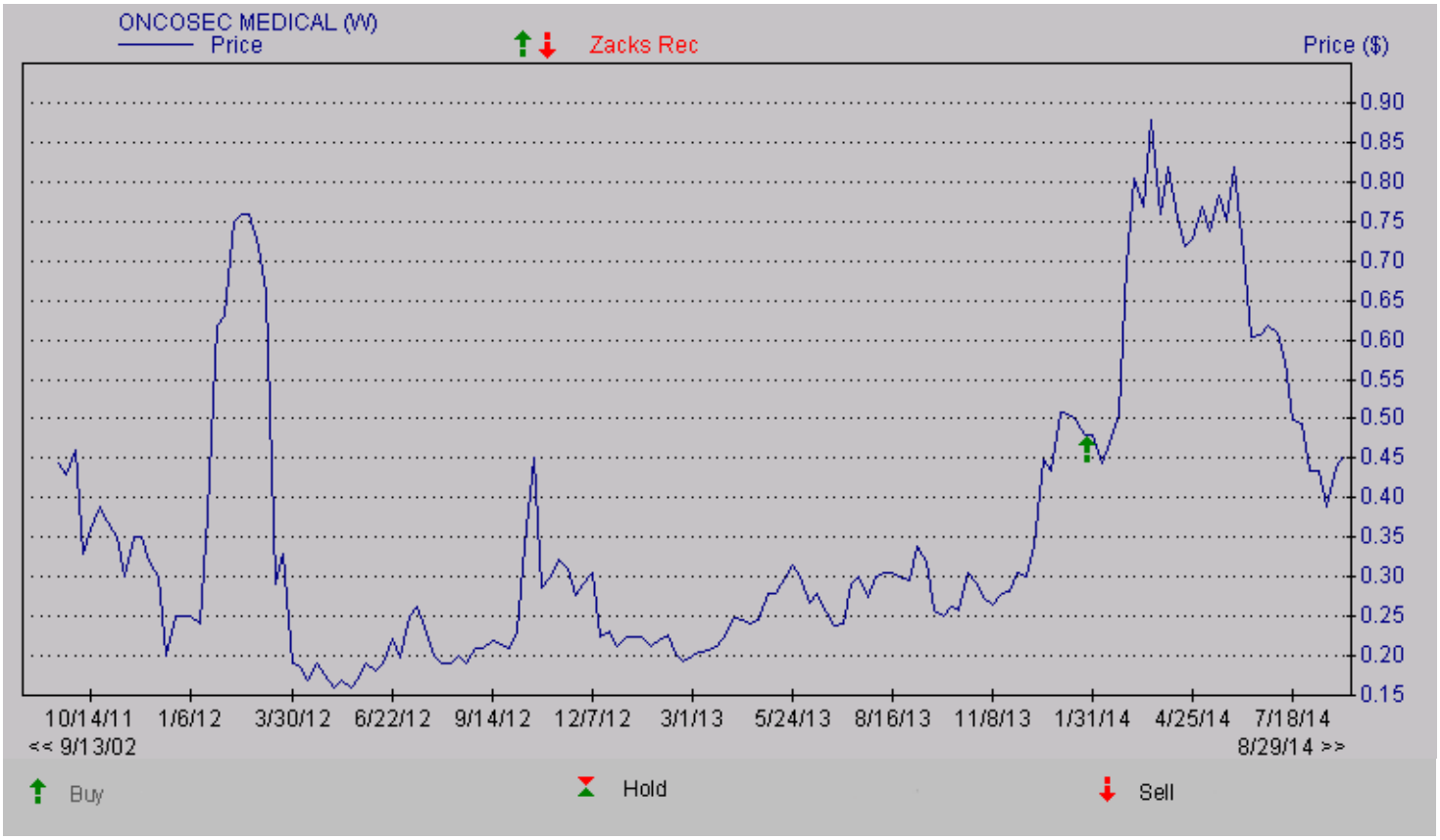
PROJECTED INCOME STATEMENT

	2012 (Jul)	2013A (Jul)	2014E (Jul)					2015E (Jul)	2016E (Jul)	2017E (Jul)	2018E (Jul)	2019E (Jul)
$ in million except per share data	FYA	FYA	Q1A	Q2A	Q3A	Q4E	FYE	FYE	FYE	FYE	FYE	FYE
Grant revenue	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Collaboration revenue	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Product revenue	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$5.00	$50.00	$100.00
Total Revenues	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$5.00**	**$50.00**	**$100.00**
YOY Growth	-	-	-	-	-	-	-	-	-	-	900.0%	100.0%
CoGS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.75	7.50	15.00
Gross Income	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$4.25**	**$42.50**	**$85.00**
Gross Margin	-	-	-	-	-	-	-	-	-	85.0%	85.0%	85.0%
R&D	$2.37	$3.16	$0.77	$1.46	$1.70	$1.55	$5.48	$5.50	$6.50	$8.50	$10.50	$13.00
% R&D	-	-	-	-	-	-	-	-	-	170.0%	21.0%	13.0%
SG&A	$3.16	$3.91	$1.21	$1.14	$2.12	$1.25	$5.72	$5.50	$6.00	$12.00	$17.50	$20.00
%SG&A	-	-	-	-	-	-	-	-	-	-	-	-
Other	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Operating Income	**($5.5)**	**($7.1)**	**($2.0)**	**($2.6)**	**($3.8)**	**($2.8)**	**($11.2)**	**($11.0)**	**($12.5)**	**($16.3)**	**$14.5**	**$52.0**
Operating Margin	-	-	-	-	-	-	-	-	-	-	29.00%	52.00%
Other Net	$3.2	($0.1)	($0.0)	($0.0)	$0.0	$0.0	($0.0)	$0.0	($0.1)	($0.1)	($0.1)	($0.1)
Pre-Tax Income	**($2.4)**	**($7.1)**	**($2.0)**	**($2.6)**	**($3.8)**	**($2.8)**	**($11.2)**	**($11.0)**	**($12.6)**	**($16.3)**	**$14.4**	**$51.9**
Income taxes(benefit)	$0.0	$0.0	$0.1	$0.0	$0.0	$0.0	$0.1	$0.0	$0.0	$0.0	$0.0	$0.5
Tax Rate	-	-	-	-	-	-	-	-	-	-	-	-
Reported Net Income	**($2.4)**	**($7.1)**	**($2.1)**	**($2.6)**	**($3.8)**	**($2.8)**	**($11.3)**	**($11.0)**	**($12.6)**	**($16.3)**	**$14.4**	**$51.4**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	256.2%
Net Margin	-	-	-	-	-	-	-	-	-			
Diluted Shares Out	67.4	106.6	144.2	176.8	207.3	231.0	189.8	265.0	300.0	400.0	450.0	500.0
Reported EPS	**($0.04)**	**($0.07)**	**($0.01)**	**($0.01)**	**($0.02)**	**($0.01)**	**($0.06)**	**($0.04)**	**($0.04)**	**($0.04)**	**$0.03**	**$0.10**
One time charge	*($3.16)*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*	*$0.00*
Non GAAP Net Income	**($5.5)**	**($7.1)**	**($2.1)**	**($2.6)**	**($3.8)**	**($2.8)**	**($11.3)**	**($11.0)**	**($12.6)**	**($16.3)**	**$14.4**	**$51.4**
Non GAAP EPS	**($0.08)**	**($0.07)**	**($0.01)**	**($0.01)**	**($0.02)**	**($0.01)**	**($0.06)**	**($0.04)**	**($0.04)**	**($0.04)**	**$0.03**	**$0.10**

Source: company filing and Zacks estimates

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HISTORICAL ZACKS RECOMMENDATIONS



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