

# Trickle Research

Every raging river, every great lake, every  
deep blue sea starts ... with a trickle



## Initiating Research Coverage



### OncoSec Medical Incorporated

(NasdaqGS: ONCS)

**Report Date: 05/15/20**

**12- 24 month Price Target: \$6.00**

**Allocation: 4**

**Closing Stock Price at Initiation (Closing Px: 05/14/20): \$1.92**

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**Trickle Research**

**Disclosure:** Portions of this report are excerpted from OncoSec's filings, website(s), presentations or other public collateral. We have attempted to identify those excerpts by *italicizing* them in the text.

## Company Overview

*OncoSec Medical Incorporated (the "Company," "OncoSec," "we" or "our") is a late-stage biotechnology company focused on developing cytokine-based intratumoral immunotherapies to stimulate the body's immune system to target and attack cancer. OncoSec's lead immunotherapy investigational product candidate – TAVO™ (tavokinogene telseplasmid) – enables the intratumoral delivery of DNA-based interleukin-12 ("IL-12"), a naturally occurring protein with immune-stimulating functions. The technology, which employs electroporation, is designed to produce a controlled, localized expression of IL-12 in the tumor microenvironment, enabling the immune system to target and attack tumors throughout the body. OncoSec has built a deep and diverse clinical pipeline utilizing TAVO™ as a potential treatment for multiple cancer indications either as a monotherapy or in combination with leading checkpoint inhibitors; with the latter potentially enabling OncoSec to address a great unmet medical need in oncology: anti-PD-1 non-responders. Results from recently completed clinical studies of TAVO™ have demonstrated a local immune response, and subsequently, a systemic effect as either a monotherapy or combination treatment approach along with an acceptable safety profile, warranting further development. In addition to TAVO™, OncoSec is identifying and developing new DNA-encoded therapeutic candidates and tumor indications for use with its new Visceral Lesion Applicator (VLA), to target deep visceral lesions, such as liver, lung or pancreatic lesions.*

The Company effectively went "public" on March 1, 2011 via a merger with a prior public entity in an unrelated business. In conjunction with that transaction, the newco appointed Dr. Avtar Dhillon chairman of the board, and brought in a new slate of C-Suite individuals as well. Prior to his appointment to OncoSec's board, Dr. Dhillon served as the President, CEO and Executive Chairman of another public company called Inovio Pharmaceuticals, Inc. (Nasdaq: INO) ("Inovio").

Also concurrent with the merger and the appointment of new management, OncoSec purchased certain assets from Inovio, which consisted of "non-DNA vaccine technology and intellectual property relating to selective tumor ablation technologies. The technology 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 tumors. The acquired assets included, among other things: certain equipment, machinery, inventory and other tangible assets of Inovio related to the OMS technology; certain engineering and quality documentation related to the OMS technology; the assignment of certain contracts; and certain of Inovio's patents, including patent applications, and trademarks, and all goodwill associated therewith related to the acquired technology". At the time of the acquisition of these assets, Inovio had completed a series of trials regarding the use of the therapy in both electroimmunotherapy and electrochemotherapy modalities. The assets and related clinical trials associated with this transaction are the basis of the Company's technology and associated intellectual property today.

We have provided a more extensive overview of the Company's technology further in this report, but in general, the Company has developed a proprietary "intratumoral electroporation" drug delivery technology. The device is called ImmunoPulse®. To edify, electroporation involves the introduction of high intensity, pulsed electric fields to cells, which can temporarily cause the cell membranes to become more permeable. One of the challenges in treating tumors with DNA encoded drugs and/or other monoclonal antibody treatments is getting enough of the drug(s) into the tumor to be effective. Electroporation creates temporary pores that allow molecules to move through the cell membrane, which allows for greater delivery of drugs into the cell.

The Company has also combined their ImmunoPulse device with DNA-based interleukin-12 ("IL-12"). IL-12 has been identified as a potential tool in boosting the immune system to fight certain cancers. However, it also has a considerable toxicity profile when delivered systemically. The Company believes that their unique approach of delivering IL-12 directly into specific tumors via their ImmunoPulse technology may provide the benefits of IL-12 without many of the toxicity challenges. They refer to the combination of the device and the drug as "TAVO™" (tavokinogene telseplasmid).

As a result of promising results along the way, the Company has spent the past few years expanding its clinical efforts around TAVO. Those efforts have included trials addressing multiple indications, iterations including TAVO as a monotherapy and other combination trials with well-established check point inhibitors such as pembrolizumab (Keytruda®). Obviously, our conclusions here are that they will continue to experience clinical success(es) that could ultimately lead to the commercialization of TAVO in one or more indications.

The Company recently completed a significant financing that substantially improved their working capital and burn rate challenges for the next 12 months or so. However, the financing was not without its challenges. Specifically, it involved a large equity investment from a single shareholder and its affiliates that by virtue of the investment is now *the majority* shareholder. The transaction was challenged by large legacy shareholders and as such was the subject of both proxy and legal battles. We will address some of those issues later in this report as well, but regardless, those battles are now largely in the rear-view mirror.

As a result of the completed financing and in light of what we see as a handful of datapoints that in our view demonstrate progress on the clinical front, we think it is reasonable to suggest that the Company has likely never been in a better spot. By extension, our “never been in a better spot” idea includes what we think is also the most favorable risk/reward posture the stock has probably ever seen. We submit, part of that conclusion is driven by the stark selloff in the stock over the past two years, *and it has been stark*. That is, conceptually, half of our favorable risk/reward notion is related to the poor performance and associated revaluation of the shares. That is not exactly something to celebrate, especially for legacy shareholders who own the shares much higher. To that end, no one can change where the company/stock has been, but we *can* focus on where it is now and where we think it has the potential to go *from here*. To reiterate, from that perspective (where it could potentially go from here) we like the risk/reward profile and we would argue it has probably never been more favorable.

To clarify, we first heard the OncoSec story two years ago, when they presented at our spring 2018 Rocky Mountain Microcap Conference. We liked the story then and have followed their progress/challenges since that time with an eye towards eventual coverage initiation. This coverage is the result of that endeavor.

### **Product/Technology Overview**

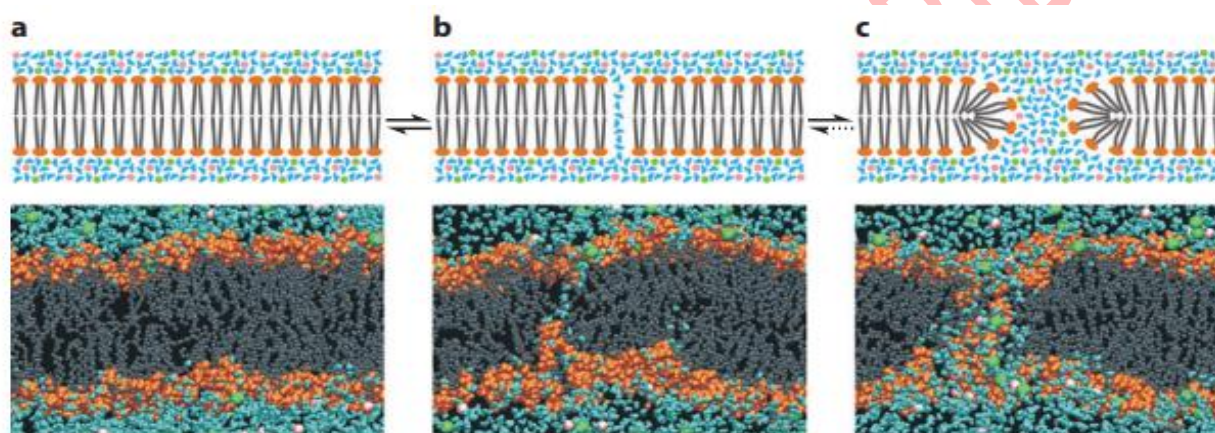
OncoSec’s core platform technology, ImmunoPulse®, “*is a drug-device therapeutic modality comprised of a proprietary intratumoral electroporation (“EP”) delivery device. The ImmunoPulse® platform is designed to deliver plasmid DNA-encoded drugs directly into a solid tumor and promote an immunological response against cancer. The ImmunoPulse® device can be adapted to treat different tumor types, and consists of an electrical pulse generator, a reusable handle and disposable applicators. Their lead product candidate is a DNA-encoded interleukin-12 (“IL-12”) called tavokinogene telseplasmid (“TAVO”). The ImmunoPulse® EP platform is used to deliver TAVO intratumorally, with the aim of reversing the immunosuppressive microenvironment in the treated tumor. The activation of the appropriate inflammatory response can drive a systemic anti-tumor response against untreated tumors in other parts of the body. In 2017, OncoSec received Fast Track designation and Orphan Drug Designation from the U.S. Food and Drug Administration (“FDA”) for TAVO in metastatic melanoma, which could qualify TAVO for expedited FDA review, a rolling Biologics License Application review and certain other benefits*”. The Company has also been granted Advanced Therapy Medicinal Product (“ATMP”) status, which is a European equivalent to the FDA’s Fast Track designation.

We tend to view OncoSec as a “platform” story built upon its electroporation technology. TAVO represents the first product/therapy established on the platform. The following is a short overview of both the platform and the TAVO “parts”, as well as some color on other emerging and perhaps future developments.

## - Electroporation

From: Electroporation-Based Technologies for Medicine: Principles, Applications, and Challenges. (<http://lbk.fe.uni-lj.si/pdfs/arbe2014.pdf>).

*“Electroporation is the increase of cell membrane permeability due to externally applied pulsed electric fields. Although observation of the effects of pulsed electric fields on biological material dates back more than 250 years, only in the past two decades have practical applications of electroporation emerged in food processing, pharmaceuticals, and medicine”.* From the same publication, the visual below reflects the molecular view of a cell membrane reacting to (opening-up) following the introduction of pulsed electric fields via electroporation. As one might imagine, there are various theories/views regarding how electroporation makes the membrane more permeable, which we will not elaborate on here, but recognize, it is generally accepted that electroporation can impact the permeability of cell membranes thus, in the case of cancer cells, making them more amenable to introducing therapies into those cells.

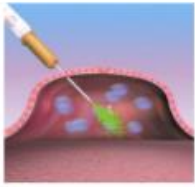


**Figure 1**

An idealized molecular-level scheme (*top*) and an atomic-level molecular dynamics simulation (*bottom*) of electroporation with the electric field perpendicular to the bilayer plane. In the simulation, a 1-palmitoyl 2-oleoyl phosphatidylcholine (POPC) bilayer surrounded by a saline solution is exposed to a field of 4 MV/cm, with the snapshots taken 0, 0.15, and 0.50 ns after the field is turned on. (a) The intact bilayer. (b) Water molecules start penetrating the bilayer, forming a water wire. (c) The lipids adjacent to the water wire start reorienting toward the wire with their polar head groups, stabilizing the pore and allowing more water, as well as other polar molecules and ions, to enter. The atoms of the lipid head groups and tails are shown in orange and gray, respectively; water molecules in cyan; sodium ions in green; and chloride ions in pink. (Top row reprinted with permission from 181; bottom row reprinted with permission from 23.)

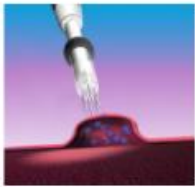
As an extension to the above, OncoSec’s electroporation technology is called ImmunoPulse®. ImmunoPulse® consists of a small box called the Genpulse Generator™. The Genpulse Generator™ is attached to a handheld device about the size of a fountain pen. The device has a series of small retractable/adjustable needles that are applied to dermal/subdermal tumors. The operator then delivers a short electric pulse from the Genpulse Generator™ into the tumor. Prior to delivering the pulse, a measured dose of IL-12 is injected into the tumor. The subsequently delivered pulse helps create pores in the cancer cell membrane that create pathways for IL-12 to enter the cell. The following visuals from OncoSec provide good examples of the product/process:





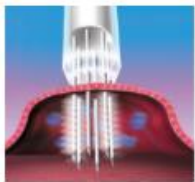
### Step 1: TAVO™ Injection

Multiple copies of IL-12 coded DNA plasmids to produce immune modulatory proteins are injected directly into the tumor using a conventional needle and syringe.



### Step 2: Applicator Insertion

The applicator's tip needle array is inserted into the tumor, up to a depth of 15mm.



### Step 3: Electroporation

Electrical pulses, activated by a foot switch administered between hexagonal needle electrodes increases the permeability of cell membranes, facilitating uptake ("transfection") of IL-12 coded DNA into cells.



## - TAVO & IL-12

As we said, TAVO represents the Company's flagship candidate and it combines the unique ImmunoPulse® delivery system with interleukin-12. As we will delineate, IL-12 is cytokine that is produced by the body, **which plays multiple roles** (referred to as "pleiotropic effects") in the operation of the immune system. Over the years the research and subsequent understanding of IL-12 has led to the recognition of its ability to help the immune system mitigate disease. Unfortunately, historically IL-12's clinical efficacy has largely been offset by its toxicity profile especially when it is applied systemically. In short, one of the reason's OncoSec chose to create TAVO around IL-12 is because of ImmunoPulse's ability to delivery therapies directly into tumors as opposed to the more traditional systemic routes. To clarify, the expectation therein is that delivering IL-12 directly to the tumor allows for the benefits of IL-12 while avoiding some if its "systemic" toxicity problems. Further, as we will address further in this report, the Company believes that not only is TAVO capable of reducing/eliminating some solid tumors, but will also in the process create a systemic response (often referred to as it "abscopal effect") of IL-12, thus perhaps mitigating additional tumors/metastases throughout the patient. Obviously, that would make TAVO highly desirable.

The following is some selected narrative that we have excerpted from various studies that we think help frame the potential cancer fighting profile of IL-12 (as well as prevailing toxicity issues) and in conjunction we think support its combination with ImmunoPulse® (TAVO).

### Interleukin 12 (IL-12) Family Cytokines: Role in Immune Pathogenesis and Treatment of CNS Autoimmune Disease

Cytokine. 2015 Oct; 75(2): 249–255. Published online 2015 Mar 18. doi: 10.1016/j.cyto.2015.01.030

Lin Sun, Chang He, Lekha Nair, Justine Yeung, and Charles E. Egwuagu (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4553122/>).

*"Cytokines play crucial roles in coordinating the activities of innate and adaptive immune systems. In response to pathogen recognition, innate immune cells secrete cytokines that inform the adaptive immune*

system about the nature of the pathogen and instruct naïve T cells to differentiate into the appropriate T cell subtypes required to clear the infection. These include Interleukins, Interferons and other immune-regulatory cytokines that exhibit remarkable functional redundancy and pleiotropic effects. The focus of this review, however, is on the enigmatic Interleukin 12 (IL-12) family of cytokines. This family of cytokines plays crucial roles in shaping immune responses during antigen presentation and influence cell-fate decisions of differentiating naïve T cells. They also play essential roles in regulating functions of a variety of effector cells... They provide the bridge between innate and adaptive immune systems by priming naïve CD4<sup>+</sup> T cells to differentiate into cytokine-producing T-helper subsets and memory T cells. In addition to their influence on cell-fate decisions of differentiating lymphocytes, IL-12 cytokines regulate cellular pathways required for proper functioning of the immune system, with some members activating pro-inflammatory responses that confer protection against infection while others restrain unbridled immune responses that cause autoimmune diseases...”

### **Re-designing Interleukin-12 to Enhance its Safety and Potential as an Anti-tumor Immunotherapeutic**

#### **Agent**

Nature Communications volume 8, Article number: 1395 (2017)

Pengju Wang, Xiaozhu Li, Jiwei Wang, Dongling Gao, Yuenan Li, Haoze Li, Yongchao Chu, Zhongxian Zhang, Hongtao Liu, Guozhong Jiang, Zhenguo Cheng, Shengdian Wang, Jianzeng Dong, Baisui Feng, Louisa S. Chard, Nicholas R. Lemoine & Yaohe Wang

*Tumor-induced immune suppression is recognized as an important mechanism by which tumors evade immune-mediated detection and destruction. A number of strategies to overcome this suppression have been evaluated, but **local IL-12 expression** consistently appears to be one of the most effective methods to achieve this due to its central role in T- and NK-cell-mediated inflammatory responses. Unfortunately, clinical application of IL-12-based therapies remains problematic due to the potential for rapid development of lethal inflammatory syndrome...*

### **New Insights Into IL-12-Mediated Tumor Suppression**

Cell Death & Differentiation volume 22, pages237–246(2015) Published: 05 September 2014

S Tugues, S H Burkhard, I Ohs, M Vrohling, K Nussbaum, J vom Berg, P Kulig & B Becher

*During the past two decades, interleukin-12 (IL-12) has emerged as **one of the most potent cytokines in mediating antitumor activity in a variety of preclinical models**. Through pleiotropic effects on different immune cells that form the tumor microenvironment, IL-12 establishes a link between innate and adaptive immunity that involves different immune effector cells and cytokines depending on the type of tumor or the affected tissue. The robust antitumor response exerted by IL-12, however, has not yet been successfully translated into the clinics. The majority of clinical trials involving treatment with IL-12 failed to show sustained antitumor responses and were associated to toxic side effects.*

#### **Facts & Questions**

- *Interleukin-12 (IL-12) regulates inflammation by linking innate and adaptive immune responses. Most of the IL-12-induced effects are mediated by the secretion of interferon - $\gamma$ .*
- *IL-12 is a potent inducer of antitumor immunity in preclinical models.*
- ***The delivery of IL-12 for therapeutic purposes focuses on novel methods to deliver this cytokine directly to the tumor site.***
- *The robust antitumor response exerted by IL-12 in preclinical models has not yet been successfully translated into the clinics.*
- ***How can we achieve durable, local, non-toxic antitumor responses with IL-12 in cancer patients? What is the best strategy to deliver this cytokine into the tumor microenvironment in a controlled manner?***

*The potential of cytokines for cancer immunotherapy has been extensively investigated. In the case of IL-12, its potent antitumor properties were already observed more than 20 years ago upon systemic administration of the cytokine in various transplantable cancer models. Since then, several studies aimed to evaluate the use of IL-12 for therapeutical purposes by specifically delivering this cytokine within the tumor site. Even though several of these approaches resulted in impressive antitumor responses, the translation into the clinics was sobering. The reasons for that are still being discussed in the oncology field. On the one hand, the schedule optimization for therapeutic IL-12 delivery in clinical trials has proved to be challenging. Even though the most successful way to administer IL-12 appeared to be in cycles of twice weekly injections, repeated administration of the cytokine could contribute to increase the immunosuppressive properties of the tumor by the induction of IL-10. On the other hand, the use of IL-12 as an adjuvant in combinatorial treatments requires a detailed knowledge of the molecular pathology of each individual tumor in order to achieve clinical benefits. In this respect, the combination of IL-12 with therapies that block the type of immunosuppressive activity characteristic of the different tumor models could be of potential use. Finally, **lasting, non-toxic anti-cancer responses with IL-12 will likely only be achieved with a controlled and tumor-targeted delivery of the cytokine.** Several of these approaches are already advancing in clinical trials. Clearly, as we only now start to understand the multiple mechanisms by which IL-12 mediates tumor protection in more detail, it is time to revisit the use of IL-12 in clinical studies. Blind systemic administration of IL-12 will not be pursued in the future, but **tumor-targeted IL-12 delivery combined with radiation-, chemo- and immunotherapy, respectively, holds great promise for the future of cancer immunotherapy.***

#### **Characterization of Abscopal Effects of Intratumoral Electroporation-Mediated IL-12 Gene Therapy**

Gene Ther. 2019; 26(1): 1–15. Published online 2018 Oct 15. doi: 10.1038/s41434-018-0044-5

Anandaroop Mukhopadhyay, Jocelyn Wright, Shawna Shirley, David A. Canton, Christoph Burkart, Richard J. Connolly, Jean S. Campbell, and Robert H. Pierce (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6514882/>) **OncoSec collaborated on this study.**

*Interleukin 12 (IL-12) is a pleotropic inflammatory cytokine, which links innate and adaptive immunity and drives Th1/Tc1 cell-mediated immune responses. IL-12, therefore, would be a good candidate for increasing tumor immunogenicity. However, systemic administration of recombinant IL-12 protein or IL-12-expressing adoptive cell therapies have led to severe immune-related toxicities in patients. As an alternative, intratumoral (IT) gene therapy with plasmids expressing IL-12 has been tested both in experimental mouse models and in the clinic. As a monotherapy in advanced melanoma, IT electroporation-mediated transfection of a plasmid encoding human IL-12 yielded a 33% best overall response rate, with 50% of patients showing regression of untreated lesions, without any reported systemic drug-related toxicity.*

*Intratumoral electroporation-mediated IL-12 gene therapy (IT-pIL12/EP) has been shown to be safe and effective in clinical trials, **demonstrating systemic antitumor effects with local delivery of this potent cytokine.** We recently optimized our IL-12 gene delivery platform to increase transgene expression and efficacy in preclinical models. Here we analyze the immunological changes induced with the new IT-pIL12/EP platform in both electroporated and distant, non-electroporated lesions. IT-pIL12/EP-treated tumors demonstrated rapid induction of IL-12-regulated pathways, as well as other cytokines and chemokines pathways, and upregulation of antigen presentation machinery. **The distant tumors showed an increase in infiltrating lymphocytes and gene expression changes indicative of a de novo immune response in these untreated lesions.** Flow cytometric analyses revealed a KLRG1hi CD8+ effector T-cell population uniquely present in mice treated with IT-pIL12/EP. Despite being highly activated, this population expressed diminished levels of PD-1 when re-exposed to antigen in the PD-L1-rich tumor. Other T-cell exhaustion markers appeared to be downregulated in concert, suggesting an orchestrated “armoring” of these effector T cells against T-cell checkpoints when primed in the presence of IL-12 in situ. These cells may represent an important mechanism by which local IL-12 gene therapy can induce a systemic antitumor immune response without the associated toxicity of systemic IL-12 exposure.*

The above references are just a few of many articles/studies demonstrating the understanding and the efficacy of IL-12 in assisting the immune system to recognize and fight cancer. On the other hand, IL-12's dubious safety profile, especially via systemically delivered protocols is perhaps equally documented. As some of the references above suggest, there are a number of researchers who have concluded that overcoming IL-12's toxicity issues might likely be a function of finding unique ways to delivery it directly into tumors. That effectively describes TAVO. Further, what is perhaps even more promising than TAVO's ability to shrink tumors, is its potential to also deliver a *systemic* immune response that can address other malignancies throughout the body. That abscopal effect, could represent a significant breakthrough for some patients facing multiple systemic malignancies. Succinctly, ImmunoPulse® may prove to be the key that unlocks (delivers) the power of IL-12.

## - “Hot” and “Cold” Tumors

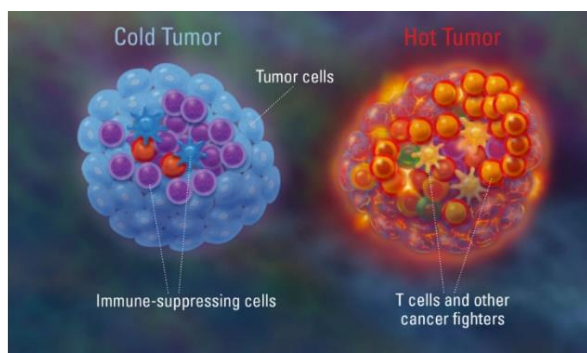
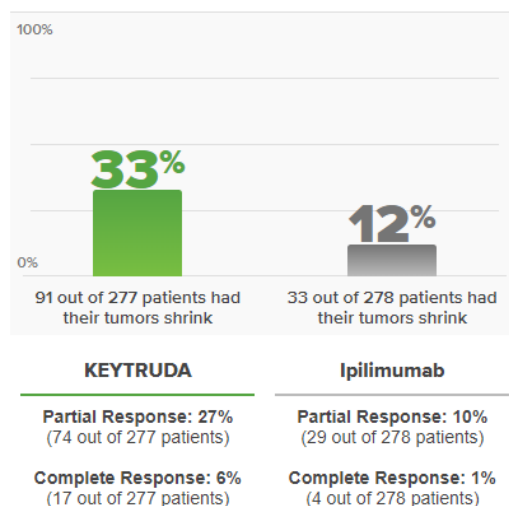


Image from the Dana-Farber Cancer Institute. Image Source.

There is some added vernacular that OncoSec references in its presentations and filings regarding TAVO's potential therapeutic effects that we think also requires some color. The Company believes that TAVO plays a role in “waking up” some tumors or more succinctly, turning them from “cold” tumors to “hot” tumors.

As we allude to throughout this report, cancer research has like many things, experienced measurable progress over the past several years/decades. Today, immunotherapy represents the “cutting edge” of that evolution and as part of that arsenal, “check-point inhibitors” like Merck and Co. Inc.’s (NYSE:MRK) Pembrolizumab (“Keytruda™”) are on the frontline of the cancer battle. For instance, according to recent narrative from Merck, Keytruda™ is “active” in over 2 dozen cancers and additional indications are likely. By another metric, some estimate that Keytruda™ will become a \$20+ billion drug over next few years. With that said, while perhaps it goes without saying, Keytruda™ does not help everyone and the voracity of that statement is impacted by several variables (cancer type, stage and other related variables). For instance, data from prior Keytruda™ melanoma trials reflect the following:



(<https://www.keytruda.com/melanoma/monotherapy-clinical-trial-results/>)

To translate, while Keytruda™ (as well as other “check point inhibitors”) may be the best available hope for many cancer patients, their respective “success rates”, of which there are multiple metrics, still leave a large portion of patients without a favorable outcome. Researchers believe that at least some portion of the unfavorable outcomes



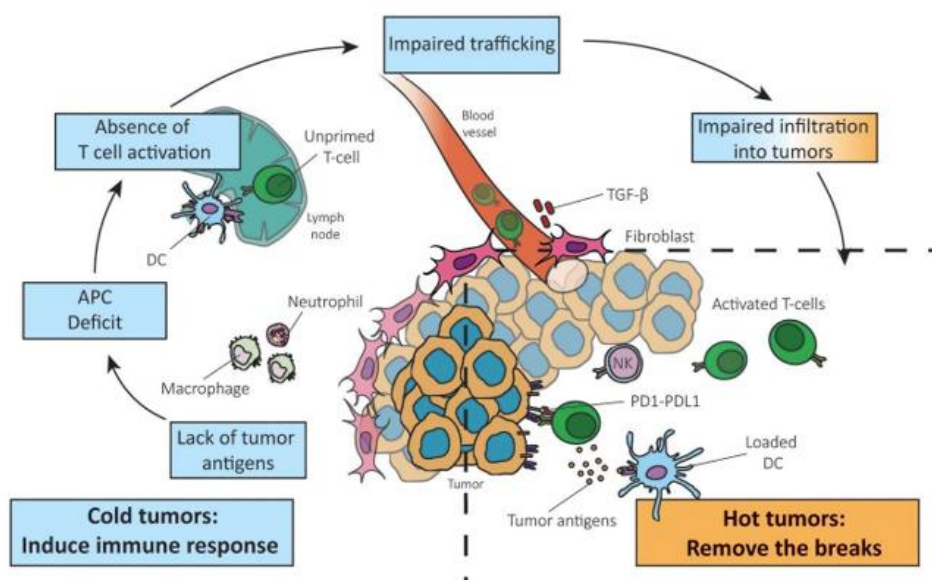
from these new therapies are related to the fact that some of the tumors they end up treating are “cold”. The following publication from the NIH, provides some background:

### **Cold Tumors: A Therapeutic Challenge for Immunotherapy**

Frontiers in Immunology Published online 2019 Feb 8.

Paola Bonaventura,<sup>1,2</sup> Tala Shekarian,<sup>1,2</sup> Vincent Alcazer,<sup>1,2</sup> Jenny Valladeau-Guilemond,<sup>2</sup> Sandrine Valsesia-Wittmann,<sup>1,2</sup> Sebastian Amigorena,<sup>3</sup> Christophe Caux,<sup>1,2</sup> and Stéphane Depil<sup>1,2,4,\*</sup>

*Immune checkpoint inhibitors (ICIs) have changed the treatment landscape of many tumors, inducing durable responses in some cases, Tumor mutational load, CD8+ T cell density and Programmed cell Death Ligand-1 (PD-L1) expression have each been proposed as distinct biomarkers of response to PD-1/-L1 antagonists. The lymphocyte infiltration and IFN- $\gamma$  status may be key factors for effective anti-PD-1/-L1 therapy by defining a “T cell inflamed” phenotype (“hot tumors”). In contrast, lack of T cells infiltrating the tumor characterizes “non-inflamed” or “cold tumors” (in which other immune populations or myeloid cells can however be observed). Immunological treatment of cold tumors is a great challenge as no adaptive immune response has been set up or maintained.*



Reversing a cold into a hot tumor. Adapted from Chen and Mellman (1). The absence of T cells in the tumor can be due to the lack of tumor antigens, APC deficit, absence of T cell priming/activation and impaired trafficking of T cells to the tumor mass (left panel). Understanding which step of the anti-cancer immune response is not functional in cancers is crucial to adapt therapies to the cancer phenotype.

Frontiers in Immunology 08 February 2019: Cold Tumors: A Therapeutic Challenge for Immunotherapy Paola Bonaventura,<sup>1,2</sup> Tala Shekarian,<sup>1,2</sup> Vincent Alcazer,<sup>1,2</sup> Jenny Valladeau-Guilemond,<sup>2</sup> Sandrine Valsesia-Wittmann,<sup>1,2</sup> Sebastian Amigorena,<sup>3</sup> Christophe Caux,<sup>1,2</sup> and Stéphane Depil<sup>1,2,4,\*</sup>

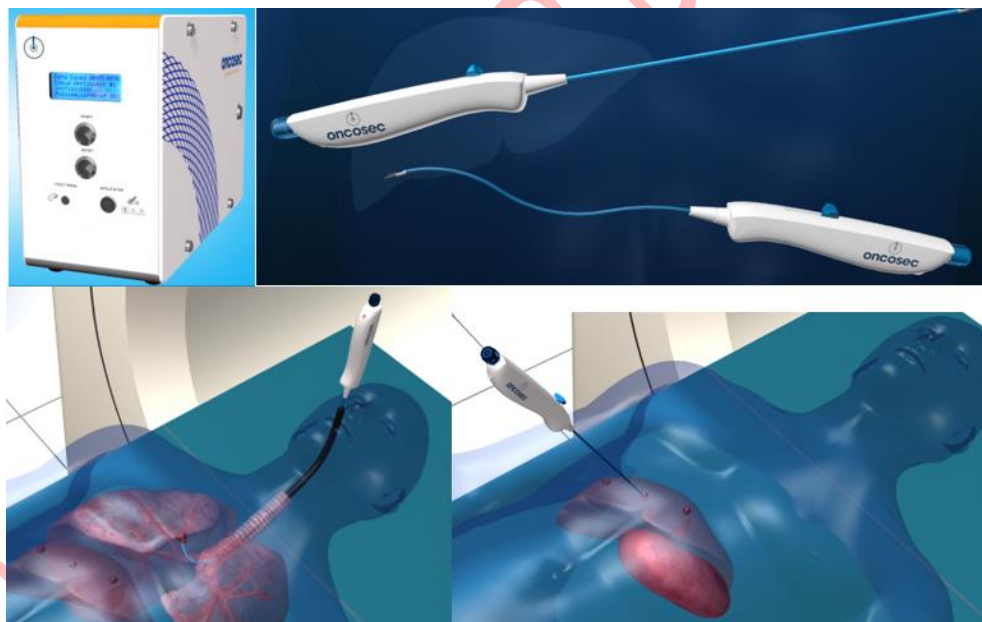
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6376112/>

To unpack this a bit, check point inhibitors like Keytruda™ work by “unblocking” overexpressed proteins that block/prohibit cancer-targeting T cells from entering cancer cells. Simply put, despite check point inhibitors’ ability to “unblock” overexpressed proteins, if tumors are cold, (per the illustration above) they may lack other characteristics necessary for ICI’s to be effective. That is, ICI’s may not be as effective on cold tumors, which may explain in part why drugs like Keytruda™ don’t help everyone and, since some types of cancers seem to involve colder/hotter tumors than others, they work better/worse on different types of cancers. That is also why the most effective cancer therapies, one to the next, will likely continue to involve combinations of available approaches. To that end, OncoSec believes that TAVO may assist in the turning of cold tumors to hot tumors, and

as such may prove effective in combination with ICI's like Keytruda™. Clearly the Company's lead combination trial with Keytruda™ ("Keynote-695") is focused on that notion.

#### - Visceral Lesions Applicator

In addition to the above, the Company recently announced some pre-clinical data from a feasibility study of its Visceral Lesion Applicator (VLA) electroporation device and APOLLO generator. The announcement referenced the following. *"The feasibility study demonstrated the capability of a rigid, trocar-like VLA applicator to safely deliver and electroporate DNA-based immunotherapy directly into target organs in a large animal model using a CT-guided approach and OncoSec's new, lower voltage APOLLO generator. The study demonstrated VLA's ability to reach deep visceral organs using laparoscopic/ultrasound and bronchoscope/steerable catheter methods in live large animal models. In the study presented online at the Annual Meeting of the SIR, OncoSec demonstrated the ability to guide and deploy the VLA under a different guidance method and electroporate with the APOLLO generator. Using CT-guidance, investigators were able to reach high value targets including liver, lung, bone, and pancreas in a live large animal model. Additionally, TAVO was safely delivered and electroporated directly into the liver. Importantly, data also showed that it had no significant effects on hemodynamics, as indicated by consistent heart rate and arterial blood pressure. Animals were survived for at least 24 hours and no adverse events were observed".* The announcement went on to note that OncoSec intends to complete preclinical trials by the end of 2020 and to commence human trials in 2021. Below are some visuals from the Company that help illustrate the applications.

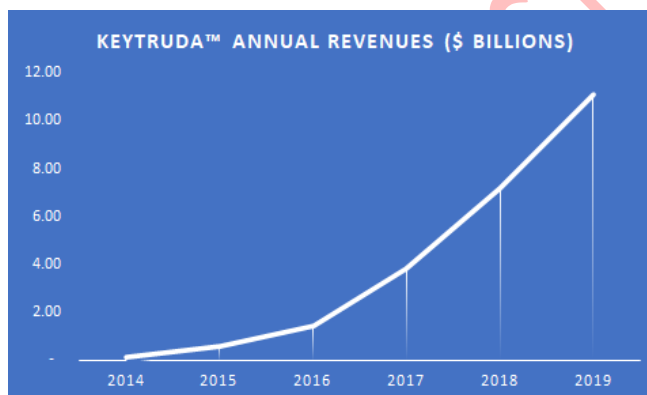


We think the Company's VLA technology is promising and that notion could prove particularly prescient if they continue to experience clinical success with TAVO. To edify, currently, ImmunoPulse®/TAVO is only able to treat cutaneous and/or subcutaneous tumors. Unfortunately, that means that even if TAVO continues to experience clinical success it is not applicable to many patients with tumors inside their bodies. Assuming VLA proves successful in subsequent human clinical trials, we think it represents a considerable addition to TAVO functionality and applicability. While it may be too early to support this assessment, we think VLA could be used as a delivery system for a number of tumor therapies. We thought this announcement deserved more attention than it ultimately received so perhaps we are overstating this, but if OncoSec's electroporation platform proves

clinically successful enough to gain an FDA approval, we think VLA could provide the pathway to address a much broader list of indications.

## Industry Overview

Generally, our industry overview involves analysis regarding market size, market growth, supply and demand nuances and other variables and associated statistical analysis aimed at framing both the magnitude and the opportunities for the relevant market(s) as well as those of the subject company within them. We are going to forgo that approach here because we think that many people are aware of the scope and the breadth of the cancer treatment market in part because unfortunately, they likely know someone (or multiple people) who has been adversely impacted by it. Succinctly, unfortunately the cancer therapy market is growing as are the costs associated with it, and that does not look like a scenario that will change anytime soon. Again, we do not think that requires much reinforcement. However, for perspective, Merck's Keytruda™ generated *\$3.3 billion in revenues* in Q1-F20 alone. Keytruda's growth since its initial approval in September 2014 has been staggering:



According to The National Center for Biotechnology Information (“NCBI”) *“cancer is a group of more than 100 diseases that develop across time and involve the uncontrolled division of the body's cells. Although cancer can develop in virtually any of the body's tissues, and each type of cancer has its unique features, the basic processes that produce cancer are quite similar in all forms of the disease. Cancer begins when a cell breaks free from the normal restraints on cell division and begins to follow its own agenda for proliferation. All of the cells produced by division of this first, ancestral cell and its progeny also display inappropriate proliferation. A tumor, or mass of cells, formed of these abnormal cells may remain within the tissue in which it originated (a condition called in situ cancer), or it may begin to invade nearby tissues (a condition called invasive cancer). An invasive tumor is said to be malignant, and cells shed into the blood or lymph from a malignant tumor are likely to establish new tumors (metastases) throughout the body. Tumors threaten an individual's life when their growth disrupts the tissues and organs needed for survival”*. ( <https://www.ncbi.nlm.nih.gov/books/NBK20362/> ).

Further the NCBI notes *“People likely have wondered about the cause of cancer for centuries. Its name derives from an observation by Hippocrates more than 2,300 years ago that the long, distended veins that radiate out from some breast tumors look like the limbs of a crab. From that observation came the term karkinoma in Greek, and later, cancer in Latin. With the work of Hooke in the 1600s, and then Virchow in the 1800s, came the understanding that living tissues are composed of cells, and that all cells arise as direct descendants of other cells. Yet, this understanding raised more questions about cancer than it answered. Now scientists began to ask from what kinds of normal cells cancer cells arise, how cancer cells differ from their normal counterparts, and what events promote the proliferation of these abnormal cells. And physicians began to ask how cancer could be prevented or cured”*.

The term “cancer” is largely generic (as noted above it includes dozens of diseases). As a result, while most “cancers” certainly share some general characteristics, they also carry unique properties that make them different, which ultimately means that the effective treatment of specific cancers requires equally specific therapies designed to address the particular indications of those individuals cancers. In that regard, we think it is fair to say that for researchers to develop specific treatments for specific cancers, they first must understand the different origins, mechanisms and characteristics of each. We also think, it is fair to say that cancer research over the past few decades has provided considerable clarity with respect to the unique characteristics of different types of cancer although that process of understanding and identifying those characteristics continues today. Historically, cancer treatments have evolved around the improved understanding of the diseases it represents.

As a result of the above quest for answers to cancer, cancer research over the years has been characterized by progress as well as setbacks and therapies have included many triumphs but also several ultimately ineffective treatments as well as others with considerable undesirable side effects. To be sure, some cancer treatments, while effective in some instances, have been described as “worse than the cure”.

Again, like medicine/science in general, cancer therapy’s expanding knowledge base has led to more effective and targeted treatments. That knowledge base has evolved over decades of various treatment protocols and modifications therein. However, as the National Institutes of Health (“NIH”) notes, some of the most common cancer protocols we continue to use today have been used in one form or another for decades and in some instances for over a century. Here are a few examples:

- **Surgery.** Surgery has been a common approach to cancer treatment. Intuitively, if a patient has a tumor, the most effective way to mitigate it is to remove it if possible. *The first radical mastectomy was performed in 1890, while the first radical hysterectomy was performed in 1906.*
- **Radiation.** In addition to surgery, radiation is another (invasive) cancer therapy that continues to be widely used today but has been around for some time. As the NIH notes, *The discovery of X-rays and radiation by Becquerel and Rontgen in the late 19th century was the first step towards radiation treatment. Marie Curie's work greatly contributed to the development of radiotherapy. The first cancer case cured exclusively by radiation occurred in 1898. Surgery and radiotherapy were the basis for solid tumor treatment into the 1960s. This led to a plateau in curability rates due to uncontrolled micrometastases. There were some promising publications about the use of adjuvant chemotherapy after radiotherapy or surgery in curing patients with advanced cancer.*
- **Chemotherapy.** As the prior paragraph above eludes, while surgery and/or radiation were the primary therapies for some time, the increased understanding of cancer lead to the revelation that metastases was a major problem in the advance of many forms of cancer and in some instances *may be related to* invasive therapies. That understanding of the need for a more systemic approach to cancer treatment paved the way for chemotherapy. *The history of chemotherapy began in the early 20th century, but its use in treating cancer began in the 1930s. The term “chemotherapy” was coined by the German scientist Paul Ehrlich, who had a particular interest in alkylating agents and who came up with the term to describe the chemical treatment of disease. During the First and Second World Wars, it was noticed that soldiers exposed to mustard gas experienced decreased levels of leukocytes. This led to the use of nitrogen mustard as the first chemotherapy agent to treat lymphomas, a treatment used by Gilman in 1943. Breast cancer was the first type of disease in which positive results with adjuvant therapy were obtained, and also the first example of multimodality treatment, a strategy currently employed for treatment of numerous types of tumors. In the late 1960s, the use of adjuvant chemotherapy changed the concept of localized treatment.*
- **Immunotherapy.** For the past 5 decades or more, oncologists have largely created their cancer strategies around the above “three pillars” of treatment; surgery, chemotherapy, and radiation (aka “slash, burn, and poison”). While cancer treatment has certainly advanced over the years, metastatic cancer remains



insidious, still accounting for the vast majority of cancer related deaths. However, we think it is fair to say that many in the cancer community would agree that immunotherapies are emerging as the “fourth pillar” in the fight against cancer. Much like the term “cancer”, “immunotherapy” is a broad label that includes many emerging/promising approaches that focus on directing and regulating the body’s own immune system to identify and destroy disease. There are currently a variety of modalities and associated adjuvants that fit under the immunotherapy label. Immunomodulators or “checkpoint inhibitors” like Keytruda® and Optivo®, cancer vaccines like HEPLISAV-B® and Cervarix® and monoclonal antibodies such as Avastin® and Erbitux® are just a few examples of FDA approved immunotherapies. *Immunotherapy is often perceived as a relatively recent advance. However, the first scientific attempts to modulate patients' immune systems to cure cancer can be attributed to two German physicians, Fehleisen and Busch, who independently noticed significant tumor regression after erysipelas infection. The next significant advances came from William Bradley Coley who is known today as the Father of Immunotherapy. It was Coley who first attempted to harness the immune system for treating bone cancer in 1891. His achievements were largely unnoticed for over fifty years, and several seminal discoveries in the field of Immunology, such as the existence of T cells and their crucial role in immunity in 1967, stepped up the research toward cancer immunotherapy known today.*

As noted, OncoSec’s lead candidate is called TAVO™, which combines their proprietary electroporation intratumoral delivery system with DNA-based interleukin-12 (“IL-12”). That being the case, industry perspectives and histories of both electroporation and IL-12 might be helpful.

The Annual Review of Biomedical Engineering (<http://lbk.fe.uni-lj.si/pdfs/arbe2014.pdf>) suggests that the study of electroporation began in the mid-18<sup>th</sup> century, however, it wasn’t until 1982 when researchers used the process to enhance the permeability of cell membranes to “*deliver foreign DNA into cells. In the following decade, the combination of high-voltage pulsed electric fields with the chemotherapeutic drug bleomycin and with DNA yielded novel clinical applications. In recent years, nonthermal irreversible electroporation (“NTIRE”) for the ablation of solid tumors has emerged as a new medical application of electroporation technology*”. The review further notes that electrochemotherapy (“ECT”) has reached an established position among local treatments in oncology, both human and veterinary, as for instance, more than 3,000 patients were treated with this application in the European Union in 2012.

In short, ECT allows for the delivery of chemotherapeutic agents directly into tumors, which allows for lower overall dosing of the agent but greater concentration of the same into the cancer cell. That is an important distinction because many chemotherapeutics include adverse side-effects, especially when delivered systemically. Unfortunately, systemic deliver leads to lesser concentration into the tumor, which leads to the dilemma of being able to dose the agent in an amount large enough to deliver a lethal concentration to the tumor, but low enough to avoid doing irreversible harm to the patient. That brings us to IL-12.

As we noted above, Interleukin-12 (“IL-12”) is one of a family of specific cytokines (proteins) referred to as “interleukins”, a termed coined in 1979. Interleukins are integral parts of the body’s immune system that collectively signal, direct and modulate immune responses. To date, researchers have identified dozens of interleukins (IL-1, IL-2...IL-36) and other interleukin subsets (IL1A, IL1B... IL1RA). IL-12 is one of these specific interleukins/proteins.

While each interleukin performs specific functions in the immune system, IL-12 has been shown to be particularly important to the body’s immune response to disease including cancer. On the other hand, historically the use of IL-12 to treat some of these diseases has not been without challenges. Specifically, researchers in various settings have encountered toxicity issues with IL-12, especially with respect to its delivery as a systemic therapy. On its simplest level, IL-12 has the similar problems that many systemic treatments (chemotherapy for instance) have in that the challenge is to deliver enough to do some good but not enough to do more harm. However, in what we view as perhaps the most intriguing aspect of OncoSec’s approach, IL-12 is delivered directly in the tumor via the

Company's electroporation technology, which allows IL-12 to mitigate the tumor. However, they have found that the process also in turn facilitates a systemic IL-12 response as well. In other words, they may have discovered a way to enhance the body's own ability to deliver a systemic IL-12 while avoiding some of the typical toxicities. In our view, if TAVO can create a systemic and sustained IL-12 response, it could represent a marked breakthrough in cancer therapy.

To summarize a bit of the above, in 1675 Sir Isaac Newton uttered his famous phrase, "if I have seen further it is by standing on the shoulders of Giants". We think that notion is certainly applicable to cancer therapies over the years. As suggested, cancer is a generic term and as such, *it* manifests itself in many forms. Consequently, over the years, effective cancer treatments for one indication to the next have often involved combinations of treatments. That approach by the way remains topical today and we suspect it will continue well into the foreseeable future. Those who follow clinical trials in the space will likely attest to the abundance of "combination trials" currently underway involving new technologies in conjunction with approved/established therapies in hopes of discovering synergistic combinations or "cocktails" of treatment. TAVO represents that sort of approach on the face (a proprietary delivery device combined with an effective and understood agent), but also in terms of current clinical trial efforts that are being conducted in combination with successful standards of care like Keytruda®. Further to that point, Merck's website provides the following graphic regarding Merck's Keytruda®, which is currently one of the top five drugs (by revenue) in the world today largely because of its success in treating several cancers. However, as the chart reflects, *success* in cancer treatment, means that a considerable majority of those treated do not respond positively. That fact underscores the drive to develop additional therapies that can increase success rates often as an adjuvant to current standards like Keytruda®.

The majority of patients with solid tumors who have been treated with anti-PD-1/PD-L1 therapies do not respond to treatment: this is one of the great challenges in oncology today. OncoSec believes TAVO™ may address this unmet medical need by increasing the proportion of patients who will respond to anti-PD-1 and other checkpoint therapies.

Tumor Type	Anti-PD1/PDL1 mAb Non-Response
Melanoma	~ 60 – 80%
Triple Negative Breast (TNBC)	~ 95% <sup>1</sup>
Head and Neck	~ 68-86% <sup>3,4</sup>
Cervical	~ 86% <sup>2</sup>
Subcutaneous T Cell Lymphoma	~ 57%

<sup>1</sup> Patients were preselected by Merck PD-L1 IHC assay

<sup>2</sup> 11% in PD-L1 (Roche) negative: 43% in PD-L1 + population

Lastly, while this may be apparent to some, we think it is worth providing a short overview of the Food and Drug Administration's drug approval process as a means of trying to frame where we believe OncoSec/TAVO sit in the process. The diagram below provides a good overview of the FDA approval process, which as indicated is appropriately laborious, time-intensive and expensive. For those wondering what the Company has been doing for the past 10 years or so, this may provide some color. Further, the following narrative from the Company's filings provides additional informative color.

## The Drug Discovery, Development and Approval Process

It takes 12-15 years on average for an experimental drug to travel from the lab to U.S. patients. Only five in 5,000 compounds that enter preclinical testing make it to human testing. One of these five tested in people is approved.

Discovery/ Preclinical Testing			Phase I	Phase II	Phase III		FDA		Phase IV
Years	6.5	File IND at FDA	1.5	2	3.5	File NDA at FDA	1.5	15 Total	Additional post marketing testing required by FDA
Test Population	Laboratory and animal studies		20 to 100 healthy volunteers	100 to 500 patient volunteers	1000 to 5000 patient volunteers		Review and approval process		
Purpose	Assess safety, biological activity and formulations		Determine safety and dosage	Evaluate effectiveness look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use				
Success Rate	5,000 compounds evaluated		5 enter trials				1 approved		

Source: Pharmaceutical Research and Manufacturers of America, [www.phrma.org](http://www.phrma.org)

<https://www.fda.gov/oc/ohrt/the-drug-development-and-approval-process/>

([https://www.sec.gov/Archives/edgar/data/1444307/000149315219016036/form10-k.htm#c\\_004](https://www.sec.gov/Archives/edgar/data/1444307/000149315219016036/form10-k.htm#c_004)) Before any new drug, device or dosage form, including a new use of a previously approved drug or biologic, can be marketed in the United States, FDA approval is required. The process required by the FDA before a product may be marketed in the United States generally involves, among other things:

- completion of non-clinical testing;
- completion of chemistry, manufacturing, and control testing, commonly known as CMC;
- submission to the FDA of an investigational new drug application (IND) for human clinical testing, which must be accepted and 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 product for each intended use;
- for a stand-alone medical device, submission to the FDA of a premarket approval application (PMA) or 510(k) premarket notification, which the FDA must review and approve; and for a therapeutic, submission to the FDA of a new drug application (NDA), or biologic license application (BLA), which the FDA must review and approve.

The pre-clinical and clinical testing and approval process can take many years and requires substantial company time, effort and financial resources. The receipt and timing of approval, if any, is 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 drugs or biologics to human subjects under the supervision of qualified investigators in accordance with good clinical practice requirements. For purposes of an NDA or BLA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

**Phase I:** The product candidate is initially introduced to 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 safety, tolerability and effectiveness.

***Phase 2:*** The product candidate 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 2 clinical trials may be conducted.

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

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

***Further, the FDA has an accelerated approval pathway for some drugs used for serious and life-threatening illnesses that do not have adequate treatment. A limitation of the accelerated approval pathway is that it allows an NDA to be approved before means are available to fully measure the drug's effectiveness — a step that would usually be required.***

Again, we apologize to those for whom this is redundant or old hat, but we think this is important to the value proposition here. Recognize, FDA approvals are, in the grand scheme, rare in terms of the number of compounds that are initially evaluated. That is a good portion of the reason that as companies continue to progress through the FDA phases with positive results (or at least results that justify continuing to move forward in the process), their stock prices often increase to reflect that progress, or perhaps from another view to reflect the “de-risking” of the process. With that said, one of our attractions to OncoSec is that *they have* demonstrated clinical progress, as demonstrated by (if nothing else) the fact that they are still doing it. Further, in terms of them getting to the filing of an NDA, we think they are much closer to that event than the street may realize, albeit in part because they have already received Fast Track designation from the FDA. To edify, (per the FDA) “*the Fast Track program facilitates the expedited development and review of new drugs or biologics that are intended to: 1) treat serious or life-threatening conditions and 2) demonstrate the potential to address unmet medical needs. Sponsors typically request Fast Track Designation during the IND phase of drug development.*” Our point is, if the clinical trials continue to support efficacy sufficient to justify regulatory approvals, we think commercialization of TAVO may better measured in months than years. We have elaborated on some of this throughout this report as well. Also, just to keep the vernacular straight, we believe that rather than filing an NDA, the Company will likely file a Biologics License Application (“BLA”) due to the “biologic” nature of their therapy.

### **Clinical Overview**

As the Company's table below reflects, OncoSec has three clinical studies underway and three additional studies in earlier stages as well. All six of the current endeavors are combination studies, and the three clinical studies are all in combination with pembrolizumab (Keytruda®), each for a different indication.



# Pipeline is Well Diversified with Multiple Growth Opportunities

	REGIMEN	TRIAL	INDICATION	N	PARTNER	PHASE 1	PHASE 2	PIVOTAL
TAVO™	TAVO + pembrolizumab	KEYNOTE-695	Advanced Melanoma	~100	MERCK	→	→	→
	TAVO + pembrolizumab	KEYNOTE-890	Triple Negative Breast Cancer (TNBC)	~25	MERCK	→	→	→
	TAVO + epacadostat + pembrolizumab	OMS-131 (INVESTIGATOR SPONSORED STUDY)	Squamous cell carcinoma head and neck (SCCHN) cancer	~34	UCSF	→	→	→
	TAVO + HER2-plasmid vaccine	Proof of Concept	HER2+ Breast Cancers		DUKE	→	→	→
	TAVO + CXCL9	Proof of Concept	Solid Tumors		ROSWELL PARK	→	→	→
CAR T Cell Therapy	CAR T Monotherapy + Combo with TAVO		Solid Tumors		DANA-FARBER CANCER INSTITUTE	→	→	→

The most advanced of these three clinical studies is **KEYNOTE-695**, which is a combination study with pembrolizumab for the treatment of advanced melanoma. The study commenced in October 2017 with an estimated study completion date of December 31, 2020. The estimated patient enrollment is 100. On May 6, 2020 the Company announced published KEYNOTE-695 data in the Clinical Cancer Research, a publication from American Association for Cancer Research (“AACR”):

(<https://clincancerres.aacrjournals.org/content/early/2020/04/23/1078-0432.CCR-19-2217>).

Below is the abstract from the AACR’s review of the available KEYNOTE-695 information:

**Purpose:** Tumors with low frequencies of checkpoint positive tumor-infiltrating lymphocytes (cpTIL) have a low likelihood of response to PD-1 blockade. We conducted a prospective multicenter phase II trial of intratumoral plasmid IL-12 (tavokinogene telseplasmid; “tavo”) electroporation combined with pembrolizumab in patients with advanced melanoma with low frequencies of checkpoint positive cytotoxic lymphocytes (cpCTL).

**Patients and Methods:** Tavo was administered intratumorally days 1, 5, and 8 every 6 weeks while pembrolizumab (200 mg, i.v.) was administered every 3 weeks. The primary endpoint was objective response rate (ORR) by RECIST, secondary endpoints included duration of response, overall survival and progression-free survival. Toxicity was evaluated by the CTCAE v4. Extensive correlative analysis was done.

**Results:** The combination of tavo and pembrolizumab was well tolerated with adverse events similar to those previously reported with pembrolizumab alone. Patients had a 41% ORR (n = 22, RECIST 1.1) with 36% complete responses. Correlative analysis showed that the combination enhanced immune infiltration and sustained the IL-12/IFN $\gamma$  feed-forward cycle, driving intratumoral cross-presenting dendritic cell subsets with increased TILs, emerging T cell receptor clones and, ultimately, systemic cellular immune responses.

**Conclusions:** The combination of tavo and pembrolizumab was associated with a higher than expected response rate in this poorly immunogenic population. No new or unexpected toxicities were observed.

*Correlative analysis showed T cell infiltration with enhanced immunity paralleling the clinical activity in low cpCTL tumors.*

We have a few observations regarding the above, KEYNOTE-695 specifically, and OncoSec's current clinical activities in general.

First, here are a few items excerpted from the KEYNOTE-695 clinical trial filing at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), which is the repository for information regarding all active and completed clinical trials filed with the FDA: (<https://clinicaltrials.gov/ct2/show/NCT03132675>).

### ***Study Description:***

*Keynote 695 will be a Phase 2 study of intratumoral tavokinogene telseplasmid (tavo; pIL-12) Electroporation (EP) plus IV Pembrolizumab. Eligible patients will be those with pathological diagnosis of unresectable or metastatic melanoma who are progressing or have progressed on pembrolizumab or nivolumab. Stage III/IV Melanoma.*

### ***Inclusion Criteria:***

*In order to be eligible for participation in this study, the subject must meet all of the following:*

- 1. Pathologically documented unresectable melanoma, American Joint Committee on Cancer (AJCC) version 8, Stage III or IV. Subjects must have histological or cytological confirmed diagnosis of unresectable melanoma with progressive locally advanced or metastatic disease.*
- 2. Subjects must be refractory to anti PD 1 monoclonal antibodies (mAb) (pembrolizumab or nivolumab either as monotherapy or in combination with other approved checkpoint inhibitors or targeted therapies according to their approved label) and subjects must meet all of the following criteria:*
  - Received treatment of FDA-approved anti PD1 mAb (dosed per label of the country providing the clinical site) for at least 12 weeks.*
  - Progressive disease after anti PD1 mAb will be defined according to RECIST v1.1. The initial evidence of PD is to be confirmed by a second assessment, no less than 4 weeks from the date of the first documented PD, in the absence of rapid clinical progression. For cases of rapid clinical progression, patients may be allowed to enroll without a confirmatory scan after discussion with the sponsor. (This determination is made by the Investigator; the Sponsor will collect imaging scans for retrospective analysis. Once PD is confirmed, the initial date of PD documentation will be considered the date of disease progression).*
  - Documented disease progression within 12 weeks of the last dose of anti PD1 mAb. Subjects who were re treated with anti PD1 mAb and subjects who were on maintenance with anti PD1 mAb will be allowed to enter the study as long as there is documented PD within 12 weeks of the last treatment date (with anti PD1 mAb).*

We think it important to point out a few things regarding the above criteria with respect to the patients enrolled in KEYNOTE-695. Recognize the patients in this study are all either Stage III or Stage IV melanoma patients. Just to clarify, *the only* Stage III patients allowed in the trial were/are those with “unresectable melanoma”, which means melanoma that could not be removed via surgery. Presumably, Stage III patients with nonresectable melanomas are likely to progress to Stage IV. Further, in a lot of words, the criteria require that patients in the study must have been treated with and essentially failed prior treatments of approved “anti PD 1 monoclonal antibodies”, which are essentially the immunotherapy checkpoint inhibitors, such as Keytruda®. Succinctly, the patients in this study are desperately ill. At this stage most have likely failed several standard protocols available to them, so they are at a point where they have few remaining options of treatment. For some of these patients

that may mean an additional round of ICI's, which typically have *very low* rates of response the second time around.

The above said, despite the health profiles of the patient population of KEYNOTE-695 being dire, the combination study has produced meaningful responses from several of these patients. Just to reiterate, per the enrollment criteria, these people failed monotherapies including Keytruda® prior to this combination therapy, so it seems reasonable to us to assume that TAVO has played a role in these responses. We would add, one additional salient conclusion to the study thus far is that despite some of the past toxicity issues we have covered regarding prior studies involving IL-12, TAVO appears to be well tolerated, as most adverse events are similar to those experienced by individuals receiving ICI monotherapies alone.

Further, we think it begs the question, “how effective might TAVO be if it were included in the front line of therapy” (prior to a tumor’s advance to later stages)? Put another way, would the results be even more robust if the patients were treated with TAVO/ICIs earlier? Unfortunately, the only way we may ever know that is if the FDA grants OncoSec a conditional approval based on these late stage results, allowing a more likely path for TAVO to eventually be approved/administered as a front-line therapy.

Clearly, OncoSec’s “success” over the next few quarters will likely be measured by the continued results/conclusions of KEYNOTE-695. We believe that is where most of the street’s attention is/has been fixed in terms of assessing the value of OncoSec. Given that 695 is the most advanced of their clinical studies, we understand that view. However, we would encourage readers to recognize a few things we know about cancer therapy, which is that each “type” of cancer (as well as other iterations therein) has some unique characteristics that speak to the need for unique therapies, which more than likely includes (will include) combinations of therapies required to treat each. From that perspective, while 695 is certainly the *timeliest* study the Company is currently engaged in, it may or may not prove to be the most successful or by extension, the most important. That is, we do not view the results of KEYNOTE-695 as indicative of TAVO’s ultimate success across other potential indications. That for instance, may be particularly true as the Company advances its VLA technology that could potentially treat a variety of internal tumors that TAVO cannot reach with their current electroporation technology. While we don’t think the Company’s valuation reflects it, and for the sake of brevity we are not covering the others clinical here in detail, we think the Company’s platform and current clinical posture provides them multiple “shots on goal”.

We would point out one additional thing about KEYNOTE-695 that may or may not be fully understood since it represents a nuance to the typical FDA approval process. Most people who have done any research/investing in the pharma and/or medical device theatres have some knowledge of the FDA approval process we covered briefly in the Industry Overview of this report. Generally, that includes a progression through stages or “phases” required to achieve an FDA approval. However, over the years and for a variety of reasons, the FDA has provided some exceptions to that process, and most of those exceptions provide for limited use and/or conditional approvals associated with diseases or stages of diseases where patients have no viable and otherwise approved treatment options. Again, these may include exceedingly rare (or newly discovered) diseases where very few other therapies exist or are even contemplated, or advanced stages of disease where existing therapies are either not specifically applicable or have failed. Those exceptions are delineated with labels like “compassionate use”, “accelerated approval”, “fast track” and others. From a practical standpoint, we have seen some application of the FDA’s “exceptions” during the current pandemic, where the Administration has specifically provided for the treatment of COVID-19 with the “off label” use of drugs approved for other indications (hydroxychloroquine) as well as the acceleration of conditional trials and/or approvals of entirely new therapies aimed at the virus (remdesivir).

In that regard, recognize that cancer research/therapy is one of the more common beneficiaries of these exceptions, typically because of the “advanced stages of disease where existing therapies are either not specifically applicable or have failed” scenario we noted above. It is important to recognize that TAVO in the context of KEYNOTE-695 has been approved for and is on that accelerated path. As a result, if KEYNOTE-695 achieves the milestones the Company hopes it will, the Company will effectively be allowed to by-pass the typical Phase III trials and

move straight to a New Drug Application (“NDA”) or a Biologics License Application (“BLA”), which effectively achieve the same “stamp of approval”. That is the reason why the Company has noted in their presentations and collateral, that an FDA approval of TAVO for melanoma over the next 12 months is conceivable. Obviously, that would represent a major milestone for the Company and likely a considerable catalyst for the value of its underlying shares.

Lastly, we would also note that beyond the FDA, the Company has also been provided some “exception” status for potential approvals in Europe and over the past year they also signed a collaboration/agreement that we believe could accelerate TAVO’s acceptance/commercialization in Australia. We will monitor/update each of these opportunities. Further, the Company recently attracted a substantial investment from a large Chinese pharmaceutical company (and its associated affiliates). We will discuss this transaction further in the Operating Overview of this report, but as part of that agreement, the purchaser (in exchange for a meaningful royalty) will be responsible for the approval and commercialization of TAVO in Asia (excluding Japan). These agreements establish additional potential distribution/commercialization of TAVO outside of the U.S.

### **Operating Overview**

We have provided a projected operating model, so we won’t belabor this section of the report with the narrative of the projected cash burn. Our expectation is that until the Company can obtain an FDA approval (or other similar international approval) they will continue to burn cash to support the general overhead of the business as well as costs associated with ongoing clinical trials. As those familiar with the space will likely attest, clinical trials are lengthy and expensive. To that point, the Company has typically supported the ongoing cash burn largely through (dilutive) equity raises. We expect that approach to continue until they can achieve commercialization. That said, the pace/breadth of clinical studies will depend on their continued access to cash, whether earned or raised. Per our attached model and based on past results, we anticipate the annual burn rate to approximate \$38 to \$40 annually.

To expand on the above, as of the most recent filing (Q2-F20 ended January 31, 2020), the Company held cash and cash equivalents of \$9.3 million. Further, subsequent to the end of the same quarter, the Company completed a \$30 million equity financing, thus we expect them to have the necessary capital to get through the next 12 months. That transaction requires some color.

The Company announced the closing of the aforementioned equity transaction on February 7, 2020. OncoSec sold 12 million shares at \$2.50 per share, which represented “an approximate 25% premium to the average share price over the 20 days prior to the signing of the deal on October 9, 2019”. The Company sold 10 million of these shares to China Grand Pharmaceutical and Healthcare Holdings Limited (“CGP”), and 2 million additional shares to its U.S. affiliate, Sirtex Medical US Holdings, Inc. (“Sirtex”). The announcement also provided the following narrative regarding the respective purchasers:

*CGP is a public company listed on the Hong Kong stock exchange with a market capitalization of approximately \$2.1 billion USD. CGP develops, manufactures and distributes pharmaceutical products and medical devices to retailers and medical organizations. CGP currently distributes its products to approximately 6,000 hospitals and approximately 30,000 pharmacies and has a sales team of more than 2,000 employees. CGP also has significant experience in R&D and product commercialization in China. Such experience dealing with the relevant Chinese regulatory bodies makes CGP an ideal strategic partner for OncoSec as it looks to gain regulatory approval to introduce TAVO™ to the Chinese market. For more information, visit [www.chinagrandpharm.com](http://www.chinagrandpharm.com).*

*Sirtex is a global healthcare business company with offices in the U.S., Australia, Europe and Asia, working to improve outcomes in people with cancer. Sirtex’s current lead product is a targeted radiation therapy for liver cancer called SIR-Spheres® Y-90 resin microspheres. More than 100,000 doses have*



*been supplied to treat patients with liver cancer at more than 1,300 medical centers in over 45 countries. Sirtex's global focus on drug development makes it a natural partner for the Company as it looks to develop and introduce TAVO™ into markets around the world. For more information, visit [www.sirtex.com](http://www.sirtex.com). SIR-Spheres® is a registered trademark of Sirtex SIR-Spheres Pty Ltd.*

In addition to the direct investment(s), the agreement also included some strategic components. For example, OncoSec and CGP entered into an agreement granting CGP a license to “develop, manufacture, commercialize, or otherwise exploit the Company’s current and future products, including TAVO and the VLA” throughout much of Asia (excluding Japan). In exchange OncoSec will receive royalties of “up to 20%” on CPG’s sales in the licensed territories. Further, Sirtex will “support and assist OncoSec with pre-marketing activities for TAVO™ and its visceral lesion applicator (VLA) in exchange for low single-digit royalties on those products”.

As a result of this transaction, CGP and Sirtex own roughly 44% and 9%, respectively, of OncoSec’s outstanding shares. Representatives of the purchaser(s) occupy three of the Company’s current nine board seats.

Given the burn rate we noted above, this transaction was critical to the Company’s continued progress. Frankly, it is not often that we see transactions on this end of the market at a premium to the prevailing public share price and a raise that exceeds the entire pre-transaction market cap of the stock at the time of the deal. We think that speaks to the buyers’ confidence in OncoSec’s platform. Having said that, the transaction was not without scrutiny, as it was challenged via proxy by (some) legacy shareholders. We suspect the change of controlling interest was a large part of that issue. However, we *would yield* to the legacy dissent that given our own bullish stance regarding OncoSec’s advanced platform, we also think the buyers struck a favorable deal. They effectively paid \$30 million for ½ of an advanced stage biopharma company *that has spent nearly \$200 million to date* getting to this point. That noted, the challenge by the legacy shareholders failed and the transaction closed. We are not going to rehash the disagreement, but again, from our perspective, the fact that the Company was able to raise the necessary capital to carry them through what could be the most critical clinical period in their history was/is paramount.

We would add, in May 2019 OncoSec announced a collaboration with Australia based Emerge Health Pty (“Emerge”), the “leading Australian company providing full registration, reimbursement, sales, marketing and distribution services of therapeutic products in Australia and New Zealand”. The agreement addresses the availability of TAVO under Australia’s Special Access Scheme (SAS) in 2019. Emerge has apparently made other products available under Australia’s SAS. The announcement further notes: “The SAS was introduced by Australia’s Therapeutics Goods Administrations (TGA) in recognition that there are circumstances where patients need access to therapeutic products that are not on the Australian Register of Therapeutic Goods (ARTG). Australia’s SAS allows physicians to prescribe and treat patients with drugs not yet approved in Australia provided those patients have a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment. In 2019, it is estimated that 15,229 new cases of melanoma skin cancer will be diagnosed in Australia (8,899 males and 6,330 females) and that it will become the ninth most common cause of death from cancer in 2019. TAVO, to be used for melanoma patients who have failed either checkpoint inhibitors or targeted therapy, could treat up to 1,000 Australian patients. As we alluded to above regarding the U.S. FDA’s trial exceptions, this is Australia version of that same approach. We believe this arrangement has the potential to generate ongoing revenues for OncoSec, although we submit, we do not have a handle on what that might be in the near term largely because the Company has refrained from providing much color to that end. However, we see this as an additional validating data point regarding TAVO.

Lastly, we would reiterate something we noted above, which is that OncoSec’s current path suggests that they may be positioned to seek expedited FDA approval in the first half of calendar 2021. That by the way has been the plan for some time now, but we submit, the current pandemic could impact that. That is just our speculation since it seems to be impacting the timelines of just about everything. In any event, if our math is reasonably correct, we anticipate that they will need to raise additional capital before an approval is likely, and that assumes

the necessary clinical success of KEYNOTE-695. While there is no guarantee that the FDA will ultimately approve an NDA or BLA, we think an FDA submission alone will make raising that additional capital much easier (and much cheaper) than the lack thereof. Again, any submission will almost certainly be predicated on an appropriate level of clinical success from KEYNOTE-695. In case it is not clear, while as we have suggested, we do not believe that all of OncoSec's eggs are in the KEYNOTE-695 basket, but we *do* believe the outcome of that trial will largely drive the valuation/direction of the Company over the next 12 months and that will include ongoing financing issues and associated dilution.

## **Management and Directors**

### **- Daniel O'Connor – CEO/Director**

*Mr. O'Connor is the Chief Executive Officer of OncoSec Medical, Inc., a biopharmaceutical company developing intratumoral cancer immunotherapies. Most recently, he served as President and Chief Executive Officer of Advaxis Inc. Mr. O'Connor successfully turned around the company, raising more than \$300 million in funding and licensing deals, transforming it into a patient-focused, leading cancer immunotherapy company. He was also instrumental in establishing major partnerships with companies that include Amgen Inc., Merck & Co. and Bristol Myers Squibb. In addition, under his leadership, the company advanced four new cancer immunotherapy drug candidates into clinical trials, as well as several PD-1 combination clinical studies with Keytruda®\* and Opdivo®\*. Previously, Mr. O'Connor was Senior Vice President for ImClone Systems where he supported the clinical development, launch, and commercialization of ERBITUX®\*, and the sale of the company to Eli Lilly in 2008. Mr. O'Connor served as General Counsel at PharmaNet (inventive Health) and was part of the senior leadership team that grew the company from a start-up contract research organization into a leader in clinical research. Mr. O'Connor is a 1995 graduate of the Penn State University's Dickinson School of Law in Carlisle, Pennsylvania and currently serves as an Entrepreneur Trusted Advisor to its Dean. He graduated from the United States Marines Corps Officer Candidate School in 1988 and was commissioned as an officer in the U.S. Marines, attaining the rank of Captain while serving in Saudi Arabia during Operation Desert Shield. Mr. O'Connor is currently the Vice Chairman of BioNJ and was a former New Jersey criminal prosecutor.*

### **- Christopher Twitty, PhD – Chief Scientific Officer**

*Dr. Twitty brings over 20 years of experience in tumor immunology and cancer immunotherapy, including the discovery and development of OncoSec's leading clinical immune monitoring and biomarker program. Dr. Twitty earned his PhD from Oregon Health & Science University where his work was focused on novel tumor vaccine strategies and was awarded an American Cancer Society fellowship training grant for his post-doctoral studies in Dr. Bernard Fox's Molecular Tumor Immunology Laboratory. After developing a pre-clinical and clinical immunological program focused on glioblastoma at Tocagen, Dr. Twitty joined OncoSec. Previously, Dr. Twitty held scientific positions of increasing responsibility at Bayer Pharmaceuticals and Cell Genesys, Inc.*

### **- Robert DelAversano, C.P.A. – Principal Accounting Officer and Controller**

*Mr. DelAversano is a certified public account and has over fifteen years of experience in accounting including thirteen years in public accounting. Prior to this appointment as OncoSec's Principal Accounting Officer and Controller, Mr. DelAversano served as OncoSec's Executive Director of Finance since 2018 where he had global responsibility for accounting, external financial reporting, and financial controls covering all aspects of OncoSec's business. Prior to joining OncoSec, he was the Director of Financial Reporting and Taxation at Brio Financial Group ("Brio"), consulting with various public companies in financial reporting, internal control*

development and evaluation, budgeting and forecasting. Prior to joining Brio, Mr. DelAversano was a manager at Bartolomei Pucciarelli, LLC and oversaw their accounting and tax practice with industry focuses in manufacturing, wholesalers and medical devices services. In addition, he performed audit services, outsourced chief financial officer functions, and consulted clients through difficult Securities and Exchange Commission comment periods particularly through application of complex accounting principles for a large public company client base. Mr. DelAversano holds a bachelor's degree in Accounting from Rider University.

- **Kellie Malloy Foerter – Chief Clinical Development Officer**

Ms. Malloy Foerter brings nearly thirty years of experience in clinical research with Syneos Health, inVentiv Health (previously PharmaNet), and Covance. Prior to joining OncoSec Kellie served as Executive Vice President and General Manager, Clinical Solutions at Syneos Health. As a member of the Syneos Health Clinical executive leadership team, Ms. Malloy Foerter was responsible for the development and growth of multiple portfolios across therapeutic areas which included a strong focus on oncology and hematology trials, for the world's leading biopharmaceutical companies. Earlier, Ms. Malloy Foerter spent 20 years at inVentiv Health (previously PharmaNet) where she held multiple positions of increasing responsibility, most recently serving as Senior Vice President, Clinical Research. Prior to inVentiv, she served as Senior Project Associate, Clinical Research Associate and Clinical Studies Assistant at Covance. Ms. Malloy Foerter has a Bachelor of Science degree from Saint Joseph's University in Philadelphia, PA.

- **Keir Loiacono - VP- Corporate Development / General Counsel**

Mr. Loiacono brings more than 17 years of success across the life sciences and medical device industries, having held commercial, legal and business roles. Mr. Loiacono draws on his extensive business, science and legal experience to head corporate development at OncoSec. Prior to joining OncoSec, Mr. Loiacono was the head of legal at Advaxis Inc., where he successfully negotiated and closed four strategic licensing transactions totaling approximately \$75 million. Prior to Advaxis Keir spent 7 years in private practice as a licensed patent attorney with the Lerner David law firm. At Lerner David he specialized in transactions, as well as the monetization and management of IP portfolios for medical device and life science clients, including Fortune 500 companies, and successfully completed numerous transactions. Prior to practicing law, Keir was part of a launching sales force at OraPharma, Inc., which was later acquired by Johnson & Johnson, where he held positions of increasing responsibility in the commercial organization. Mr. Loiacono hold a bachelor's degree in biology (Cum laude) from Manhattan College and a Juris Doctorate from the Elisabeth Haub School of Law.

- **Robert Ashworth, PhD – Senior VP Regulatory Quality and CMC**

With more than 35 years of experience in the pharmaceutical industry, Dr. Ashworth is well-versed in drug development and global regulatory strategies and has made significant contributions to the FDA approval of 12 new drugs. Prior to joining OncoSec, Dr. Ashworth served as Vice President, Regulatory Affairs, Quality & Compliance for Advaxis, Inc., where he developed and executed the global regulatory strategy for the company's immunotherapy platform and served as the company's regulatory representative for clinical development programs involving Amgen, Bristol-Myers Squibb and Merck. Importantly, Dr. Ashworth was instrumental in securing a groundbreaking investigational new drug application (IND) for a personalized medicine, neo-epitope program. Before Advaxis, Dr. Ashworth was Vice-President, Global Regulatory Affairs at NPS Pharmaceuticals, Inc., where he built the company's international regulatory department and was instrumental in negotiating the approval of NATPARA (PTH) for hypoparathyroidism. As Vice-President, Global Regulatory Affairs for Otsuka

Pharmaceutical Development, Inc., Dr. Ashworth was responsible for the regulatory strategy for the company's flagship product, ABILIFY®. Dr. Ashworth's career experience also includes regulatory positions at Biovail Corporation, Forest Laboratories, Inc., Knoll Pharmaceutical Company (BASF), and CIBA-Geigy Corporation. Dr. Ashworth earned a B.S. in Chemistry from St. John's University and his Ph.D. in Organic Chemistry from MIT.

- **John Rodriguez – VP Product Engineering**

Mr. Rodriguez is a leader in product development with over 30 years of experience heading teams in the design, development and manufacture of products for the biomedical industry. Prior to joining OncoSec, Mr. Rodriguez served as Senior Director of Product Development for Cytos Therapeutics, where he was responsible for the development of Cytos's stem and regenerative cell products. Mr. Rodriguez biomedical product manufacturing experience includes both domestic and OUS manufacturing with specific experience in Europe, South America and Asia. Mr. Rodriguez has held positions of increasing responsibility in the biomedical and product development fields since beginning his career at Johnson & Johnson Medical Inc in 1987. In addition to Mr. Rodriguez relevant immunotherapy and oncology experience with electroporation product at both Inovio Biomedical and Genetronics, Mr. Rodriguez tenure includes development of product with Advanced Sterilization Products, Gynecare, Ethicon Endo-Surgery and Ethicon Inc. Mr. Rodriguez has a bachelor's degree in manufacturing Engineering from National University, and a degree in Executive Perspective for Scientists and Engineers from the University of California, San Diego.

- **Kim Jaffe, PhD – Senior Director of Operations**

Dr. Jaffe brings nearly 20 years of experience in both academia and industry to OncoSec. As Senior Director of Operations, Dr. Jaffe translates her extensive science experience as a backdrop for business development, operational management, and corporate strategy. She oversees numerous programs, including our CAR-T collaboration with the Marasco lab at DFCI, Emerge Health SAS program for TAVO in Australia, and our new visceral lesion applicator (VLA) platform. She is also extensively involved with search and evaluation and identifying new partnering opportunities. Prior to OncoSec, Dr. Jaffe held various positions of increasing responsibility, including Director of Research, at several private and public biotech companies in the oncology sector. In addition to her research roles, she has broad experience interacting with U.S. and European regulatory authorities and has overseen the development and manufacturing operations of a neoantigen-based immuno-oncology platform. Dr. Jaffe earned her PhD in Molecular and Cell Biology from Northwestern University and performed her post-doctoral research at Princeton University.

- **Gem Hopkins – Head of IR and Corporate Communications**

Ms. Hopkins brings over a decade of experience leading strategic investor relations and corporate communications programs for early-to-late stage and commercial biotechnology companies. Prior to joining OncoSec in July 2019, Ms. Hopkins served as VP, Investor Relations and Corporate Communications at Synergy Pharmaceuticals where she was responsible for building and leading innovative IR/communications programs during the company's transformation and rise in market capitalization from less than \$300 million to over \$1.5 billion. In this role, she successfully marketed over \$800 million in capital transactions and led IR/communications strategies for the launch of the company's first commercial product. Prior to that, Ms. Hopkins ran a boutique communications firm providing comprehensive IR/PR strategy, video production and marketing solutions to emerging growth companies. In this role, she led media training for dozens of C-level executives, created and delivered high-impact communications initiatives that ran the gamut from CEO interviews



to new product launches and patient testimonials. Ms. Hopkins started her career as a Reporter/Producer for the NBC news affiliate covering the Northern Nevada and Sierra areas. She holds a B.A. from the Walter Cronkite School of Journalism at Arizona State University.

- **Margaret R. Dalesandro PhD - Chairman of the Board**

Dr. Dalesandro brings more than 25 years of drug development experience in the pharmaceutical, biotechnology and diagnostics industries. She currently serves as the President of Brecon Pharma Consulting, a full-service pharmaceutical and biotech consultancy firm. She previously served as Business Director of Corning Integrative Pharmacology. Before that, Dr. Dalesandro held an executive leadership role at ImClone Systems where she oversaw project management for the clinical development of ERBITUX® (cetuximab), making significant contributions to the sale of ImClone to Eli Lilly in 2008. Prior to that, Dr. Dalesandro served as an Executive Director at GlaxoSmithKline, managing cardiovascular, urology, and oncology drug product commercialization. Earlier in her career, she was a senior consultant at Cambridge Pharma Consultancy and a Director of Immunobiology and Diagnostic Research at Centocor. Dr. Dalesandro holds a Ph.D. and M.A. in Biochemistry from Bryn Mawr College and an A.B. in Biology and Chemistry from Rosemont College, where she graduated summa cum laude.

- **Robert E. Ward - Director**

Mr. Ward is currently the Chief Executive Officer and Chairman of the Board of Eloxx Pharmaceuticals, Inc., roles he has held since December 2017. He was a Director and Chair of the Governance Committee of Akari Therapeutics from October 2016 to August 2018. Mr. Ward previously served as the Chief Executive Officer, President and member of the board of directors at Radius Health, Inc. from December 2013 to July 2017. Prior to joining Radius, Mr. Ward was Vice President for Strategy and External Alliances for the New Opportunities iMed of AstraZeneca from 2011 to December 2013. He has held a series of progressive management and executive roles with established companies such as NPS Pharmaceuticals, Schering-Plough (Merck), Pharmacia (Pfizer), Bristol-Myers Squibb and Genentech. Mr. Ward has been a Director of Akari Therapeutics, Plc since October 2016. Mr. Ward received a B.A. in Biology and a B.S. in Physiological Psychology, both from the University of California, Santa Barbara, a M.S. in Management from the New Jersey Institute of Technology and an M.A. in Immunology from The Johns Hopkins University School of Medicine. Mr. Ward's extensive experience and expertise in the biopharmaceuticals industry are the primary qualifications the Board considered in nominating him as a director of the Company.

- **Herbert Kim Lyerly, M.D. - Director**

Dr. Herbert Kim Lyerly is the George Barth Geller Professor of Cancer Research, professor of surgery, immunology and pathology, and director of the surgical sciences applied therapeutics section at Duke University, and former director of the Duke Comprehensive Cancer Center. He is an internationally recognized expert in cancer therapy and immunotherapy, has published over 300 scientific articles and book chapters, and has edited ten textbooks on surgery, cancer immunotherapy and novel cancer therapies. He serves on the editorial board of 12 scientific journals. Dr. Lyerly was appointed in 2008 by President George Bush to serve on the National Cancer Advisory Board, which oversees the National Cancer Institute, where he served until 2014. He has served as chair of the Cancer Centers Subcommittee and served on the Global Health Subcommittee of the National Cancer Advisory Board. He has served on the National Institutes of Health (NIH) Council of Councils, and on the board of the NIH Office of AIDS Research. He has also been a member of the scientific advisory boards of Susan G. Komen and the Burroughs Wellcome Foundation. He is a highly sought-after consultant and advisor and has served on the Cancer Center's external advisory boards for the M.D. Anderson Cancer Center, University

of Michigan, University of Chicago, University of Alabama, University of Arizona, Boston University and Purdue University. He has served as an advisor to the University of Washington and Case Western Reserve Clinical and Translational Science Institutes.

- **Chao Zhou - Director**

Chao Zhou is currently the Executive Deputy Officer of China Grand Pharmaceutical and Healthcare Holdings Limited, a public company listed on the Hong Kong stock exchange that develops, manufactures and distributes pharmaceutical products and medical devices to retailers and medical organizations with significant experience in R&D and product commercialization in China. Since 2018, Mr. Zhou has served on the Board of Directors of Grand Pharma Sphere Pty Ltd, a Singapore based company that indirectly wholly-owns the Australian based global medical device company, Sirtex Medical Pty. Ltd. Prior to his role as Executive Deputy Officer, Mr. Zhou served as a Management Director in the Department of Legal Security for China Grand Enterprises, Inc., an investment company engaged in the operation and management of businesses covering pharmaceuticals and healthcare, commodity trading, real estate investment, financial service and other sectors. He earned his Bachelor in Law from Ocean University of China and a Master in International Law from the University of International Business and Economics.

- **Kevin R. Smith – Director**

Kevin R. Smith is currently the Chief Executive Officer of Sirtex Medical US Holdings, Inc. He combines more than 20 years of sales and marketing experience in the medical device industry with the keen instincts of an entrepreneur. Prior to his appointment to CEO, Mr. Smith was Executive Vice President of Sales & Marketing, Americas. Before joining Sirtex, Mr. Smith was Executive Vice President of Business Development at Gel-e, Inc., a company based at the University of Maryland specializing in advanced material hemostasis products. His previous positions include Chief Commercial Officer of Sensium Healthcare along with Global Vice President of Sales & Marketing at Teleflex, where he was the senior sales and marketing executive in the company's cardiac business unit. Kevin holds a Master of Business Administration in Global Management from the University of Phoenix and a Bachelor of Science in Marketing from the University of Kentucky.

- **Jim DeMesa, MD, MBA – Director**

Dr. DeMesa has served as a senior executive with several international pharmaceutical and biotech companies in the areas of corporate management, regulatory affairs, and pre-clinical and clinical pharmaceutical and medical device product development. Most recently, Dr. DeMesa served as President, CEO, and Director of Migenix Inc., a public biotechnology company. Dr. DeMesa was also president, CEO and Director of GenSci Regeneration Sciences Inc., a public biotech company, Vice President of Medical and Regulatory Affairs at Biodynamics International, Inc., and Vice President of Medical and Regulatory Affairs at Bentley Pharmaceuticals. He has been a practicing physician and is a Co-Founder of CommGeniX, a medical communications company, and MedXcel, a medical education company.

- **Yuhang Zhao, PhD, MBA - Director**

Dr. Yuhang Zhao, a graduate from Peking University, received her Doctorate in Molecular Biology from Rockefeller University and her MBA in Finance from NYU Stern Business School. Dr. Zhao was most recently a member of the Bayer Global Leadership Circle. She established one of Bayer's four Global Clinical Development sites, located in Beijing, China in 2009. She then became Head of Global Strategy for Bayer Consumer Health, reporting to the President. Prior to her positions in the pharmaceutical industry, Dr. Zhao held positions as a

stock analyst at PaineWebber and was a management consultant specializing in strategies for life science companies. Dr. Zhao currently serves on the board of R2 Technologies and is a senior adviser to China Grand Enterprises.

- **Joon Kim – Director**

Joon Kim is a highly accomplished attorney and partner in Lee & Ko's Corporate, International Litigation and Dispute Resolution, and White-Collar Crime Practice Groups. Mr. Kim advises clients, both domestic and international, on a broad range of litigation, dispute-resolution and transactional matters. With a particularly strong background in representing clients in court proceedings, Mr. Kim has a comprehensive understanding of every stage of the litigation process, including all aspects of initial investigatory/discovery proceedings, settlement negotiations, hearings, motions, trials, evidentiary issues and the handling of post-judgment challenges and appeals. Prior to joining Lee & Ko, Mr. Kim worked for several years as a litigation lawyer and served from 2008 to 2017 as a public prosecutor in California. Mr. Kim has first-chaired both jury and non-jury trials, and has been trained in all aspects of litigation. During his time as a public prosecutor, Mr. Kim also had the experience of serving in 2016 as a research fellow in Korea at the Institute of Justice, under the auspices of the Korea Ministry of Justice, where he worked together with Korean public prosecutors. Joon received his J.D. from Berkeley School of Law and his B.S. from the Berkeley School of Business.

### **Risks and Caveats**

We will preface this section of the report with a bit of a caveat regarding our own aptitudes in the biopharma space. Recognize, Trickle Research is a generalist microcap platform. That is, we are not biopharma industry analysts, rather, we follow generally small, underappreciated companies from “soup to nuts”. As a result, we do not always have the same understanding/insights into the minutia of some analysts in some industries and biopharma is most certainly one of those. On the other hand, *we have written* our share of biopharma stories over the years, so we are also not neophytes to the space. Our experience in covering biopharma stories is that the industry is rife with theories. Theories about how the human body and its almost immeasurable number of “moving” parts and interactions therein work. Further, when we add external/environmental factors, the analysis becomes exponentially more complex. Succinctly, we do not always fully understand all the machinations of the theories and explanations posited by researchers in the biopharma space, however, we are not so sure that the researchers always fully understand them either. Afterall, there is a reason why medical papers/studies in the space get “peer reviewed” and it is because that process provides a forum for *experts* to challenge the assessments and conclusions of *other* experts. Quite often there is considerable disagreement amongst those experts regarding the “machinations” we alluded to. These complexities and the many variables that create them embody the risks associated with biopharma investing. It is the quintessential high risk/high reward environment.

On the face, OncoSec certainly fits in the high risk/high reward category we just described. However, in our view, the most imminent of those risks is probably the outcome of the KEYNOTE-695 trial. Given that OncoSec shares have lost over 90% of their value since they commenced the KEYNOTE-695 trial in October 2017, we think it is safe to assume that much of the street does not believe that TAVO will achieve an approval, at least not through KEYNOTE-695. Our other assumption is that at least some of that assessment must be based on the trial results we have seen to date, which we covered above. That may be one of the more perplexing things about the stock to us, because we have generally viewed those results as positive. Obviously, others may be reading something into the data that we are not.

From another angle, we generally view the FDA approval process as a bit of an enigma. That is, while we have seen plenty of approvals, we have also seen companies fail to gain approvals that we thought were likely. The fact that OncoSec is pursuing an approval through the “exceptions” path we described above is a bit of a wild card to us. In our view, the visibility regarding what results the FDA might be looking for out of KEYNOTE-695 is not specifically clear to us. That includes perhaps the “conditions” of any “conditional approval”. That is, our assumption is that a favorable approval might initially only apply as a third or fourth line therapy, which could at least limit the market for TAVO as well as perhaps its reimbursement rates and other such metrics. Ultimately, the goal is for TAVO to prove successful as a first/second line therapy, and perhaps ultimately a monotherapy, and for the FDA to provide a reasonable approval pathway to that end(s).

The clinical results to this point have demonstrated that TAVO appears to have a favorable safety profile. On the other hand, as we noted in this report, prior clinical efforts involving systemic administration of IL-12 have encountered marked safety challenges. While we do not anticipate negative safety issues from TAVO trials, we cannot rule out the possibility of that event. Moreover, adverse safety events would be decidedly negative for the trials and by extension OncoSec.

As we noted above, we think it is quite likely that the Company will need to return to the capital markets before it is generating any measurable revenues. Their ability to continue to attract capital (and limit dilution) remains a critical element to the story. Their inability to continue to attract required capital could at least negatively delay or otherwise impact their clinical endeavors and in the worst case could be potentially catastrophic.

As we said, over the past 2½ years the stock has lost a considerable portion of its value. We expect the stock to continue to be volatile. Investors should assess that volatility in the context of their own risk tolerances and investment horizons.

These are just some of the more obvious risks associated with OncoSec. There are most certainly others we have either overlooked or are not apparent at this time.

### **Summary, Valuation and Conclusion**

As we alluded to above, we are microcap generalists so over the that past three decades we have covered dozens of companies in a multitude of industries including biotech/biopharma. Our goal as generalists is to find companies that we think may have some unique characteristics and/or are largely unrecognized by the street in hopes of being early in the story. To clarify typically “being early” is more about being willing to initiate coverage on the stock when important elements to the story still lack visibility than it is about prescience or somehow figuring out something that others can’t or haven’t. We submit, there are marked inherent risks associated with getting involved in emerging companies that lack visibility. That said, we view our charge as trying to identify and understand the visibility issues as best we can, and then to try to ascertain the potential for positive outcomes around that visibility. In that regard, determining the *likelihood* of positive events is difficult at best, and it explains in part why many emerging companies trade at modest valuations. Consequently, recognizing the difficulty of handicapping those positive outcomes, our approach is to try to identify opportunities where if the positive outcomes come to fruition, the reward for getting it right will be extraordinary from a return perspective. In roulette parlance, we are not looking to put our chips on red or black, but rather on green. Moreover, we would like to think that over the years we have at least developed some aptitudes to help us recognize when green may be queuing up.

Frankly, we think the approach we just described is a reasonable summation for investing in the biopharma space in general. Most who follow the space can attest that the odds of getting from the “drawing board” to an FDA approval are slim, which is why (retrospectively and collectively) biopharma stories that actually achieve FDA



approvals are among some of the most prolific investments on the board. However, to put those risks into perspective, industry assessments suggest that:

*“In the United States, it takes an average of 12 years for an experimental drug to travel from the laboratory to your medicine cabinet. That is, if it makes it. Only 5 in 5,000 drugs that enter preclinical testing progress to human testing. One of these 5 drugs that are tested in people is approved. The chance for a new drug to actually make it to market is thus **only 1 in 5,000**....* (<https://globalforum.diaglobal.org/issue/may-2019/what-are-the-chances-of-getting-a-cancer-drug-approved/>).

To compare that back to our roulette analogy, the odds of hitting “green” on the roulette table are **1 in 36**...

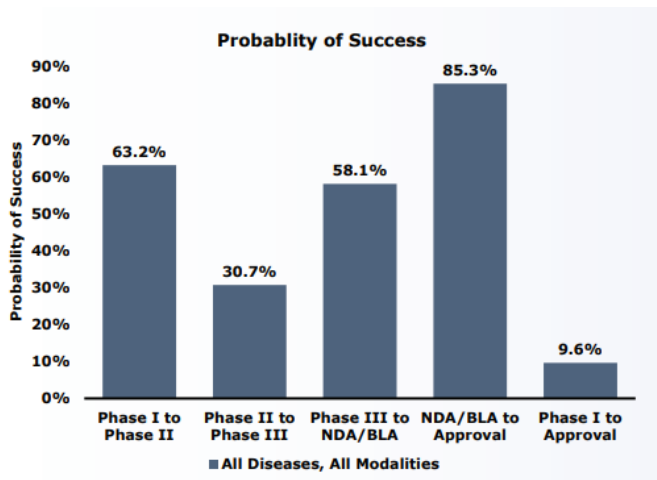
The above noted following are some points regarding why we are optimistic about OncoSec’s prospects as well as what we view as some unique characteristics that contribute to our bullishness.

- We think some observers have a hard time putting OncoSec in the right box. On the face, OncoSec’s platform is a medical device and we don’t think most people think of devices when they think of cancer therapies. In addition, TAVO is the combination of the device (ImmunoPulse) with a natural occurring molecule (IL-12). To edify, as the Supreme Court has addressed, naturally occurring molecules cannot generally be patented/protected *per se*. So then, TAVO is the combination of an unconventionally applied medical device with a naturally occurring cytokine that is difficult to provide protection around, which by the way, while demonstrating clinical efficacy in prior studies has also demonstrated marked toxicity issues when delivered systemically. In short, we understand the skepticism.
- Before we address that “skepticism” we would segue just a bit to cover the “protection” issue we raised. We submit, the TAVO combination is a bit abstract. For instance, we think the Company has wrestled with issues like pursuing a medical device approval from the FDA (typically an easier, faster and cheaper path than the current approach) as well as how to patent or otherwise protect their application of a natural occurring molecule. These nuances have certainly provided some complexities and perhaps even some risks for OncoSec *and the underlying story*. We believe they have addressed those issues from a business perspective (patent protection and approvals), while the story/investor part is perhaps still a work in progress. On the business side of that notion, we would just submit that there is a good reason why Keir Loiacono, the Company’s VP of Corporate Development and General Counsel’s resumé includes medical device and life science patent and IP law. We think this part of the business, while challenging, has been well thought out.
- Moving on, our answer to the street’s skepticism is that we think the uniqueness of both the device, the cytokine and their combination are *exactly* the point. We think it is fair to say that combination therapies will continue be the answer to addressing cancer going forward. That is not particularly insightful since combination therapies have been the answer to cancer therapy for the past several decades as well. Put another way, there is no silver bullet for “cancer” and there likely never will be. However, we do know that on their own, electroporation has been proven to make cancer cells more permeable and thus receptive to the uptake of cancer therapies, and we also know that IL-12, has been proven to be an affective enabler of the body’s immune response. The trick, then is to figure out how to get the two promising approaches to work together to make  $1+1 = 3$ . *We think*, TAVO may achieve that synergy, which would mean that it could prove effective as a combination therapy (KEYNOTE-695 for instance) or ultimately as a monotherapy as well. Either/both of those outcomes would likely prove to be watershed events for OncoSec, while the latter (monotherapy) would be extraordinary.
- We are not sure the investment community fully appreciates how far the Company has taken TAVO in terms of clinical success and *in multiple indications*. That notion includes what we think could be an NDA or BLA within the next 12 months. That is, we are not sure everyone is recognizing that the Company’s “accelerated approval” status means that it will likely jump from the current Phase II to an

FDA filing following the completion of KEYNOTE-695, which per [www.Clinicaltrials.gov](http://www.Clinicaltrials.gov) is slated for the end of this calendar 2020. Granted, submission of the NDA/BLA will be predicated on the successful results of the trial. We submit, while we think the glimpses we have seen of the trial have been quite positive, (which we think is supported by the American Association for Cancer Research's review of the same), we do not know what the final summation of the study will be and that lack of visibility remains one of the major and most imminent risks in the story. However, the fact remains that *in our view*, the market capitalization of OncoSec seems relatively low for a Company with a therapy that has performed well enough to get through several layers of the FDA process and is now knocking on the door of submission with KEYNOTE-695. Moreover, as we noted, this is not their only shot on goal. We think that combination of progress and nominal market capitalization speaks to the risk/reward analogy we laid out above.

- While we covered this issue above, we think it is important to reiterate because we think it may represent one of the more important aspects of TAVO if it proves to be clinically significant. The Company believes that TAVO not only helps to shrink the electroporated tumor, but also provides an “abscopal effect” throughout the rest of the body. That is, TAVO creates a systemic IL-12 response to help fight other tumors that may have metastasized in other areas. As the Company sometimes describes it, their primary goal is not to shrink a tumor, but rather, use a tumor to prime or jump start the immune system to create a systemic response. They liken it to “pulling a fire alarm” and alerting the rest of the immune system. In short, it would be of tremendous value if TAVO in fact proves able to illicit a meaningful systemic response. With respect to most stage IV melanoma patients out there as well as many with other stage IV indications, a systemic therapy is likely paramount to their survival.
- Along with TAVO's potential abscopal effect, we think their electroporation technology's ability help turn cold tumors to hot tumors makes it a particularly valuable combination for some immunotherapies and/or checkpoint inhibitors like Keytruda™. As we noted, Keytruda™ is regarded as the most widely effective checkpoint inhibitor available today. Some estimates suggest that over the next few years it could command a \$20 billion market, which would likely make it the biggest drug on the planet. However, as we also illustrated, Keytruda™ is only effective for *roughly* 30% of the patients treated with the therapy (depending on the indication). As we understand it, some of the limits of checkpoint inhibitors stem from their inability to impact cold tumors. If TAVO can in fact help to make unresponsive tumors responsive, thus allowing the ICI's to successfully treat a larger portion of tumors/patients, its value as an adjuvant therapy could be substantial. Consider this. If Keytruda™ can be a \$20 billion drug while succeeding less than 1 time out 3, what would the value of an adjuvant therapy be that could improve Keytruda's success to 1 out 2 or 3 out 5? We will not try to defend a specific answer to that question, but we are highly confident suggesting that the value is *substantially more* than the current OncoSec market capitalization of roughly \$40 million.
- Lastly, the Company's initial clinical approach has been to establish TAVO as an effective adjunct to other standard therapies like check point inhibitors or other immunotherapies. That is clearly the focus of their current clinical programs. We think that approach is almost certainly the critical path to an initial FDA approval because of the Fast Track status they were able to obtain from the FDA in 2017. As we discussed, that Fast Track approach may allow them to skip Phase III, which certainly compresses their potential path to commercialization. We submit, that path will likely be limited initially to the treatment of Stage III/Stage IV melanoma patients. However, if they are able to get their foot in the door through the Fast Track exemption, we think that could provide the opening for the acceleration of TAVO's ultimate use as a first/second line therapy, in additional indications, and perhaps even as a monotherapy for some cancer types. Further, clinical success with their Visceral Lesions Applicator could also provide new opportunities/indications for TAVO.

While we are obviously optimistic about OncoSec's prospects, especially relative to the current market capitalization of the Company, we submit, valuing clinical stage biopharma assets is difficult. That being the case, there are a few datapoints we know that we think are germane to that process. First, we think most biopharma valuations operate off the assumption that as a company successfully moves a candidate through the various stages of the FDA approval, it becomes more valuable. Part of that logic is framed by the statistical data that delineate the odds of success/failure, of getting through each stage:



<https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf>

Succinctly, since the odds of failure are often considerable, successfully transitioning from one stage to the next effectively de-risks the process, which we think supports better valuations as the company advances through the process. While OncoSec has in fact managed to advance through the clinical process (on multiple fronts) the stock trades *at or near all-time lows*. That seems a bit counterintuitive to us, but we submit, that still does not tell us what OncoSec might be worth and we would reiterate, that number is difficult to ascertain at this point.

Generally, our approach to valuation is relatively straightforward. We attempt to develop a projected operating/cash flow model and then we apply steep discounts to that model to account for the risks associated with the notion that those projections will be wrong/overstated. We then derive our valuations/price targets based on the NPV conclusions of that DCF analysis in the context of likely future dilution and capitalization. In the case of OncoSec (and other biopharma companies for that matter) our discount rates are sometimes in the 30% to 35% range, which reflects the marked risks associated with FDA approvals and subsequent commercialization results. Obviously, if the Company *never gets* an approval, there is no discount rate that will reconcile that outcome. Put another way, if the Company is never able to achieve enough clinical success to gain an approval somewhere, then it will ultimately fail. We also use some additional valuation nuances to blend our conclusions, for example, we consider DCF iterations that include industry/peer EBITDA multiples based terminal values as well as some future price to sales valuations again based on industry metrics of the same. To reiterate, we are not suggesting any of these are perfect approaches when it comes to biopharma valuations, but *we will* add that this approach likely understates the value of those companies that *actually do achieve* approvals/commercialization rates within reasonable proximities to our assumptions because in that case the discount rates will have been substantially overstated. To translate, our price target includes a substantial discount to account for negative outcomes but if it all works the way our model projects, our price targets will likely be understated. That speaks to the favorable risk/reward profile we addressed above.

The above noted, we are initiating coverage of OncoSec Medical Incorporated with an allocation of 4 and a 12-24 month price target of \$6.00. We will reassess these conclusions as additional datapoints emerge and associated visibility improves.

### Projected Operating Model

<b>Projected Operating Model</b>						
<b>OncoSec Medical Incorporated</b>						
<b>By: Trickle Research</b>	(actual)	(actual)	(estimate)	(estimate)	(estimate)	(estimate)
	<u>10/31/19</u>	<u>1/31/20</u>	<u>4/30/20</u>	<u>7/31/20</u>	<u>Fiscal 2020</u>	<u>Fiscal 2021</u>
Revenue			\$ -	\$ -	\$ -	\$ -
Expenses:						\$ -
Research and development	\$ 5,420,159	\$ 6,055,218	\$ 6,115,770	\$ 6,176,928	\$ 23,768,075	\$ 25,331,612
General and administrative	\$ 4,418,217	\$ 7,468,375	\$ 3,600,202	\$ 3,636,204	\$ 19,122,997	\$ 14,912,089
Loss from operations	\$ (9,838,376)	\$ (13,523,593)	\$ (9,715,972)	\$ (9,813,131)	\$ (42,891,072)	\$ (40,243,701)
Other income, net	\$ 82,387	\$ 46,768	\$ -	\$ -	\$ 129,155	\$ -
Interest expense	\$ (992)	\$ (78)	\$ -	\$ -	\$ (1,070)	\$ -
Foreign currency exchange (loss) gain, net	\$ (3,503)	\$ (154,672)	\$ -	\$ -	\$ (158,175)	\$ -
Realized loss on sale of securities, net	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Loss before income taxes	\$ (9,760,484)	\$ (13,631,575)	\$ (9,715,972)	\$ (9,813,131)	\$ (42,921,162)	\$ (40,243,701)
Provision for income taxes	\$ -	\$ 2,450	\$ -	\$ -	\$ 2,450	\$ -
Net loss	\$ (9,760,484)	\$ (13,634,025)	\$ (9,715,972)	\$ (9,813,131)	\$ (42,923,612)	\$ (40,243,701)
Basic and diluted net loss per common share	\$ (0.92)	\$ (1.27)	\$ (0.43)	\$ (0.43)	\$ (2.57)	\$ (1.18)
Weighted average shares basic and diluted	10,648,540	10,712,022	22,633,043	22,930,663	16,731,067	34,192,581



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## Rating System Overview:

There are no letters in the rating system (Buy, Sell Hold), only numbers. The numbers range from 1 to 10, with 1 representing 1 "investment unit" (for my performance purposes, 1 "investment unit" equals \$250) and 10 representing 10 investment units or \$2,500. Obviously, a rating of 10 would suggest that I favor the stock (at respective/current levels) more than a stock with a rating of 1. As a guideline, here is a suggestion on how to use the allocation system.

Our belief at Trickle is that the best way to participate in the micro-cap/small cap space is by employing a diversified strategy. In simple terms, that means you are generally best off owning a number of issues rather than just two or three. To that point, our goal is to have at least 20 companies under coverage at any point in time, so let's use that as a guideline. Hypothetically, if you think you would like to commit \$25,000 to buying micro-cap stocks, that would assume an investment of \$1000 per stock (using the diversification approach we just mentioned, and the 20-stock coverage list we suggested and leaving some room to add to positions around allocation upgrades. We generally start initial coverage stocks with an allocation of 4. Thus, at \$1000 invested per stock and a typical starting allocation of 4, your "investment unit" would be the same \$250 we used in the example above. Thus, if we initiate a stock at a 4, you might consider putting \$1000 into the position ( $\$250 \times 4$ ). If we later raise the allocation to 6, you might consider adding two additional units or \$500 to the position. If we then reduce the allocation from 6 to 4 you might consider selling whatever number of shares you purchased with 2 of the original 4 investment units. Again, this is just a suggestion as to how you might be able to use the allocation system to manage your portfolio.

**For those attached to more traditional rating systems (Buy, Sell, Hold) we would submit the following guidelines.**

**A Trickle rating of 1 thru 3 would best correspond to a "Speculative Buy" although we would caution that a rating in that range should not assume that the stock is necessarily riskier than a stock with a higher rating. It may carry a lower rating because the stock is trading closer to a price target we are unwilling to raise at that point. This by the way applies to all of our ratings.**

**A Trickle rating of 4 thru 6 might best (although not perfectly) correspond to a standard "Buy" rating.**

**A Trickle rating of 7 thru 10 would best correspond to a "Strong Buy" however, ratings at the higher end of that range would indicate something that we deem as quite extraordinary..... an "Extreme Buy" if you will. You will not see a lot of these.**