

FIGHTING INFECTIONS WHERE ANTIBIOTICS DON'T!<sup>TM</sup>

APRIL 30, 2006

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## **MAJOR INVESTMENT FACTORS**

## **Pros**

+ Key compounds—trade-marked Aganocides—appear to fulfill major unmet medical needs

+ These chemicals circumvent major clinical problems like biofilm formation and resistance generation, where most other anti-infectives stumble

+ Its drugs have proven efficacious and non-toxic, although testing so far has been on a limited basis

+ These compounds have applicability across a broad spectrum of large-market medical needs

+ Company's IP cache could prove very attractive to big pharma enterprises seeking significant new product and market opportunities

# **Cons**

 Although the Company plans to pursue fast-track approval wherever possible, moving through the vagaries of the FDA can present many unforeseen challenges

- Substantial additional financing will be required to carry out the planned drug and medical device program, planned licensing and partnering programs notwithstanding





#### FIGHTING INFECTIONS WHERE ANTIBIOTICS DON'T!TM

**CONCEPT:** NovaCal is an early clinical stage pharmaceutical company that has recently developed a novel class of non-antibiotic antimicrobial solutions, termed Aganocide<sup>TM</sup> compounds by the Company. These products are capable of fighting many types of widespread infections that cannot be touched by many antibiotics and antiseptics. Besides being broadly efficacious, Aganocides have low toxicity quotients and do their work rapidly; most important, they are effective against resistant bacteria, and as well do not generate resistance. NovaCal's products have overcome the deficiencies of existing antibiotics and antiseptics by mimicking the chemicals produced by white blood cells to destroy invading pathogens. Key to their success is their inherent stability at room temperature, where naturally produced compounds are transient. In order to maximize value, NovaCal is pursuing a three-prong strategy of licensing, partnering, and in-house development of its intellectual property. In order to accelerate this process, the Company is seeking fast-track approval for several clinical uses ("indications") of its products as *medical devices*, where the FDA requires significantly less clinical trial data than in the case of new drugs. The *potential* market for Aganocides is huge-possibly running to multi-billions of dollars over time. The clinical areas in which NovaCal intends to operate currently have no *effective* treatments, and thus competition could be disadvantaged by the laboratory-proven infection-fighting superiority of Aganocides (although clinical trials so far have been on a very limited basis). The prospects for this Company would appear to be bright indeed.





**Aganocides—Harnessing The Antimicrobial Power of Active Halogens** 

Halogens, a class of chemicals that usually exhibit a valence of -1, i.e. a singlycharged negative ion in the pure state, are very powerful microbe inhibitors. They consist of the common elements Chlorine, Fluorine, Bromine and Iodine, and the extremely rare and radioactive Astatine. Chlorine and its derivative Chloramine are used in disinfecting the water supply. Iodine and Chlorine are used extensively in antiseptic applications, such as in Dakin's Solution (Cl) and Betadine® (I), but their usefulness is limited due to their toxicity to human tissue.

Active halogens are also made by white blood cells. *Neutrophils* are white blood cells produced in the bone marrow, which constitute about 60% of the blood; they are critically important to an immune response and migrate to tissues during an infection. They produce the halogens hypoclorous acid, taurine-chloramine, and taurine-dichloramine. Other white blood cells called *eosinophils* aggregate wherever allergic reactions take place, although their function is to defend against parasites; they produce the antimicrobial hypobromous acid.

The problem with naturally produced halogens like those produced by white blood cells is that they are too unstable for use in drugs. At room temperature, they undergo the process of dehydrohalogenation during which halogens are quickly deactivated by chemical transformation.

<sup>1</sup>Registered trademark of *Purdue Pharma L. P.* 



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A common occurrence in up to 80% of all infections is the presence of a biofilm, according to the NIH. A biofilm is a community of microorganisms attached to a surface. Microorganisms that are part of a surface-attached complex behave radically different than when in a free-floating (planktonic) state. In essence, a biofilm is a defense mechanism for dealing with perceived threats within the tissue environment. Encased in a biofilm, microbes can resist very high levels of commonly used antibiotics and antiseptics. Infections relating to the development of biofilms are numerous: chronic sinusitis, otitis media and externa (common ear maladies), cystic fibrosis, chronic wounds; as well as device-related infections, such as those that develop with usage of urinary tract catheters, central venous catheters, and dialysis access shunts.

By definition, antibiotics are substances produced by microorganisms that kill or inhibit other microorganisms. The first antibiotic—Fleming's penicillin—became widely available just after World War II. Almost from the outset it was noticed that a number of microbial strains developed resistance to the drug. Today, virtually all significant bacterial infections throughout the world have become resistant to the most ubiquitous antibiotics, including penicillin. This has become one of the most serious problems that medicine faces currently.

**Enter the Aganocides.** This new class of antimicrobial compounds developed by NovaCal appears to solve efficiently all of the major problems encountered by the use of conventional antiseptics and antibiotics. By mimicking the action of the body's natural defenses, the white blood cells, to produce key halogens, and engineered by the Company into a form stable at room temperature, these compounds provide the most important links to healing by:





- **△** Overcoming Bacterial Biofilm
- **▲** Killing Resistant Bugs
- **▲** Being Safe and Non-irritating
- ▲ Providing Universal Relief Against All Microbes
- **A** Having No Propensity For Resistance
- **▲** Working Relatively Rapidly
- **A** Having Broad Clinical Applicability
- **A** Being Practical For Use In Both Devices and Drugs
- **▲** Being Stable at Room Temperature

### <u>Aganocides—The Killer App</u>

NovaCal currently has two key compounds—NVC-101 and NVC-422. While both are rapid acting and have good-to-excellent safety records, NVC-101 is used in shorter time-frame applications and NVC-422 in longer time-frame applications. The Company has one issued U.S. patent, seven U.S. patent applications, and foreign analogs covering claims for both of these products. Wherever applicable complementary intellectual property will be licensed in order to provide any other necessary elements to bring Aganocide<sup>TM</sup> products to market. Of special note is that NovaCal uses the eminent life science firm Heller Ehrman LLP as patent attorneys. Heller Ehrman has more than 700 attorneys, and employs a highly respected patent team experienced in handling "bet-the-company" litigation in the IP area. In the January 2006 edition of *The American Lawyer*, Heller Ehrman's Intellectual Property Litigation practice was recognized as one of the top five in the U.S.





# **Intellectual Property**

Title	Patent/Application	Date	Attorney
Use of Physiological balanced, ionized, acidic solution in wound healing	US Patent: US 6,426,066	Issued: 7/30/02	
Physiologically balanced, ionized, acidic solution and methodology for use in wound healing	US Application: US 2003/0185704	Published: 10/02/03	39164-0002 P1
Physiologically balanced, ionized, acidic solution and methodology for use in wound healing	US Application: US 2004/0137078	Published: 7/15/04	39164-0004 CIP
N,N-dihalogenated amino acids and derivatives	US Application: US 2005/0065115	Published: 3/24/04	39164-0005
N,N-dihalogenated amino acids and derivatives	Internat'l Application: WO 2005/020896	Published: 3/10/005	39164-0005

NovaCal has an exclusive option in the field of medical applications for the following patents:

Title	Patent	Date
Polymer protein composites and methods for their preparation and use	US Patent: US 5,914,367	Issued: 6/22/99
Polymer protein composites and methods for their preparation and use	US Patent: US 6,291,582	Issued: 9/18/01

In addition, the Company has filed three other patent applications, which presently are in confidential status until they are published.





## AGANOCIDETM ACTION ON BACTERIAL BIOFILM





Staining for live bacteria (data from Center for Biofilm Engineering, Montana State University, Bozeman). Green indicates live bacteria and red indicates dead bacteria. A: Treated with Saline. B: Treated with NVC-422 <sup>2, 3,4, 5</sup>

<sup>2</sup>Usnic acid, a lichen derivative, appears to inhibit some forms of biofilm growth. Francolini et al http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=525405

<sup>3</sup>The enzyme dispersin B appears to clear medical devices of biofilm. Kaplan et al http://www.nidcr.nih.gov/NewsAndReports/NewsReleases/NewsRelease08112004.htm

<sup>4</sup>Sequoia Sciences of San Diego lays claim to several compounds that inhibit microfilm formation and that are synthetically accessible. There is a legal dispute between Sequoia Sciences and one of its researchers with regard to ownership rights to at least one of these biofilm inhibitors (AAAS, Science & Policy, 1/19/06). http://sippi.aaas.org/ipissues/updates/?res\_id=623

<sup>5</sup> Cumbre Inc., Dallas, TX and Quorex Pharmaceuticals, Carlsbad, CA, are taking other directions in their work on the biofilm issue.



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The topic of biofilms is widely researched. Just for example, the Website of PubMed, a joint service of the National Institutes of Health and the National Library of Medicine<sup>5</sup> lists abstracts for 125 articles relating to the subject appearing since the beginning of 2006. There are 35 articles discussing the destruction of biofilms that have appeared since 2001. Dealing with these phenomena, in our opinion, lies at the crux of the efficacy of the Aganocides, although NovaCal has mapped out possible uses for these products that are non-biofilm related. At any rate, management feels that the Company is well ahead of competition in the biofilm area, having safe products that can destroy biofilm, and backed up by convincing clinical data.

<sup>5</sup>Link: <u>http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed</u>

### **Biofilm-Related Applications—Prevention of Infection in Medical Devices**

Aganocides potentially may be used to inhibit the build-up of biofilms on medical devices. Hospital-acquired infections are a growing problem, especially due to increasing ascendance of bacteria that are resistant to standard antibiotics. The overwhelming majority of these cases involve bacteria that attach themselves to a medical device and form a biofilm culture. The application to use of Aganocides to prevent the growth of bacteria biofilms on or in medical devices will be submitted by NovaCal to the FDA as Investigational Device Exemptions or IDEs. An (IDE) allows the device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification (501-k) submission to the FDA. In essence this process cuts down the time frame for final approval, because less clinical data is required than in an IND (Investigational New Drug) application.



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Aganocides Have Potential for Preventing Infections in Patients Involving:

- **∆** Urinary Tract Catheters
- **∆** Central Venous Catheters
- **∆** Dialysis Shunts
- **A** Mechanical Ventilators (Pneumonia)
- **▲** Surgical Sites
- **∆** Skin Grafts
- **▲** Extensive Burns

**Urinary Tract Catheters**—The Company has been testing NVC-422 in varying strengths in collaboration with the Center for Biofilm Engineering at Montana State University—Bozeman, against bacteria in dynamic flow urinary tract catheters with encouraging results.

**Central Venous Catheters**—There is a high incidence of blood stream infection in hospitals through use of these devices, which are usually filled with saline and/or other solutions, in order to prevent coagulation when not in the process of delivering drugs. Such mixtures are referred to as "lock" solutions and are considered Medical Devices by the FDA. NovaCal thinks that the risk of infection can be significantly reduced if NVC-422 were included in the lock solution.

**Dialysis Shunts**—Chronic hemodialysis patients are at high risk of infection, because this process requires vascular access for long periods. The Company expects to develop a lock solution (see above) containing NVC-422 to reduce or eliminate the incidence of such problems in this group of users.

**Mechanical Ventilators**—Ventilator-associated pneumonia is an airway infection that develops in patients whose breathing needs to be assisted by mechanical ventilators, because their respiratory functions have been compromised by conditions that do not permit breathing on their own. NovaCal has not yet mapped out a strategy to deal with this condition, but its profile would fit the generally anticipated use of Aganocides.

**Surgical Sites**—NovaCal expects to devise a solution of saline and Aganocides for use as a surgical irrigant prior to closure of incisions. This is expected to reduce significantly the number of bacteria entering the site during the procedure.





**Skin Grafts**—Subject to high infection rates, skin grafts are a logical area for use of Aganocides, either in artificial or autologous types (where the patient provides a graft to himself). Treatment with NVC-101 has been employed with success in a small sample of artificial graft patients. Management thinks that disinfection of artificial grafts would be considered a medical device by the FDA.

**Extensive Burns**—A safe product that can destroy biofilm is a critical requirement in this application, which, of course, is a prime characteristic of Aganocides. This is a limited market, and The Company might seek government and/or charitable funding with such a development program.



Source: http://www.fda.gov/cder/handbook/develop.htm



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During *pre-clinical* drug development, a sponsor must first submit data showing that the drug is reasonably safe for use in initial, small-scale clinical studies. The drug's toxic and pharmacologic effects are determined through *in vitro* and *in vivo* laboratory animal testing. If testing proves successful on this micro scale, an *IND* would be filed. Clinical testing would then begin.

**Phase 1** would include the initial introduction of the new drug into humans. These studies are closely monitored and may be administered to patients, but are usually conducted in healthy volunteers. **Phase 2** includes the early controlled clinical studies conducted to obtain preliminary data on the effectiveness of the drug in patients with the targeted disease or condition. Short-term side effects and risks associated with the drug, if any, would be determined. These studies are highly controlled, closely monitored, and conducted in an expanded though relatively small number of patients, usually involving several hundred people. **Phase 3** clinical studies are performed after preliminary evidence in Phase 2 suggests effectiveness of the drug. Phase 3 studies are intended to gather the additional information needed to evaluate the overall benefit-risk relationship of the drug, and usually include several hundred to several thousand people. It also must be shown that there is sufficient basis for extrapolating the clinical results to the general population and translating that information into specific physician labeling.

At this point, an *NDA* (New Drug Application) would be filed with sufficient information, data, and analyses to permit FDA reviewers to reach several key conclusions, including:





- Whether the drug is safe and effective for its proposed use(s)
- If the benefits outweigh the risks
- Whether the drug's proposed labeling is appropriate
- If the methods used in manufacturing are sufficient to preserve the drug's distinctive therapeutic qualities, strength, and purity

According to Dr. Neal Masia, the director of economic policy at Pfizer, Inc.: "Overall, the discovery and development of a new medicine takes about 12 to 15 years. Patents are granted along the way, and it usually takes at least a few years between the granting of patents and marketing approval...Estimates about the cost of developing a new drug vary widely, from a low of \$800 million to nearly \$2 billion per drug."<sup>6</sup>

CMR International—a major provider of R&D metrics to the global pharma industry<sup>7</sup>—carried out a survey of drug development between 1984 and 1999 and found that, in general, new molecular entities (NMEs—separately distinguishable chemicals) of *the anti-infective class had the fastest development times*. "Overall mean drug development times lay around the 12 to 13 year period, but for the anti-infective drug class this was between the 9.6 and 11.7 years. In fact, the fastest development time recorded for the 719 successfully launched drugs surveyed by CMR International over this time period, was for an anti-infective NME (at an astonishing 3.2 years!)"<sup>8</sup> Refer to chart in Appendix *iv* re development times.

<sup>&</sup>lt;sup>8</sup> http://www.inpharm.com/External/InpH/1,2580,1-3-32527-0-inp\_intelligence\_art-0-128425,00.html



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<sup>&</sup>lt;sup>6</sup> Jan. 2006 at USINFO.STATE.GOV http://usinfo.state.gov/products/pubs/intelprp/cost.htm

http://www.cmr.org

The Aganocides are anti-infective products. The development route for this class of drugs is well established, since so many antimicrobials have been approved by the FDA over the years. The vast majority of these drugs that are shown to be safe in initial studies obtain approval. And as indicated in the earlier referred-to CMR International study on drug development times, it is logical that FDA approval for these products might follow a relatively fast track. Partnering and licensing could defray a good deal of the capital costs of development programs. (Management's intention to sell the Company prior to product launch, if a ready buyer were found, certainly would accelerate the investor's exit time considerably.)

### Aganocides Have Potential as Prescription Drugs In Patients Involving:

- **△** Chronic Wounds
- **▲** Pre-Surgical Nasal Disinfection
- **▲** Chronic Sinusitis
- **∆** Otitis Media & Externa
- **▲** Periodontal Disease

**Chronic Wounds**—In areas where there is poor circulation bacteria may enter a wound and quickly establish a biofilm, thus preventing healing either by topical or systemic antibiotics. So far no product has been approved for this application. However, NovaCal's early studies seem to indicate that NVC-101 is effective for use in such applications, and accordingly the Company is developing a solution for ameliorating the healing process in chronic wounds. If development proves successful, an NDA could be filed in 2009.

**Pre-Surgical Nasal Disinfection**—Nasal bacteria, particularly MRSA (Methicillin-Resistant Staphyloccus Aureus), are a source of infection during surgical procedures. The chief product currently on the market for this application is of low efficacy and requires several days of use to disinfect the nasal passages. The Company thinks an Aganocide<sup>TM</sup> formulation in spray form could be highly effective and reduce the bacteria deactivation time to perhaps less than an hour.





**Chronic Sinusitis**—This is a large market affecting more than 30 million people in the U.S. In consort with a multinational pharma enterprise, the Company is conducting extensive animal safety and efficacy studies using NVC-422, with promising results to date.

**Otitis Media & Externa (middle & outer ear infections)**—Otitis media accounts for one-third of all doctor visits in children aged one through five. Management thinks that suitable formulations of Aganocides may be able to be used effectively against both of these maladies.

**Periodontal Disease**—Dental plaque is a biofilm that forms between teeth and gums. Since Aganocide<sup>TM</sup> compounds are effective against biofilm, as well as microbes that cause tooth decay, it appears that these products will be efficacious in both treating and preventing periodontal problems.

### **Non-Biofilm-Related Applications**

- **△ Ophthalmic Infections**
- **▲** Dermal Infections (MRSA)
- ▲ Mouth & Throat Infections
- ▲ Pulmonary Infections (Cystic Fibrosis Patients)

The safety and effectiveness of Aganocides present a number of opportunities for use against non-biofilm-related infections. NVC-422 is currently being tested in conjunction with a major drug firm for use in ophthalmic applications. A topical solution or ointment suggests itself for application in dermal conditions. Aganocide<sup>TM</sup> use is implied for many other types of infections.

Much of the Anti-infective Market Fair Game for "Aganocidal" Treatment

Statistics on the size of various medical markets are fragmentary at best. Mountains of data are kept by hospitals, clinics, pharma companies, physicians, public health intermediaries, and others, and collated into estimates with exceptionally broad ranges, where upper bounds often exceed several hundred percent of lower bounds.





While it is fairly easy to find the dollar volumes for specific classes of drugs, or specific drugs per se, since most market research is categorized in this fashion, it is not an easy task to size up specific clinical needs. Some individual hospitals conduct studies on various infections in their patient populations, and this data is frequently extrapolated to indicate market size by induction.

According to IMS Health, the leading pharma market data company (imshealth.com), nearly half of world market audited spending on systemic antibiotics occurs in the U.S., and equates to nearly \$15 billion.<sup>9, 10</sup> As previously mentioned, antibiotics increasingly generate resistance, and if solutions to numerous medical problems using non-antibiotic antimicrobials like NovaCal's Aganocide<sup>TM</sup> compounds prove out, it is clear that the opportunities in just this one segment of anti-infectives is mammoth.

*Grosvenor* has provided U.S. estimates for the size of various major clinical applications targeted by NovaCal, and collated them into the pie chart shown in Figure 1 on page 16, below. We have listed some of the sources used in making our estimates; but Grosvenor is solely responsible for the final numbers, which in our judgment were the most representative and authoritative of the large number of resources consulted.



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<sup>9</sup> http://pharmalicensing.com/articles/disp/1115636372\_427f42944efa9

<sup>&</sup>lt;sup>10</sup> For a different take on the market, please see Swiss pharma company Arpida Ltd. (ARPN.SWX) Website: http://www.arpida.ch/index.php?MenuID=13&UserID=1&ContentID=12&way2go=5cdff21fbf4a6a808b2e58 b4fda337c9



Estimates provided by Grosvenor Financial Partners, LLC; some resources identified below.

1-OTITIS MEDIA & EXTERNA: <u>http://www.progressivehealth.com/catalog/Anistil.htm</u> <u>http://www.emedicine.com/emerg/topic351.htm</u>

2-CHRONIC SINUSITIS:

http://www.stonecrestmedical.com/CustomPage.asp?guidCustomContentID={71B7E787-0404-4C67-9DE5-1102543485E0}

http://www.clevelandclinicmeded.com/diseasemanagement/allergy/sinusitis/sinusitis.htm#pathophysiology 3-CHRONIC WOUNDS: <u>http://www.o-wm.com/article/4755</u>

4-URINARY TRACT CATHETER INFECTIONS: <u>http://www.kanebiotech.com/press\_release112305.htm</u> 5-CENTRAL VENOUS CATHETER INFECTIONS: <u>http://www.migenix.com/newsreleases/020319.pdf</u> 6-VENTILATOR-ASSOCIATED PNEUMONIA: <u>http://www.jhconline.com/article-julaug2005-</u> dirtysecret.asp

7-MRSA DISINFECTION: ibidem

8-OPHTHALMIC INFECTIONS: http://www.bccresearch.com/biotech/B183.html

9-DERMATOLOGICAL INFECTIONS: IMS National Prescription Audit 2001 (May 2002 Revision), Connetics 2005 Annual Report 10K, Page 7, ¶1.

![](_page_16_Picture_10.jpeg)

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![](_page_16_Picture_13.jpeg)

### Prospects for Aganocides Appear Promising—But Not Necessarily a Slam-Dunk

In Addition to huge costs and protracted timelines for developing new drug products, "only about 30% of new medicines actually earn enough revenue during their patented product lifecycle to cover the average upfront cost of development," according to Pfizer's Dr. Neal Masia (please refer to footnote <sup>6</sup>). Sizable amounts of research dollars in the competitive pool are, in many cases, chasing after remedies to similar problems. In the U.S. alone, over \$50 billion of investments in biotech and biomedical R&D was made in 2005, representing more than 2000 compounds under development, according to a study done by Burrill & Co. for PhRMA—Pharmaceutical Research and Manufacturers of America.<sup>11</sup> Literally, hundreds of companies, many of them promising startups, are seeking out the next blockbuster, should such a thing exist anymore, with caution increasingly entering the picture with regard to unforeseen deleterious side effects.

In some of the market segments that NovaCal expects to compete in there is currently very little or no known competition. For example, in infections involving biofilm, there are no effective treatments except the profligate and extended use of antibiotics, which may not necessarily be a guaranteed curative. Known research in this area is proceeding along several lines that differ from the Aganocide<sup>TM</sup> approach (please see footnotes <sup>2, 3, 4, 5</sup>, page 7). Some of these may also prove promising, and NovaCal's cachet in this area might depend on being first to market.

<sup>&</sup>lt;sup>11</sup><u>http://www.phrma.org/news\_room/press\_releases/r%26d\_investments\_by\_america%92s\_pharmaceutical\_research\_companies\_nears\_record\_%2440\_billion\_in\_2005/</u>

![](_page_17_Picture_4.jpeg)

![](_page_17_Picture_6.jpeg)

There presently is no approved drug for the prevention and inhibition of bacteria in chronic wounds. Systemic antibiotics are the primary method of dealing with infection in chronic wounds, but these products have little effect on wound surfaces. Ointments and bandages containing silver derivatives have also been used in this application, but with limited success.

A number of small pharma have experimented with various forms of chlorine in solution<sup>12</sup> or with certain modified chlorine molecules and compounds.<sup>13</sup> The former approach may be somewhat useful, but is limited by its cytotoxicity. The latter approach, in the Company's estimation, would provide an unstable product, since NovaCal has experimented in this direction extensively.

Medical device companies, in general, have substantial resources at their disposal, and continue to incorporate means to reduce or eliminate the survival of pathogens during the use of catheters, shunts, etc. According to the Company, these techniques so far have met with little success beyond the first few days of implementation.

As mentioned previously, NovaCal is pursuing a three-prong strategy of licensing, partnering, and in-house development of its intellectual property. The schedule contemplated by the Company is outlined in Appendix *iv*, near the end of this report. It is important to remember that this blueprint is a projection, and its actual execution might take longer than presently anticipated. Much of its preclinical work is outsourced to qualified contractors.

 <sup>&</sup>lt;sup>12</sup> Oculus Innovative Sciences, Dermacyn<sup>TM</sup> Wound Care, Microcyn<sup>TM</sup> Disinfectant, Sterilant and Antiseptic, <u>www.oculusis.com</u>
<sup>13</sup> Pathogenics, Inc., Hingham MA, OTC Pink PTGN.PK

![](_page_18_Picture_5.jpeg)

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![](_page_18_Picture_8.jpeg)

For large-scale Phase 3 studies, NovaCal expects to use Contract Research Organizations, or CROs, to ensure that studies are completed in a timely manner. The Company does not expect to be a manufacturer of its finished products. There are numerous outside manufacturers capable of producing drugs under the FDA-mandated Good Manufacturing Practices code.

Partnering and licensing are crucial to the success of NovaCal, in order that it may carry out its clinical studies on its planned timetable. The Company currently has very limited resources, and is need of completing an additional financing within the next few months. Additionally, the process of negotiating licensing and partnering agreements can be a protracted procedure, so there is no assurance that management will be able to fulfill its objectives and devote the resources to direct program costs as currently projected in Figure 2 on page 20 below. Figures 3, 4, and 5, pages 21 and 22, respectively graph the direct program costs, projected partnering payments, and the difference between the two, on a quarterly basis for the 2006—2008 time period.

A projected partnering payment of \$125 million anticipated for the Q3 2008 has been omitted because of its relative disproportionateness to other quarterly payments, in view of the uncertainty in timing for negotiating these contracts.

![](_page_19_Picture_3.jpeg)

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![](_page_19_Picture_6.jpeg)

![](_page_20_Figure_0.jpeg)

CLINICAL STUDIES: 2-CHRONIC ULCERS 3-CENTRAL VENOUS CATHETERS 4-URINARY TRACT CATHETERS 5-DIALYSIS ACCESS CATHETERS 6-VENTILATOR ENDOTRACHEAL TUBES 7-MRSA DISINFECTION

![](_page_20_Picture_2.jpeg)

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![](_page_20_Picture_5.jpeg)

![](_page_21_Figure_0.jpeg)

![](_page_21_Figure_1.jpeg)

![](_page_21_Figure_2.jpeg)

![](_page_21_Picture_3.jpeg)

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![](_page_21_Picture_6.jpeg)

![](_page_22_Figure_0.jpeg)

Note: Omits a projected \$125 million payment in Q3 08 for licensing out MRSA Disinfection, CVC, Urinary Tract Catheter, and Dialysis Access Shunt applications, due to the outsize nature of the amount.

![](_page_22_Picture_2.jpeg)

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![](_page_22_Picture_5.jpeg)

#### **Management**

**Ron Najafi, Ph.D.**, Founder, Chairman and CEO. In 1996, Dr. Najafi founded Cal Pac Lab, Inc. from which NovaCal was spun out in 2001. At Cal Pac Lab, he invented the patented ECO-Funnel, now a standard safety product for major pharmaceutical and chemical companies, as well as inventing the core technology of NovaCal and co-inventing NVC-101. He also founded and later sold Cal Pac Lasers, Inc. that developed and marketed lasers and LED products. Since 1994, he has been a consultant on electrolysis technology and its related chemistry to a number of Japanese companies and is currently a consultant to Panasonic Corp. Prior to founding Cal Pac Lab and Cal Pac Lasers, Dr. Najafi worked for Perkin Elmer Applied Biosystems, where he was responsible for the synthesis of DNA components and where he was recognized as "Perkin Elmer Scientist of the Year". He has also worked for Aventis (then Rhone Poulenc Rorer) synthesizing a new generation of asthma drugs, and for Aldrich Chemical Co. as team leader in Organo-Silicon development. Dr. Najafi has a Ph.D. in Chemistry from the University of California at Davis and a B.S. and M.S. in Chemistry from the University of San Francisco. He has written numerous articles in peer-reviewed journals and has been inventor on several US patents.

**Jack O'Reilly,** Senior Vice President, Corporate Development & CFO. Prior to joining the Company in 2002, Mr. O'Reilly was Founder and Chairman of Xomol Inc., a healthcare software company. He was Senior Vice President Corporate Development and Chief Financial Officer at Health Hero Network, Inc. where he raised over \$29 million in three rounds of financing for this company that focused on deploying an Internet appliance for communication with the chronically ill. Prior to Health Hero, he served as President of Vectorpharma International Corporation, a physical chemistry-based drug delivery company successfully sold to a European pharmaceutical company, Chief Executive Officer of Spectra Biomedical, Inc. where he established a new strategic direction that led to its sale to Glaxo and Chief Financial Officer of Abaxis, Inc., where a secondary offering was successfully completed. From 1975 to 1992, he held various positions at Syntex Corporation, including heading Corporate Development and serving as Group Finance Director, Pharmaceuticals and Animal Health. Mr. O'Reilly was also a consultant with McKinsey & Company, Inc. Mr. O'Reilly holds an M.B.A. from Stanford University and a B.A. from Oxford University.

**Behzad Khosrovi, Ph.D.,** Vice President, Research and Development, joined the company at the end of 2003. He continues to support, on a consulting basis, pharmaceutical development at Neurobiological Technologies, Inc.(NTII), where he was Vice President of Pharmaceutical Development. Prior to joining Neurobiological Technologies, Dr. Khosrovi worked for fifteen years at Cetus Corporation, where he held a variety of Development positions with the last five years there as Vice President of Development, taking products through from research into manufacturing and product registration. Dr. Khosrovi was educated in the UK with a B.A./M.A. in Natural Sciences from Cambridge University and a Ph.D. in Applied Microbiology from the University of Manchester Institute of Science and Technology.

![](_page_23_Picture_4.jpeg)

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![](_page_23_Picture_7.jpeg)

**Colin Scott, M.D.,** Vice President Clinical Research and Development. Dr. Scott joined NovaCal in January 2006 from Glycomimetics, Inc., where he was Vice President, Drug Development focused on the development of drugs targeting antibiotic resistance. Prior to that he was Vice President, Clinical and Regulatory Affairs at Arriva Pharmaceuticals, focused on hereditary emphysema. He was also Vice President, Clinical and Regulatory Affairs at Emisphere Technologies concentrating on the clinical development of oral drug delivery products for insulin and an asthma drug. He held similar positions at other companies, including Fisons, CytoMed and ASTA Medica. He managed European clinical trials for Sterling Winthrop and worked on worldwide regulatory affairs for Wyeth. Dr. Scott completed his medical studies at Glasgow University, and his medical positions included House Officer, Infectious Diseases.

**Kenneth Krantz, M.D., Ph.D**, Vice President Medical Affairs, joined the company in January 2004 on a part-time basis. He has very broad experience organizing and conducting clinical trials, having been involved in 23 INDs and 16 NDAs. He was Director of Clinical Pharmacology and Pharmokinetics at G.D.Searle, Senior Director, Immunology and Anti-Infective Clinical Research at Schering-Plough, Vice-President, Clinical Research and Biostatistics at Ayerst Laboratories, Executive Director, Biotech Clinical Research at Ortho Biotech (J & J) and Vice President, Clinical and Regulatory Affairs at Neurocrine Biosciences. He has also been a consultant to many companies. He has an M.D. and a Ph.D. in Pharmacology from the University of Chicago Medical School.

**Mansour Bassiri, Ph.D.**, Senior Director of Microbiology and Cell Biology. Dr. Bassiri joined NovaCal (then Cal Pac) in 2000 from the University of California at Davis, School of Medicine, where he served as a research faculty member in the department of Dermatology and supervised the research of doctoral and post-doctoral students. He conducted post-doctoral research in Immunology, Microbiology and gene therapy at UC Davis. He had been a consultant to Cal Pac since 1996 and was responsible for much of the pre-clinical work on NVC-101. He holds a Ph.D. in Microbiology from UC Davis, M.S. in Clinical Microbiology at Cal State, Fresno and a B.S. in Biochemistry from Oklahoma State University. He has published several articles in peer-reviewed journals and is the inventor of NVC-201.

**Rakesh Jain, Ph.D**., Director of Research. Dr. Jain joined NovaCal in January 2006 having previously been Associate Director at Vicuron Pharmaceutical, Inc. (sold to Pfizer for \$1.9 billion.) During his six years at Vicuron, he led drug discovery efforts that resulted in new antibiotics, one of which is currently in clinical trials. He also managed an R & D collaboration with Novartis. Prior to Vicuron, he was at Intercardia Research Labs, focusing on structural modification of antibiotic drugs. He has also worked at Roswell Park Cancer Institute, Buffalo, NY, the National Institute of Immunology in New Delhi and the Central Drug Research Institute in Lucknoiw, India, from where he obtain a Ph. D. in Synthetic Organic Chemistry.

![](_page_24_Picture_4.jpeg)

![](_page_24_Picture_6.jpeg)

Lu Wang, Ph.D., Director of Chemistry. Dr. Wang joined NovaCal from the Department of Chemistry, Purdue University, where she worked with Professor Dale Margerum (Company Scientific Advisor) on the chemistry of products similar to NVC-101. In addition to a Ph.D. from Purdue University, Dr. Wang has an M.S. in Chemistry from the University of Central Florida, an M.S. in Physics from the University of Science and Technology, China and a B.S. in Chemistry from Peking University, Beijing.

**Michael Mueller, Ph.D.**, Director of Intellectual Property and Business Development, joined NovaCal in 2005. He has worked at the Office of Technology Licensing, Stanford University, managing a portfolio of patents. Dr. Mueller was Vice-President, US Operations for the Swiss bioinformatics company, Genedata, and held different positions at Molecular Applications Group (acquired by Celera). He has a Ph.D. in Molecular Biology from the University of Zurich .

**Luana Staiger,** Consultant, Regulatory Affairs. Ms. Steiger is an independent consultant and has been working with NovaCal since 2002, when she was Senior Director of Regulatory Affairs at ICON Clinical Research. Prior to that, she was Vice President of Regulatory Affairs at Matrix Pharmaceuticals. She has also held management positions in Regulatory Affairs at Gilead Sciences, Landec, Syntex and Zoecon. Ms. Steiger has a B.S. from the University of California at Davis.

**Herwig von Morze, Ph.D.** Consultant, Patent Strategy. Dr. von Morze is International Patent Consultant for Heller, Ehrman, White & McAuliffe. He has over 30 years of patent experience with the last ten years focused on designing effective patent strategies for life science companies. He combines experience of inorganic electrochemistry with very wide life science experience. He holds a Ph.D. in Inorganic Chemistry from the University of Vienna, Austria.

![](_page_25_Picture_4.jpeg)

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![](_page_25_Picture_7.jpeg)

#### **Glossary**

**Antibacterial**—Capable of fighting bacterial infections, as opposed to infections due to other microbes.

Antibiotic—A substance, such as penicillin or streptomycin, produced by or derived from certain fungi, bacteria, and other organisms, that can destroy or inhibit the growth of other microorganisms.

**Anti-infective**—A drug capable of killing or inhibiting the spread of an infectious agents; a generalized term that encompasses antibacterials, antibiotics, antifungals, antivirals, and antiprotozoans.

Antimicrobial: Another generalized term for chemicals, or other substances that either kill or slow the growth of microbes.

Antiviral—Differentiated as a drug that fights viruses, as distinct from other microbes like bacteria or fungi.

**Biofilm**— Biofilm forms when bacteria adhere to surfaces in aqueous environments and begin to excrete a slimy, glue-like substance that can anchor them to all kinds of material – such as metals, plastics, soil particles, medical implant materials, and tissue; plaque, slippery rocks in water, and residue in sink drains are some examples (courtesy of MSU—Bozeman.)

Cytotoxicity—The quality of being toxic to cells.

![](_page_26_Picture_8.jpeg)

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![](_page_27_Picture_0.jpeg)

# **OPERATING PLAN—TIMELINE**

![](_page_27_Figure_2.jpeg)

![](_page_27_Picture_3.jpeg)

Appendix *i* 

![](_page_28_Picture_0.jpeg)

### Statement of Operations for the Years 2004 & 2005 and from 1/20/2000 (Inception) to December 31, 2005

	For the year ended December				
		December 31,		Inception to	
		2005	2004	December 31, 2005	
Operating Expenses:					
Salaries and benefits	\$	1,511,817	1,097,343	3,243,276	
Professional services		681,486	481,407	1,513,762	
General and administrative expenses		657,561	509,402	1,413,179	
Research and development		670,739	579,285	1,456,098	
Write-off and disposal of property and equipment		355	120,002	120,357	
Depreciation and amortization		47,171	39,065	144,133	
Total operating expenses		3,569,129	2,826,504	7,890,805	
Interest and other investment income, net	_	106,079	22,294	103,188	
Net loss before income taxes		(3,463,050)	(2,804,210)	(7,787,617)	
Income tax expense	_				
Net loss	\$	(3,463,050)	(2,804,210)	(7,787,617)	

![](_page_28_Picture_3.jpeg)

### Appendix *ii*

![](_page_29_Picture_0.jpeg)

## Balance Sheets December 31, 2005 & 2004

Asset	S		2005	2004
Current assets:				
Cash and cash equivalents		\$	2,208,396	4,046,823
Marketable securities			1,003,723	_
Prepaid expenses and other current asse	ts		82,542	119,090
	Total current assets		3,294,661	4,165,913
Property and equipment, net			267,129	193,541
	Total assets	\$	3,561,790	4,359,454
Liabilit	ies			
Current lighilities.				
Accounts navable and accrued liabilities		2	310 179	246 098
Canital lease obligation		Φ	510,177	11 757
Capital lease obligation	Total current liabilities		310 170	257 855
Canital lass abligation noncurrent	Total current natinities		510,179	7 967
Capital lease obligation - noncurrent	Total liabilities		310 170	265 822
Stockholder	- Fourty		510,177	203,022
Common stock \$0.01 per value: 64.000.000 and 44	000 000 shares authorized:			
at December 31, 2005 and 2004, respect	volv: 10 000 001 and 8 000 621			
shares issued at December 31, 2005 and 2004, respect	2004 respectively	Φ	100 000	80.006
Duefenned steek \$0.01 new value: 30.000.000 and 10	2004, respectively	Φ	100,990	09,900
at December 21, 2005 and 2004 respect	volve 17 499 222 and 16 219 066			
at December 51, 2005 and 2004, respect	2004 mappatively		174 002	162 101
Additional noid in conital	2004, respectively		1/4,000	103,101
Additional paid-in capital			10,707,705	0,954,102 94,500
Stock subscriptions received			_	84,500 (972,550)
Stock subscriptions receivable			(1.2.10)	(8/3,550)
Accumulated other comprehensive loss			(4,348)	
Accumulated deficit during developmen	t stage		(7,787,617)	(4,524,567)
	Total stockholders' equity		3,251,611	4,093,632
	Total liabilities and stockholders' equity	\$	3,561,790	4,359,454

![](_page_29_Picture_3.jpeg)

Appendix *iii* 

![](_page_30_Picture_0.jpeg)

# SUCCESS RATE FIRST HUMAN DOSE TO MARKET

![](_page_30_Figure_2.jpeg)

**SOURCE: CMR INTERNATIONAL (2003)** 

![](_page_30_Picture_4.jpeg)

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Appendix *iv*