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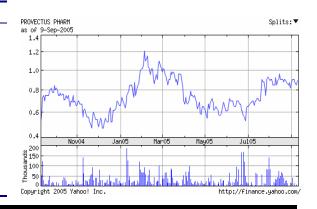
# **Developing Advanced Therapies in Oncology and Dermatology**

Snapshot September 12, 2005

Provectus Pharmaceuticals, Inc. ("Provectus" or "the Company") is developing advanced prescription drugs in the fields of oncology and dermatology, which are designed to target and destroy the deadliest of cancers and to treat severe skin diseases such as **psoriasis**<sup>T</sup>, respectively. The Company is also developing biotechnologies to augment vaccine production and detect viruses (including an innovative "virus hunter" method). To supplement its development efforts, Provectus produces and markets over-the-counter (OTC) skin care products, and licenses patented technologies for therapeutic and cosmetic medical devices. Its oncology portfolio contains Provecta™, an injectable oncology drug in development to treat melanomas, and focal tumors of the breast, liver, and prostate. Its dermatology portfolio contains Xantryl™, a topical drug in development to treat psoriasis and other dermatology disorders including acne, actinic keratosis (AK), and eczema. The Company's therapeutic device technologies are focused in three main areas: (1) the treatment of ocular melanomas; (2) the improvement of multiphoton microscopy and diagnostic devices; and (3) devices that cut tissue for precise surgical applications, such as laser vision correction. Provectus currently markets an antibacterial hand and surface spray called Pure-ific™, which immediately eradicates up to 99.9% of germs on the skin and prevents regrowth for six hours. The Company has also conducted a pilot-scale run on the manufacturing of a hand cream, which contains both antiperspirant and antibacterial properties, called GloveAid™, to treat the irritation associated with wearing disposable gloves. A secondstage product, called **Pure-Stick™**, is a non-toxic, topical agent to treat acne.

## **Recent Financial Data**

B)



### **Key Points**

- Provecta<sup>™</sup>, when injected into tumor tissue, concentrates in the tumor at cytotoxic levels while quickly dissipating from healthy tissue, making it safer and more effective than conventional therapies, such as chemotherapy and radiation. Tumor ablation with Provecta<sup>™</sup> may also stimulate an immune response that can eliminate tumor tissue spreading from the treatment site. Provecta<sup>™</sup> can be combined with radiation, increasing its effect on tumor tissue and potentially enabling less radiation use.
- In August 2005, Provectus announced that the first group of subjects had completed treatment in a Phase I clinical trial for malignant melanoma (the most deadly type of skin cancer) with Provecta™ and that the treatment was well tolerated at the initial lower dose level.
- Like Provecta<sup>™</sup>, Xantryl<sup>™</sup> is only active in abnormal or diseased tissue, making it safer to use than existing products. Xantryl<sup>™</sup> is delivered directly to diseased tissue through the skin and may be activated with ambient light, reducing the potential for side effects in healthy tissue. Xantryl<sup>™</sup> successfully completed Phase I clinical studies for psoriasis and actinic keratosis and is expected to begin Phase II for psoriasis early next year.
- As part of its growth and development strategy, Provectus is pursuing partnerships for the development of its products. Its core technology has attracted the attention of some of the larger pharmaceutical and biomedical technology companies, including Schering-Plough Corporation (SGP-NYSE), Varian Medical Systems, Inc., (VAR-NYSE), and Carl Zeiss, Inc. (CZMWF.PK), among others.
- The Company holds 12 issued and 3 pending patents from the U.S. Patent and Trademark Office (USPTO), with an additional 19 U.S. patents under examination.

<sup>\*</sup>BOLD WORDS IN TEXT ARE REFERENCED IN GLOSSARY ON PAGES 41-42.



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### **Executive Overview**

Provectus Pharmaceuticals, Inc., ("Provectus" or "the Company") is developing advanced prescription drugs in the fields of oncology and dermatology, which are designed to target and destroy the deadliest of cancers and to treat severe skin diseases such as psoriasis. The Company is also developing biotechnologies to augment vaccine production and detect viruses (including an innovative "virus hunter" method). To supplement its development efforts, the Company produces and markets over-the-counter (OTC) skin care products, and licenses patented technologies for therapeutic and cosmetic medical devices. The Company is divided into four operating subsidiaries that are highlighted in Table 1 and subsequently described below. Extensive details on each of these subsidiaries and the products/technologies either in development or on the market are provided within this Executive Informational Overview™ (EIO™).

### **Corporate Structure**

	Table 1
	Provectus Pharmaceuticals, Inc.
COR	PORATE STRUCTURE: FOUR OPERATING SUBSIDIARIES
Provectus Pharmatech, Inc.	Prescription drugs, which encompass the areas of dermatology and oncology
Provectus Devicetech, Inc.	Medical device systems, which include therapeutic and cosmetic lasers
Provectus Biotech, Inc.	Patented, cost-effective methods used to improve the yield or performance of recombinant DNA products (including enzymes, antigens, drugs, or other proteins) and vaccines
Pure-ific, Corp.	Over-the-counter (OTC) products, which address markets primarily involving skin care applications
Source: Provectus Pharmaceutica	ils, Inc.

### Provectus Pharmatech. Inc.

Cancer treatments that are currently on the market typically destroy healthy cells along with the cancer cells they are meant to attack. Further, they can be very ineffective at stopping **metastasis**, the often-fatal spread of the disease to remote locations in the body. Provectus is developing a novel pharmaceutical approach to cancer that has been the subject of extensive pre-clinical studies and has recently completed treatment in patients enrolled in a Phase I clinical trial.

Provecta<sup>™</sup> is an injectable oncology drug in development to treat melanoma and focal tumors of the breast, liver, and prostate. This drug is comprised of a sterile saline solution of **Rose Bengal (RB)**—a stable, non-toxic substance that exhibits therapeutic effects solely in tumor tissue. When injected into tumor tissue, Provecta<sup>™</sup> concentrates in the tumor at cytotoxic levels while quickly dissipating from healthy tissue, making it safer and more effective than conventional therapies, such as chemotherapy and radiation. Simultaneously, tumor ablation with Provecta<sup>™</sup> may stimulate an immune response that can eliminate tumor tissue which has spread from the treatment site (metastatic tumors). At lower dosages, Provecta<sup>™</sup> can also be combined with radiation, increasing the effects of radiation on tumor tissue and potentially enabling less radiation to be used, thereby subjecting patients to fewer side effects.

In August 2005, the Company announced that the first group of subjects had completed treatment in a Phase I clinical trial for malignant melanoma (the most deadly type of skin cancer), and that the treatment was well tolerated at the initial lower dose level. Additionally, preliminary therapeutic effects were characterized as being comparable to those observed in preclinical studies. The study is being conducted at two dosage levels with both dosage levels having the potential to show safety, preliminary efficacy, and the "bystander effect"—potential effects on nearby untreated tumors.



Like Provecta<sup>™</sup>, Provectus' other pharmaceutical candidate in development, Xantryl<sup>™</sup>, is only active in abnormal or diseased tissues, potentially making it a safer alternative than existing products. Xantryl<sup>™</sup> is delivered directly to diseased tissue through the skin and may be activated with ambient light, reducing the potential for side effects in healthy tissue. Xantryl<sup>™</sup> is applied topically as a gel that targets chronic, severe skin afflictions such as psoriasis as well as eczema and acne.

The active ingredient in Xantryl™ is RB, the same substance used in Provecta™. To date, Xantryl™ has been the subject of three Phase I clinical trials for psoriasis and two additional Phase I trials for actinic keratosis. In the Phase I trials for psoriasis, after 30 days a single-dose treatment yielded an average reduction in plaque thickness (patches of raised skin) of 51%; this response further improved to 60% by 90 days. No pain or significant side effects were observed in any of the Phase I trials.

### Provectus Devicetech, Inc.

Provectus has developed a number of intellectual properties and technologies in the area of medical devices, with six U.S. patents and six pending patent applications held in two market sectors: therapeutic and cosmetic devices. The therapeutic device technologies are focused in three main areas: (1) the treatment of ocular melanomas; (2) the improvement of multiphoton microscopy and diagnostic devices; and (3) devices that cut tissue for precise surgical applications, such as laser vision correction. Provectus' devices are intended to increase ease of use and performance of multiphoton microscopes; make multiphoton devices practical for *in vivo* diagnosis; give superior performance for next-generation laser ablation procedures such as eye surgery; and to become a highly effective tool in treating melanoma, precisely targeting only the tumor. The Company has stated its intent to license these technologies rather than to develop them internally.

### Provectus Biotech, Inc.

Provectus is developing biotechnologies to augment vaccine production and to detect viruses (including an innovative "virus hunter" method) used to identify dangerous new viruses. This technology may play a crucial role in discovering the underlying cause of certain cancers and other serious diseases, and ultimately in producing preventative vaccines. For example, the recent demonstration that vaccination against **human papillomavirus (HPV)** may prevent cervical cancer illustrates that many cancers may be caused by viruses. Provectus' technology may be used by pharmaceutical companies to discover the cause and develop preventative vaccines against cancers of the breast, prostate, and other parts of the body.

### Pure-ific Corp.

Provectus markets over-the-counter (OTC) products that are designed to be safer and more specific than competing products on the market. The Company's OTC products typically use compounds with potent antibacterial and antifungal activity as building blocks, and then combine these building blocks with anti-inflammatory and moisture-absorbing agents. Products with these properties can be used for treating many dermatologic conditions, including hand irritation and mild-to-moderate acne. The most advanced OTC product, Pure-ific™ Anti-bacterial Hand Spray, is marketed and is both effective and convenient—killing over 99.9% of germs and improving upon conventional messy gel products. Additionally, GloveAid™ is a hand cream designed to reduce the discomfort of wearing disposable gloves. A second-stage product, Pure-Stick™, is a non-toxic, topical agent to treat acne.

### **Corporate History**

Provectus Pharmaceuticals, Inc. was incorporated in Colorado on May 1, 1978, as SPM Group, Inc. SPM Group ceased operations in 1991 to become a development-stage company on January 1, 1992, with the corporate mission of seeking out acquisitions of properties, businesses, or merger candidates. A decade later, on April 1, 2002, SPM Group changed its name to Provectus Pharmaceutical, Inc. and reincorporated in Nevada for the purpose of merging with Provectus Pharmaceuticals, Inc., a privately-held Tennessee corporation, referred to as PPI.



On April 23, 2002, an Agreement and Plan of Reorganization between Provectus Pharmaceutical and PPI was approved by the written consent of a majority of the outstanding shares of Provectus Pharmaceutical. As a result, holders of 6,680,000 shares of common stock of Provectus Pharmaceutical exchanged their shares for all of the issued and outstanding shares of PPI. As part of the acquisition, Provectus Pharmaceutical changed its name to "Provectus Pharmaceuticals, Inc." and PPI became its wholly-owned subsidiary. For accounting purposes, the transaction was treated as a recapitalization of PPI.

On November 19, 2002, the Company acquired Valley Pharmaceuticals, Inc., a privately-held Tennessee corporation formerly known as Photogen, Inc., by merging the subsidiary PPI with Valley and naming the surviving corporation Xantech Pharmaceuticals, Inc. With the acquisition of Valley, the Company acquired its most important intellectual property—issued U.S. patents and patentable inventions. As a development-stage organization, the Company had not generated any revenues from the assets acquired.

On December 5, 2002, Provectus acquired the assets of Pure-ific LLC, a Utah limited liability company. The Company created a wholly-owned subsidiary, Pure-ific Corporation, to operate that business. It acquired the product formulations for Pure-ific<sup>™</sup> personal sanitizing sprays, along with the "Pure-ific<sup>™</sup>" trademarks, which it continued to develop under the "Pure-ific<sup>™</sup>" brand name.

### Headquarters, Manufacturing, and Employees

Provectus Pharmaceuticals, Inc. has its corporate office and operations in Knoxville, Tennessee, where it leases approximately 6,000 square feet of office and laboratory space. The Company works with outside organizations to manufacture its prescription drugs and OTC products. Provectus has ongoing relationships with two OTC product manufacturers, EXAL, Inc. and 220 Laboratories, Inc., and several other OTC service vendors that manufacture, package, warehouse, and distribute the Company's OTC products. The Company has four full-time employees.



# **Growth Strategy**

### **Revenue Model**

Provectus has a portfolio of both marketed products and candidates in development, which provide a diversified revenue structure. The Company's near-term operating strategy is to launch several OTC products that could generate growing income streams to help fund capital requirements for longer-term projects in the prescription drug and medical device arenas. Once these products have progressed, the goal is to license them to marketing partners, sell them, or spin them off. The Company has no plans to develop its own sales effort for prescription drugs or medical devices. Figure 1 provides a depiction of this structure followed by descriptions of the Company's overall growth strategy, by subsidiary.

# Figure 1 Provectus Pharmaceuticals, Inc. REVENUE OPPORTUNITIES

#### **Near-Term Revenues**



### OTC Products

- Pure-ific™
- GloveAid™
- Pure-Stick™
- Other Skin Applications

### Licensable IP

- Laser Microscopy
- Melanoma Treatment
- Vision Correction
- · Biotech (Vaccines)



### **Longer-Term Growth**



### Oncology

- Melanoma
- Liver Cancer
- Breast Cancer
- Prostate Cancer

### **Dermatology**

- Psoriasis
- Severe Acne
- Actinic Keratosis
- Eczema



Source: Provectus Pharmaceuticals, Inc.

Oncology and Dermatology (Provectus Pharmatech, Inc.)

Provectus entered the cancer therapy market with the goal of addressing the limitations of current treatments and to deliver improved efficacy, lower toxicity, and little to no side effects. The Company intends to develop Provecta™ to treat melanoma, and focal tumors of the breast, liver, and prostate. The global cancer market is one of the most far-reaching pharmaceutical markets in the world, representing \$20 billion per year and expected to increase to over \$45 billion by 2011, according to Research and Markets Ltd. (<a href="www.researchandmarkets.com">www.researchandmarkets.com</a>). As part of the development strategy for this product, the Company intends to pursue joint development or licensing agreements with major pharmaceutical partners.

Similar to its growth strategy in oncology, Provectus has entered the dermatology market in order to address the limitations of current treatments, with a goal of delivering improved efficacy, lower toxicity, and few to no side effects. The Company intends to develop Xantryl™ to treat psoriasis and other skin



disorders such as acne, actinic keratosis, and eczema. The principle issues with current treatments are their high costs and limited specificity, which can cause collateral damage to the surrounding health tissue. According to the National Psoriasis Foundation, psoriasis affects some 2.1% of the U.S. population and has been diagnosed in 4.5 million American adults. Synonymous with its development strategy in oncology, the Company intends to pursue joint development or licensing agreements with major pharmaceutical partners.

Medical Device Systems (Provectus Devicetech, Inc.)

Provectus has developed a number of intellectual properties and technologies in the areas of medical devices and biotechnology. Its devices include multiphoton microscopes and diagnostic instruments; laser ablation technologies, such as for eye surgery; and devices for the treatment of ocular melanomas. The combined market for these in both therapeutic and cosmetic therapies is believed to exceed \$1 billion (Source: *Medical Laser Report, Vol. 14, No. 1, January 2000, PenWell Publications*). The Company intends to develop these devices in collaboration with pharmaceutical and biotechnology company partners.

Biotechnology (Provectus Biotech, Inc.)

The Company is developing biotechnologies to augment vaccine production and to detect viruses (including an innovative "virus hunter" method) used to identify dangerous new viruses. This technology may play a crucial role in discovering the underlying cause of certain cancers and other serious diseases, and ultimately in producing preventative vaccines.

OTC Products (Pure-ific, Corp.)

Provectus owns a portfolio of OTC products, some of which currently provide revenue to the Company. The Company intends to continue to file patent applications and seek intellectual property protection for these formulations. While modest amounts of these products have been sold, developing and monetizing these OTC products are an important component of the Company's overall growth strategy.



## **Intellectual Property**

Provectus holds patent protection within the following areas: laser microscopy, melanoma treatment, vision correction, biotechnology, and vaccines. Specifically, the Company holds 12 U.S. patents (and 3 pending patents) from the U.S. Patent and Trademark Office (USPTO) on the technology it has developed (and is developing) for the production of prescription drugs, medical devices, and OTC pharmaceuticals. Also, the Company has 19 additional U.S. patent applications under examination. Some of these patents were first filed under the aegis of Photogen Technologies, Inc. and are now held by Provectus. These principal U.S. patents are listed in Table 2.

Table 2
Provectus Pharmaceuticals, Inc.
U.S. PATENTS HELD

Patent No.	U.S. Patent Title	Issue Date	Expiration Date
5,829,448	Method for improved selectivity in photo-activation of molecular agents	November 3, 1998	October 30, 2016
5,832,931	Method for improved selectivity in photo-activation and detection of molecular diagnostic agents	November 10, 1998	October 30, 2016
5,998,597	Method for improved selectivity in photo-activation of molecular agents	December 7, 1999	October 30, 2016
6,042,603	Method for improved selectivity in photo-activation of molecular agents	March 28, 2000	October 30, 2016
6,331,286	Methods for high energy phototherapeutics	December 18, 2001	December 21, 2018
6,451,597	Method for enhanced protein stabilization and for production of cell lines useful for production of such stabilized proteins	September 17, 2002	April 6, 2020
6,468,777	Method for enhanced protein stabilization and for production of cell lines useful for production of such stabilized proteins	October 22, 2002	April 6, 2020
6,493,570	Method for improved imaging and photodynamic therapy	December 10, 2002	December 10, 2019
6,495,360	Method for enhanced protein stabilization and for production of cell lines useful for production of such stabilized proteins	December 17, 2002	April 6, 2020
6,519,076	Methods and apparatus for optical imaging	February 11, 2003	October 30, 2016
6,525,862	Methods and apparatus for optical imaging	February 25, 2003	October 30, 2016
6,541,223	Method for enhanced protein stabilization and for production of cell lines useful for production of such stabilized proteins	April 1, 2003	April 6, 2020

Source: Provectus Pharmaceuticals, Inc.

### **Trademarks**

Provectus owns the following trademarks: Xantryl™, Provecta™, GloveAid™, and Pure-ific™ (including Pure-ific™ and Pure-ific™ Kids). The Company also owns the registered trademark PulseView®. Trademark rights are perpetual provided that the Company can continue to keep the mark in use.

### **Material Transfer Agreement**

On July 31, 2003, Provectus entered into a Material Transfer Agreement with Schering-Plough Animal Health Corporation, the animal-health subsidiary of Schering-Plough Corporation. Under this agreement, the Company provides Schering-Plough with access to some of its patented technologies to permit Schering-Plough to evaluate those technologies for use in animal-health applications. This Material Transfer Agreement involves four U.S. patents that cover biological material manufacturing technologies. If Provectus' technologies are able to be commercialized by Schering-Plough, Provectus will license these technologies to Schering-Plough in exchange for progress payments upon the achievement of goals.



## **Management and Board of Directors**

### **Management and Board of Directors**

Provectus was founded in 2002 and has four full-time employees. Principals Craig Dees, Timothy Scott, and Eric Wachter have worked together for more than a decade, previously as founders of Photogen Technologies as well as at the Oak Ridge National Laboratory (ORNL). Chief financial officer (CFO) Peter Culpepper joined Provectus in February 2004. The management team and Board of Directors are outlined in Table 3, followed by detailed biographies.

# Table 3 Provectus Pharmaceuticals, Inc.

### MANAGEMENT AND BOARD OF DIRECTORS

H. Craig Dees, Ph.D. Chief Executive Officer and Member of the Board of Directors

Timothy C. Scott, Ph.D. President and Member of the Board of Directors

Eric A. Wachter, Ph.D. Vice President of Pharmaceuticals and Member of the Board of Directors

Stuart Fuchs Member of the Board of Directors

Source: Provectus Pharmaceuticals, Inc.

### H. Craig Dees, Ph.D., Chief Executive Officer and Member of the Board of Directors

Dr. Dees is chief executive officer (CEO) and a member of the Board of Directors of Provectus. He joined the Company in April 2002, when it acquired Provectus Pharmaceuticals, Inc. (PPI). Previous to that, Dr. Dees was a senior member of management at Photogen Technologies (1997-2002) and a member of the Board of Directors (1997-2000). Prior to joining Photogen, Dr. Dees served as a Group Leader at the ORNL. He was previously a senior member of management at LipoGen Inc., which used genetic engineering technologies to manufacture diagnostic assay kits for auto-immune diseases, and at TechAmerica Group Inc., now a part of Boehringer Ingelheim Vetmedica, Inc., a subsidiary of Boehringer Ingelhem GmbH, an international chemical and pharmaceutical company headquartered in Germany. He has developed ethical vaccines, human diagnostics, cosmetics, and OTC pharmaceuticals. Dr. Dees developed and commercialized the world's first live viral vaccine produced by recombinant DNA technologies and licensed the first recombinant antigen human diagnostic assay using an FDA Class II licensure. While at TechAmerica, he developed and obtained U.S. Department of Agriculture (USDA) approval for the first *in vitro* assay for releasing "killed" viral vaccines. He earned a bachelor's degree in microbiology from Brigham Young University, a master's degree in immunology from Auburn University, and a doctorate in molecular virology from the University of Wisconsin at Madison, in 1984.

### Timothy C. Scott, Ph.D., President and Member of the Board of Directors

Dr. Scott is president of Provectus and a member of the Board of Directors. He joined the Company in April 2002, when it acquired Provectus Pharmaceuticals, Inc. Previous to that, Dr. Scott was a senior member of management at Photogen Technologies (1997-2002), serving as Photogen's chief operating officer (1999-2002), as director (1997-2000), and as interim CEO in 2000. Prior to joining Photogen, he served as senior management of Genase LLC, a developer of enzymes for fabric treatment, and held senior research and management positions at the ORNL. Dr. Scott was involved in developing numerous high-tech innovations in a broad range of areas, including separations science, biotechnology, biomedical, and advanced materials. He has licensed several of his innovations to the oil and gas and biotechnology industries. As director of the Bioprocessing R&D Center at ORNL, Dr. Scott achieved a national presence in the area of advanced biotechnology for the production of energy, fuels, and chemicals. He earned a bachelor's degree in chemical engineering at the University of Tennessee and a doctorate in chemical engineering from the University of Wisconsin at Madison, in 1985.



### Eric A. Wachter, Ph.D., Vice President of Pharmaceuticals and Member of the Board of Directors

Dr. Wachter is vice president of pharmaceuticals and a member of the Board of Directors. He joined the Company in April 2002, when it acquired Provectus Pharmaceuticals. Previous to that, Dr. Wachter was a senior member of management at Photogen Technologies, serving as secretary and a director from 1997, and as vice president from 1999. Prior to joining Photogen, Dr. Wachter served as a senior research staff member at the ORNL. Dr. Wachter was extensively involved in pre-clinical development and clinical testing of pharmaceuticals and medical device systems, as well as with coordination and filing of patents. He earned a bachelor's degree in chemistry at Indiana University at Bloomington and a doctorate in chemistry from the University of Wisconsin at Madison, in 1988.

### Peter R. Culpepper, CPA, MBA, Chief Financial Officer

Mr. Culpepper was appointed CFO in February 2004. Previous to that, Mr. Culpepper was CFO of Felix Culpepper International, Inc. (2001-04); a registered representative with AXA Advisors, LLC (2002-03); and chief accounting officer and corporate controller for Neptec, Inc. (2000-01). Prior to that, Mr. Culpepper served in various senior director positions with Metromedia Affiliated Companies (1998-2000) and with Paging Network, Inc. (1993-98), as well as in a variety of financial roles in public accounting and industry from 1982 to 1993. He earned a bachelor's degree from the College of William and Mary, in 1982, and an MBA in finance from the University of Maryland at College Park, in 1992. He is a licensed Certified Public Accountant (CPA) in both Tennessee and Maryland and is a faculty member with the University of Phoenix.

### Stuart Fuchs, Member of Board of Directors

Mr. Fuchs has served as a member of the Company's Board of Directors since January 2003. He has been the co-founder and managing principal of Gryffindor since January 2000, a Chicago-based venture capital firm. Before joining Gryffindor, he was a founding stockholder of several biotechnology companies, including Angiogen LLC (since 1998), which develops combinations of drugs to stimulate *in vivo* production of factors that inhibit the growth of blood vessels in tumors, and Nace Pharma LLC (since 1996), which develops drugs that employ novel drug delivery technologies. Through Nace Resources Inc., a Delaware corporation providing strategic and financial advice to companies in the technology sector, Mr. Fuchs has formed or participated in groups of investors on behalf of several companies, including Miicro Inc., Celsion Corp., and Photogen. Before founding Nace Resources Inc., he served for 19 years as an investment banker with Goldman, Sachs & Co. (GS-NYSE), where he co-managed the firm's public finance activities for the Midwest region. Before joining Goldman, Sachs & Co., Mr. Fuchs was a lawyer in private practice with Barrett Smith Schapiro & Simon in New York. Mr. Fuchs holds an A.B. degree from Harvard College and a J.D. from Harvard Law School and is a member of the Association of the Bar of the City of New York.



## **Core Story**

Provectus is Latin for "advanced." Provectus develops advanced prescription drug products, which encompass the areas of dermatology and oncology; its medical device systems include therapeutic and cosmetic lasers; and the Company develops and markets OTC products, which address markets primarily involving skincare applications.

The Company's oncology therapies are designed to target and destroy the deadliest of cancers—such as melanoma, and focal tumors of the breast, liver, and prostate—while causing few side effects. The dermatology therapies are designed to treat severe psoriasis, as well as other skin disorders such as acne, actinic keratosis, and eczema. Provectus is also developing biotechnologies to augment vaccine production and detect viruses.

Cancer and psoriasis are similar in that they both involve the increased metabolic activity of cells and severe alteration of the chemistry in local tissue. Both diseases put the body's metabolism into hyperdrive and increase the uptake of nutrients, which are the building materials for cell function and growth. When the uptake mechanisms are increased, there is a modification of membranes to facilitate this increased activity and, frequently, an over-replication of cells. This causes tissue to be highly disordered, which induces the clinical symptoms of these diseases.

Provectus' oncology candidate, Provecta<sup>™</sup>, has completed treatment in a Phase I clinical trial for malignant melanoma in the first group of subjects and the treatment was well tolerated at the initial lower dosage level. The Company's dermatology candidate, Xantryl<sup>™</sup>, is expected to begin Phase II clinical trials in psoriasis early next year. Provectus' pharmaceutical development pipeline is illustrated in Figure 2.

Figure 2
Provectus Pharmaceuticals, Inc.
PRODUCT DEVELOPMENT PIPELINE

DRUG	INDICATION	DEVELOPMENT	PRE-CLINICAL	PHASE I	PHASE II/III
Provecta™	Melanomas, and focal tumors of the breast, liver, and prostate				
Xantryl™	Psoriasis, and other disorders such				
	as acne, actinic keratosis, and eczema				

Source: Provectus Pharmaceuticals, Inc.

Within the biotechnology portfolio, the Company's vaccine technology is currently available and Provectus has a non-exclusive license for veterinary vaccine production. On the device side, the imaging and tissue ablation technology are currently available for license and the Company has developed a variant of the imaging technologies for Carl Zeiss, Inc., which is assessing its use in the laboratory for biomedical microscopy. On the OTC side, Pure-ific™ is marketed as an antibacterial hand spray. The Company has also conducted a pilot-scale run on the manufacturing of a hand cream, which contains both antiperspirant and antibacterial properties, called GloveAid™, to treat the irritation associated with wearing disposable gloves. Also, Pure-Stick™ for acne will require minimal clinical trials before approval.

The accompanying sections provide details on each of the Company's key operating subsidiaries:

- Provectus Pharmatech, Inc.
- Provectus Devicetech, Inc.
- Provectus Biotech, Inc.
- Pure-ific Corp.



### PROVECTUS PHARMATECH, INC.

#### Cancer

Cancer is a disease characterized by the uncontrolled growth of abnormal cells. These cells, which mutate from normal tissues within the body, are not recognized as abnormal by the body's defense systems. Since the body's immune system is unable to make this important differentiation, it does not respond through a typical immune response. This enables the cancerous cells to multiply freely, invading and replacing healthy cells and destroying important tissues. Cancer may be caused by patient-specific factors, such as genetic predisposition, immune deficiency, hormones, diet and smoking, or external factors, such as exposure to a toxic environment or excess sun exposure.

Cancer is manifested as either solid tumors or blood-borne cancerous cells, which, over time, tend to invade or metastasize to other tissues and organs of the body. Typically, cancer that is detected early in its progression has the best prognosis. In this circumstance, if the cancer has not spread to other organs and tissues, surgical removal of the tumor can be effective. Conversely, cancer that is detected at a later stage has a worse prognosis as it has often already spread to other organs and tissues within the body.

When detected early, cancer cannot always be cured through surgery since, in many situations, the disease will have already spread to other parts of the body, rendering surgery incapable of completely excising the cancer. In such cases, even if the bulk of the tumor is removed, the prognosis may be poor due to the spread of undetectable cancer cells, or **micrometastasis**, through the blood or lymphatic system to establish new tumors at other sites. Cells and tumors formed at these new sites are extremely difficult to treat.

### Prevalence

Cancer is a global health threat, with an estimated 10 million new diagnoses each year and approximately 6 million deaths, 40% of which occur in the developed world. The incidence is expected to increase by 50% over the next 20 years. The American Cancer Society (ACS) estimates that there are currently 8.9 million people in North America with a history of cancer, and approximately 3 million projected diagnoses occurring annually. In the U.S. this year, approximately 570,280 people (more than 1,500 per day), are predicted to die from cancer.

Following cardiovascular diseases, cancer remains the most common cause of death, with about one out of every four U.S. deaths linked to this disease. The relative lifetime risk of a male developing cancer is one in two; for women the risk is one in three. Furthermore, the National Cancer Institute (NCI) anticipates that cancer may exceed cardiovascular disease as the leading cause of death within the next decade. Table 4 (page 13) provides an overview of the estimated new cases of cancer and estimated deaths, projected by the ACS in 2005, highlighting those sites to which Provectus has targeted its development efforts—mainly metastatic melanoma, and focal tumors of the breast, liver, and prostate.

### Global Market

The global cancer market represents the most far-reaching pharmaceutical market in the world. According to Datamonitor (a business information company), this market was estimated to represent approximately \$20 billion in 2003, and could increase to more than \$45 billion by 2011. This expansion is forecasted to occur as a result of improvements in traditional therapies combined with the introduction of new and innovative treatments that display improved efficacy and lower toxicity, and at the same time, take a more targeted approach at eliminating specific forms of cancer. Provectus is developing Provecta™, a sterile injectable form of **PV-10** (or Rose Bengal, RB), for direct injection into tumors. Since PV-10 is retained in diseased or damaged tissue but quickly dissipates from healthy tissue, the Company believes it can develop therapies that confine treatment to cancerous tissue and reduce collateral impact on healthy tissue.



# Table 4 Provectus Pharmaceuticals, Inc. ESTIMATED NEW CANCER CASES AND DEATHS FOR ALL SITES, 2005\*

		ted New Cases			nated Deaths	
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,372,910	710,040	662,870	570,280	295,280	275,000
Oral cavity & Pharynx	29,370	19,100	10,270	7,320	4,910	2,410
Tongue	7,660	5,050	2,610	1,730	1,120	610
Mouth	10,070	5,370	4,700	1,890	1,100	790
Pharynx	8,590	6,520	2,070	2,130	1,490	640
Other oral cavity	3,050	2,160	890	1,570	1,200	370
Digestive System	253,500	134,370	119,130	136,060	75,020	61,040
Esophagus	14,520	11,220	3,300	13,570	10,530	3,040
Stomach	21,860	13,510	8,350	11,550	6,770	4,780
Small Intestine	5,420	2,840	2,580	1,070	580	790
Colon	104,950	48,290	56,660	56,290	28,540	27,750
Rectum	40,340	23,530	16,810	0	0	0
Anus, anal canal, & anorectum	3,990	1,750	2,240	620	230	390
Liver & intrahepatic bile duct	17,550	12,130	5,420	15,420	10,330	5,090
Gallbladder & other billiary	7,480	3,330	4,150	3,340	1,270	2,070
Pancreas	32,180	16,100	16,080	31,800	15,820	15,980
Other digestive organs	5,210	1,670	3,540	2,400	950	1,450
Respiratory System	184,800	102,420	82,380	168,140	93,990	74,150
Larynx	9,880	7,920	1,960	3,770	2,960	810
Lung & bronchus	172,570	93,010	79,560	163,510	90,490	73,020
Other respiratory organs	2,350	1,490	79,300 860	860	540	320
Bones & Joints	2,570	1,480	1,090	1,210	670	540
Soft Tissue (including heart)	9,420	5,530	3,890	3,490	1,910	1,580
	9,420		28,420	10,590	6,920	6,970
Skin (excluding basal & squamous)	,	37,580	•			
Melanoma-skin	59,580	33,580	26,000	7,770	4,910	2,860
Other nonepithelial skin	6,420	4,000	2,420	2,820	2,010	810
Breast	212,930	1,690	211,240	40,870	460	40,410
Genital system	321,050	241,570	79,480	59,920	31,010	29,810
Uterine cervix	10,370	0	10,370	3,710	0	3,710
Uterine corpus	40,880	0	40,880	7,310	0	7,310
Ovary	22,220	0	22,220	16,210	0	16,210
Vulva	3,870	0	3,870	870	0	870
Vaginal & other genital, female	2,140	0	2,140	810	0	810
Prostate	232,090	232,090	0	30,350	30,350	0
Testis	8,010	8,010	0	390	390	0
Penis & other genital, male	1,470	1,470	0	270	270	0
Urinary System	101,880	71,090	30,790	26,590	17,420	9,170
Urinary bladder	63,210	47,010	16,200	13,180	8,970	4,210
Kidney & renal pelvis	36,160	22,490	13,670	12,660	8,020	4,640
Ureter & other urinary organ	2,510	1,590	920	750	430	320
Eye & orbit	2,120	1,090	1,030	230	110	120
Brain & other nervous system	18,500	10,620	7,880	12,760	7,280	5,480
Endocrine	27,650	7,550	20,100	2,370	1,080	1,290
Thyroid	25,690	6,500	19,190	1,490	630	860
Other endocrine	1,960	1,050	910	880	450	430
Lymphoma	63,740	33,050	30,690	20,610	10,930	9,680
Hodgkin's disease	7,350	3,980	3,370	1,410	780	630
Non-Hodgkin's	56,390	29,070	27,320	19,200	10,150	9,050
Multiple myeloma	15,980	8,600	7,380	11,300	5,660	5,640
Leukemia	34,810	19,640	15,170	22,570	12,540	10,030
Acute lymphocytic leukemia	3,910	2,180	1,790	1,490	850	640
Chronic lymphocytic leukemia	9,730	5,780	3,950	4,600	2,520	2,080
	11,960	6,530	5,430	9,000	5,040	3,960
Acute myeloid leukemia						
Acute myeloid leukemia Chronic myeloid leukemia						
Acute myeloid leukemia Chronic myeloid leukemia Other leukemia	4,600 4,550	2,640 2,510	1,960 2,040	850 6,630	430 3,700	420 2,930

<sup>\*</sup> Rounded to the nearest 10; excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. About 58,490 carcinoma in situ of the breast and 46,170 melanoma in situ will be newly diagnosed in 2005.

Areas targeted by Provectus Pharmaceuticals, Inc.

Source: American Cancer Society, Inc. (2005).

<sup>‡</sup> Estimated deaths for colon and rectum cancers are combined. More deaths than cases suggests lack of specificity in recording underlying causes of death on death certificates.



### Rose Bengal

Rose Bengal, or RB, is the active ingredient in Provectus' pharmaceutical candidates, Provecta™ and Xantryl™. RB is a synthetic small molecule agent that is highly stable at room temperature and long-lasting. RB is excreted from the bloodstream without metabolizing and is, for the most part, non-toxic to normal tissue. RB has a long history as a diagnostic agent and also as a food dye. It was used intravenously as a diagnostic agent for liver disease as far back as the 1920s. A half-century later, it became used as a topical agent to diagnose eye injuries, such as corneal abrasions. In either application, RB is not known for any significant deleterious side effects. Despite the long history of RB, the Company is not aware of any therapeutic drugs that have been previously based on RB.

Since it is a known substance, RB cannot be patented by Provectus. Nonetheless, the Company filed U.S. patent applications to protect its proprietary formulations and methods of use (refer to page 8). The Company holds patents on its use as a radiosensitizer and as a contrast agent for Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), while it simultaneously pursues patents on its use as a chemoablative agent, a topical dermatologic agent, and a chemotherapeutic agent.

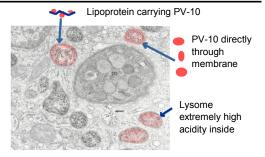
### Provecta<sup>™</sup> (PV-10)

Figure 3
Provectus Pharmaceuticals, Inc.
PROVECTA™



Source: Provectus Pharmaceuticals, Inc.

Figure 4
Provectus Pharmaceuticals, Inc.
PROVECTA™ IN THE CELLS



Source: Provectus Pharmaceuticals, Inc.

Current cancer treatments typically destroy healthy cells along with the cancer cells they are meant to attack. Additionally, they do little to stop metastasis, the often-fatal spread of the disease to remote locations in the body. Provecta™, illustrated in Figure 3, is a sterile form of RB (also known as PV-10) that is comprised of an injectable saline solution at 10% weight per volume and can be imaged using CT or ultrasound to facilitate image guided delivery.

Provecta™ is injected into and around focal tumors, killing the tumors via a process called chemoablation, shown in Figure 4. Preclinical studies to date have shown that Provecta™ targets the tumors with minimal side effects and may even elicit an anti-tumor immune response that could lead to the elimination of metastases.

### Development Status

In August 2004, Provectus filed an Investigational New Drug (IND) application, which received clearance in October 2004 by the U.S. Food and Drug Administration (FDA). Provecta™ is being evaluated for safety and preliminary efficacy in a total of 20 subjects with Stage III metastatic melanoma, which is the most aggressive form of skin cancer. Current treatments for melanoma include surgical excision, chemotherapy, and radiation therapy. Incidence of the disease continues to increase at a rate of more than 2% annually in the U.S. Five-year survival rates are less than 50% for locally metastatic forms of the disease, and approximately 10% once distant metastasis has occurred.

### Phase I

The Company announced on August 17, 2005 that the first group of subjects had completed treatment in a Phase I clinical trial in metastatic melanoma, and that the treatment was well tolerated at the initial lower dose level. Additionally, preliminary therapeutic effects were characterized as being comparable to those observed in preclinical studies. The study is being conducted at two dosage levels, with both



dosage levels having the potential to show safety, preliminary efficacy, and the "bystander effect"—potential effect(s) on nearby untreated tumors. The authorized dosage will be increased to the maximum level for treatment of the remaining subjects.

The study is being conducted at two of the world's leading melanoma treatment and research centers, both located in New South Wales, Australia, a country where the incidence of melanoma is more than twice that of the U.S. Each subject enrolled in the study is having one to three tumors treated with a single injection of Provecta™ and the local response to the treatment is then being observed for a period of 12 to 24 weeks. Potential effects on nearby untreated tumors (the "bystander effect") are also being monitored.

It is believed that since the toxic effects of Provecta<sup>™</sup> appear to be confined only to diseased cells (i.e., cancer cells), these Phase I studies, if successful, could shorten the path for approval. The Company expects to complete the trial in early 2006. Subsequently, Phase II/III trials could require another two to three years. The ultimate success for this indication would be determined during the Phase III trial. There is also the possibility of sale or licensure of Provecta<sup>™</sup> to a larger company.

### Key Properties

Key properties of Provecta™ are summarized in Table 5.

#### Table 5

Provectus Pharmaceuticals, Inc.
KEY PROPERTIES OF PROVECTA™

Stablity-based, nontoxic small-molecule agent (Rose Bengal)

Targets unique feature of tumor cell membrane common to all focal tumors

Exhibits prolonged retention (24 hours or more) in tumor tissue

Provides contrast for CT and ultrasound imaging

Useful for direct ablation of tumor tissue at high dose, radiosensitization at lower dose

Capable of stimulating anti-tumor immunity

Rapidly cleared from healthy tissues

Not metabolized

Rapidly excreted from the bloodstream

Source: Provectus Pharmaceuticals, Inc.

### Additional Potential Indications

In addition to metastatic melanoma, Provectus is exploring advancement to clinical studies in the following areas:

### **Breast Cancer**

In the U.S., breast cancer is the most common cancer occurring in women (excluding cancers of the skin) and is the second most common cause of death from cancer in women after lung cancer. If diagnosed at an early stage, breast cancer has an encouraging cure rate, with up to 97% of women diagnosed surviving five years after their diagnosis. Even if the cancer is discovered at a more advanced stage, new therapies have enabled many people with breast cancer to experience the same quality of life as before their diagnosis. In 2005, an estimated 212,930 Americans (primarily women) are expected to be diagnosed with the disease, resulting in an estimated 40,870 deaths (Table 4, page 13).

Surgical resection, chemotherapy, radiation therapy, and **immunotherapy** comprise the standard treatments for the majority of breast cancer cases, resulting in serious side effects that may become permanent conditions. Moreover, current treatments are relatively ineffective against metastasis, which in many cases is the eventual cause of patient mortality.



Development status. Pre-clinical studies at Provectus using human breast tumors implanted in mice have shown that direct injection of Provecta™ into these tumors ablates the tumors, and, as is the case of liver tumors, may elicit an anti-tumor immune response that eradicates distant metastases. Since fine-needle biopsy is a routine procedure for diagnosing breast cancer, and since the needle used to conduct the biopsy also could be used to direct an injection of Provecta™ into the tumor, localized destruction of suspected tumors through direct injection of Provecta™ has the potential to become a primary treatment. In August 2005, the Company announced its intention to commence a Phase I study of Provecta™ for treatment of recurrent breast carcinoma later this year.

### **Liver Cancer**

Primary liver cancer occurs when cancerous (malignant) cells begin to grow in the liver tissues. While many cancers are on the decline, the incidence of primary liver cancer in the U.S. rose by more than 70% between 1975 and 1995, linked to rising rates of hepatitis B and C infections—the most common causes of liver cancer. More common than primary liver cancer, however, is cancer that occurs when tumors from other parts of the body spread (metastasize) to the liver. The liver is especially vulnerable to invasion by tumor cells and, with the exception of the lymph nodes, is the most common site of metastasis. Since liver cancer is rarely discovered early, the prognosis is often poor, though treatment can help relieve symptoms and improve quality of life. In addition to standard treatments, such as surgery, chemotherapy, and radiation, new and less invasive therapies may be an option for some people. Risk of contracting liver cancer can be reduced by receiving a vaccine that protects from the hepatitis B virus (HBV). New cases of primary liver cancer in the U.S. are forecast at 17,550, while deaths expected in 2005 are forecast at 15,420 (Table 4, page 13).

The current standard of care for liver cancer is ablative therapy which seeks to reduce a tumor by poisoning, freezing, heating, or irradiating it, using either localized injection of ethanol (alcohol), cryosurgery, radiofrequency ablation, or ionizing radiation, such as X-rays. Where effective, these therapies have many side effects; however, selecting therapies with fewer side effects tends to reduce overall effectiveness. Combined, ablative therapies have a five-year survival rate of 33%.

Development status. In pre-clinical studies, Provectus found that direct injection of Provecta™ into liver tumors quickly ablates treated tumors and can trigger an anti-tumor immune response leading to eradication of residual tumor tissue and distant tumors. Because of the natural regenerative properties of the liver and the highly localized nature of the treatment, the Company believes that this approach may produce few to no significant side effects.

### **Prostate Cancer**

The prostate is a gland in the male reproductive system located just below the bladder (the organ that collects and empties urine) and in front of the rectum (the lower part of the intestine). It is approximately the size of a walnut and surrounds part of the urethra (the tube that empties urine from the bladder). The prostate gland produces fluid that makes up part of the semen. Prostate cancer is found mainly in older men and is the most common cancer, excluding skin cancers, in American men. The American Cancer Society estimates that during 2005, approximately 232,090 new cases of prostate cancer will be diagnosed in the country. About one in six men will be diagnosed with prostate cancer during their lifetime, but only one in 33 will die of this disease. The American Cancer Society also estimates that 30,350 men in the nation will die of prostate cancer during 2005 (Table 4, page 13).

As with breast cancer, surgical resection, chemotherapy, radiation therapy, and immunotherapy comprise the standard treatments for the majority of cases of prostate cancer, and can result in serious, permanent side effects, including permanent erectile dysfunction.

Development status. The direct injection of Provecta™ into prostate tumors may selectively ablate such tumors, and, as in the case of liver and breast tumors, may also elicit an anti-tumor immune response capable of eradicating distant metastases. Since trans-urethral ultrasound, guided fine-needle biopsy, and immunotherapy, along with brachytherapy implantation have become routine procedures for diagnosis and treatment of these cancers, Provectus believes that localized destruction of suspected tumors through direct injection of Provecta™ may become a primary treatment.



### Types of Tumors in Clinical Studies

Cancer cells implanted into laboratory animals and allowed to grow are tumor models. These grow in a short amount of time to a size at which they can be studied. This artificial setting for study, however, does not closely match that of spontaneous tumors, which may take months or years to grow to a size at which they can be studied. This means that tumor models and spontaneous tumors may react differently to a specific treatment.

There are two types of tumor models: **xenografts**, tumors obtained from different and incompatible species of animal, and **homografts**, tumors obtained from the same or compatible species. Xenografts are less representative of human cancers, because they are often implanted in animals that do not have advanced immune systems that may reject the tumors outright. Still, such tumor models provide a means to obtain an important initial assessment of potential drug performance.

Provectus has gained limited data on the treatment of spontaneous tumors in dogs, cats, and horses with Provecta<sup>™</sup>. Because the results with the spontaneous tumors approximate those results in studies using tumor models, the Company believes the drug has shown uncommon efficacy. Additionally, as RB has exhibited a previous history of human use, the Company has confidence in Provecta's <sup>™</sup> safety. Success in the targeted areas of melanoma and breast, liver, and prostate tumors (as described on pages 14-16) is foreshadowed by studies using mouse homografts and human tumor xenografts in mice and spontaneous tumors in companion animals.

## Types of Cell Lines Tested

Provecta<sup>™</sup> has been found to have "successfully treated" a range of particular tumor models and spontaneous tumors. The Company defines "successfully treated" as complete tumor eradication, or ablation, with a single treatment of the drug, as well as eradication in at least half of all the tumors treated. Table 6 illustrates the tumor models in mice that were treated successfully.

### Table 6

### Provectus Pharmaceuticals, Inc.

### TUMOR MODELS TREATED SUCCESSFULLY IN MICE

murine hepatocellular carcinoma (HCC), a common liver tumor

murine renal adenocarcinoma (RAG), a common kidney tumor

murine melanoma (MeWo, A375, and B160F10 tumor lines)

human breast (MCF-7, HTB-133, and T-47D lines; ER+ and ER- lines responsive)

human prostate (PC3 tumor line)

human lung carcinoma (H69-AR, non small cell, multi-drug resistant)

Source: Provectus Pharmaceuticals, Inc.

Table 7 illustrates spontaneous tumors in other veterinary subjects that were treated successfully.

### Table 7

Provectus Pharmaceuticals, Inc.

### SPONTANEOUS TUMORS IN OTHER VETERINARY SUBJECTS

canine recurrent fibrous histocytoma (a recurrent tumor that had previously been treated with surgery and 60 Gray of radiation)

canine mast cell

feline squamous epithelial

equine melanoma

equine sarcoid

murine mammary carcinoma



### **Psoriasis**

Psoriasis is a skin disease characterized by raised red lesions, covered with a white build-up of dead skin cells. It can appear anywhere on the body, such as on the face, scalp, genitals, hands, and feet. According to the National Psoriasis Foundation, the skin disease affects some 2.1% of the U.S. population and has been diagnosed in 4.5 million American adults. Worldwide, the disease affects some 1% to 3% of the global population. There is no known cause and no known cure for the disease.

Psoriasis appears to have a genetic link. A child of one parent with psoriasis has a 10% to 25% chance of developing the disease; two parents pass along a 50% chance. The disease generally affects patients between the ages of 15 and 35. Close to 30% of Americans are diagnosed with moderate to severe psoriasis, which generally indicates that it affects more than 3% of the body. In the U.S., dermatologists report almost 2.4 million visits per year, and the accumulative cost of treatment may exceed \$3 billion annually.

### Market Opportunity

Provectus is in the process of developing a topical dermatology drug called Xantryl™. Preclinical studies have demonstrated its ability to target diseased tissue without adverse side effects. The leading developers in this category have no direct comparison with Xantryl™, since they target psoriasis with potent immunosuppresants that have potentially severe side effects. The fundamental problems with most of the current technologies are that these products are seen to have limited specificity. According to Provectus, this immune system suppression inadequately targets the diseased tissue by reducing immune system function, potentially leading to inadequate immune response in treated tissues and elsewhere in the body. Provectus believes that serious side effects in normal tissue are a relevant safety concern. In addition, the Company believes that these approaches have demonstrated to be complex and costly.

Provectus notes that there are important similarities between cancer and psoriasis. For example, there is increased metabolic activity of cells under both conditions, with severe chemical alterations of the local tissue, i.e., low oxygen and high acidity.

### XantryI™

Figure 5
Provectus Pharmaceuticals, Inc.
XANTRYL™



Source: Provectus Pharmaceuticals, Inc.

Xantryl™, illustrated in Figure 5, is a topical dermatology drug, comprising an aqueous hydrogel formulation of RB (also known as PV-10), at 0.001% weight per volume. Xantryl™ is used to treat serious skin diseases, such as psoriasis. Applied topically, the compound penetrates the top layers of skin, or epithelial tissue, but does not show undue systemic uptake.

RB, the active element in Xantryl™, is "photoactive" at low concentration, meaning that it reacts to light of certain wavelengths, increasing its therapeutic effects. RB concentrates in diseased or damaged tissue but is not taken up by healthy tissue. By developing a "photodynamic" treatment regimen (one which combines a photoactive substance with activation by a source emitting a particular wavelength of light) around these two properties of RB, the Company is able to deliver a higher therapeutic effect at lower dosages of active ingredient, thus minimizing potential side effects, including damage to nearby healthy tissues.

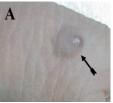
RB is especially responsive to green light, which is strongly absorbed by the skin and thus only penetrates the body to a depth of about three to five millimeters. For this reason, the Company has developed Xantryl™ combined with green-light activation for topical use in surface applications, where serious damage could result if medicinal effects were to occur in deeper tissues. Furthermore, no costly light delivery devices are required. A depiction of RB's effects confined to diseased tissue is provided in Figure 6 (page 19).



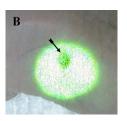
Approximately one-quarter to one-third of psoriasis patients who suffer from severe cases generally are treated with intensive drug therapies, often **Psoralen and ultraviolet A light (PUVA)**, a light-based therapy that combines the drug Psoralen with exposure to ultraviolet A light. While PUVA is one of the more effective treatments, it increases a patient's risk of skin cancer. The Company asserts that Xantryl™, activated with green light, offers a superior treatment for acute psoriasis because it selectively treats diseased tissue with negligible potential for side effects in healthy tissue. The therapy has shown promise in comprehensive Phase I clinical trials.

To date, clinical tests conducted using Xantryl™ for dermatology have utilized a number of commercially available lasers for activating the drug. This approach has several advantages, including leveraging an extensive base of installed

# Figure 6 Provectus Pharmaceuticals, Inc. RB EFFECTS CONFINED TO DISEASED TISSUE









Source: Provectus Pharmaceuticals, Inc.

devices present throughout the pool of potential physician-adopters for Xantryl™, where access to such a base could play an integral role in early market capture.

However, since the use of such lasers, which were designed for occasional use in other types of dermatologic treatments, is potentially too cumbersome and too costly for routine treatment of the large population of patients with psoriasis, Provectus has begun investigating the use of other types of **photoactivation** hardware, such as light booths. The use of such booths is consistent with current care standards in the dermatology field, and may provide a cost-effective means for addressing the needs of patients and physicians alike. It is possible that such photoactivation hardware would be developed, manufactured, and supported in conjunction with one or more third-party device manufacturers.

### Clinical Status

Xantryl™ successfully completed preclinical and Phase I clinical studies. Provectus expects to launch Phase II testing early next year, which could be completed in 2007. Table 8 provides detailed information on the clinical testing status of this compound.

# Table 8 Provectus Pharmaceuticals, Inc. CLINICAL TESTING OF PV-10

Study	Indication	When	Where	Who	Subjects
Pilot	Psoriasis	2000-2001	Aarhus, DK	Dr. Peter Bjerring	10
Phase 1a	Psoriasis	2001	Encinitas, CA	Dr. Richard Fitzpatrick	21
Phase 1b	Psoriasis	2001	Rutherford, NJ	Dr. Manuel Norman	9
Phase 1a	Actinic Keratosis (AK)	2001-2002	Santa Monica, CA	Dr. Nicholas Lowe	24

Source: Provectus Pharmaceuticals, Inc.

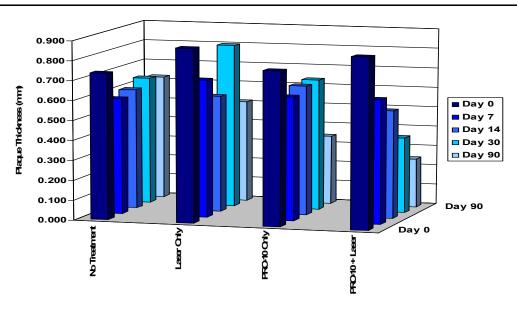
Among the pivotal results of the Phase I studies of Xantryl™ was that there were no damaging side effects to the treatment, pain was negligible, and after 30 days, a single-dose treatment yielded an average reduction in plaque thickness (patches of raised skin) of 51%; this response further improved to 60% by 90 days.



### Phase I

The objective of the Phase I clinical trial was to determine if there was a safety concern with the therapy. In these studies, involving more than 40 test subjects, Xantryl™ was applied topically once to psoriatic plaques and then illuminated with green light. In the first study, a single-dose treatment yielded an average reduction in plaque thickness of 51% after 30 days, with further response noted at the final follow-up examination 90 days later, illustrated in Figure 7.

Figure 7
Provectus Pharmaceuticals, Inc.
XANTRYL™ TREATMENT OF PSORIASIS



Source: Provectus Pharmaceuticals, Inc.

Furthermore, there was no pain, significant side effects, or evidence of "rebound" (increased severity of a psoriatic plaque after the initial reduction in thickness) observed in any treated areas. This degree of positive therapeutic response is comparable to that achieved with potent steroids and other anti-inflammatory agents, but without the serious side effects associated with such agents.

### Phase II/III Design

The Company is in the process of designing two studies with 50 subjects each for a total duration of 24 months in patients with psoriasis.

### Additional Potential Indications

Provectus may also study additional applications for Xantryl™. These include eczema, severe acne, chronic skin lesions, and actinic keratosis.

### Eczema

Eczema, or dermatitis, is a range of skin conditions that can affect all age groups. In the United Kingdom, up to one-fifth of all school-aged children have eczema, along with about one in twelve adults. The severity of the disease can vary. In mild forms, the skin is dry, hot, and itchy, while in severe forms, the skin can become broken, raw, and bloody. With treatment, the inflammation of eczema can be reduced. Based on Phase I results for psoriasis, the Company believes that Xantryl™ may also prove to be a useful treatment for eczema.



### Severe Acne

Serious forms of acne affect approximately 17 million people in the U.S., causing pain, disfigurement, and social isolation. The U.S. prescription acne care market is estimated at \$1.3 billion (Source: *Berson et al., "Current concepts in the treatment of acne: report from a clinical roundtable," Cutis. 72 (2003) 5-13; "US Prescription Dermatology Pharms − Anti-Acne Mkt," Frost & Sullivan, October 31, 1996*). Moderate to severe forms of acne have proven responsive to several photodynamic regimens, and the Company believes that Xantryl™ may be used as an advanced treatment for this disease. Pre-clinical studies have demonstrated that the active ingredient in Xantryl™ is highly potent against the bacteria associated with acne. Provectus seeks to make a clinical assessment of Xantryl™, with green-light photoactivation as a treatment for acne, perhaps as a follow-on effort to the psoriasis studies. If successful, this could become an important advance over currently available products for severe acne.

### Chronic Skin Lesions

Xantryl™ may also prove to be a useful treatment for chronic skin lesions such as leg ulcers, diabetic foot ulcers, pressure ulcers, and bedsores, as well as other chronic infections of the skin and underlying tissue. Wound care expenditures within the U.S. healthcare industry are estimated at between \$5 billion and \$7 billion annually, with more than five million chronic wound patients (Source: Frost and Sullivan. Executive Summary: U.S. Wound Management, Product Markets. Mountain View, Calif: 1996:1-2). Worldwide, this market is estimated at \$11.8 billion (Source: MedMarket Diligence).

### Actinic Keratosis (AK)

According to a study in *Fitzpatrick's Dermatology in General Medicine* (1999), actinic keratosis (AK), also called solar keratosis or senile keratosis, is the most common pre-cancerous skin lesion among fair-skinned people and is estimated to occur in more than half of elderly, fair-skinned persons living in sunny climates. Researchers noted that nearly half of the approximately five million cases of skin cancer in the U.S. may have begun as AK. The standard treatments for AK (primarily excision, cryotherapy, and ablation with topical 5-fluorouracil) are often painful and yield unacceptable cosmetic outcomes due to scarring. Based on its experience with psoriasis, Provectus assessed the use of Xantryl™ with green-light activation as a possible improvement in treatment of early and more advanced stages of AK.

Provectus completed initial Phase I clinical trials of the therapy for this indication in 2001 through a company that was acquired in 2002 and made into a subsidiary. This study, involving 24 subjects, examined the safety profile of a single treatment using topical Xantryl™ with green-light photoactivation; no significant safety concerns were identified.



### PROVECTUS DEVICETECH, INC.

Provectus has developed a number of valuable intellectual properties and technologies in the area of medical devices. Six U.S. patents and six pending patent applications are held by the Company in two market sectors: therapeutic and cosmetic devices. The Company expects to develop medical devices through partnerships with third-party device manufacturers or, if appropriate opportunities arise, through acquisition of one or more device manufacturers. The combined market for both therapeutic and cosmetic therapies in these areas targeted by Provectus is estimated to exceed \$1 billion (Source: *Medical Laser Report, Vol. 14, No. 1, January 2000, PennWell Publications*).

Provectus DeviceTech has a number of proprietary technologies that address three main markets in biomedical photonics:

(1) Treatment of ocular melanomas. One of the priorities in the medical devices field for Provectus is commercialization of its laser-based product for the treatment of melanoma. The current five-year survival rate for melanoma therapies is 13% once metastasis has occurred. Provectus' technologies allow the selective destruction of cancerous lesions based on the inherent light absorption of these tissues.

Research conducted in ocular melanoma at the Massachusetts Eye and Ear Infirmary (a teaching affiliate of Harvard Medical School) using the Company's new laser treatment demonstrated a significant advantage over current treatment options. A single quick non-invasive treatment of ocular melanoma tumors in a rabbit model resulted in the elimination of over 90% of tumors. While ocular melanoma is rare, with approximately 2,000 new cases annually (Table 4, page 13) in the U.S., the laser treatment may afford significant advantage over invasive alternatives, such as surgical excision, **enucleation**, or radiotherapy implantation.

Provectus has performed similar laser treatments on large (averaging approximately 3 millimeters thick) cutaneous melanoma tumors implanted in mice and has been able to eradicate over 90% of these pigmented skin tumors with a single treatment. Moreover, the Company has shown that this treatment stimulates an anti-tumor immune response that may lead to improved outcome at both the treatment site and at sites of distant metastasis. From these results, the Company believes that a device for laser treatment of melanomas of the eye is nearly ready for human studies, and the Company is looking to partner with a medical device manufacturer to bring it to market.

- (2) Improvement of multiphoton microscopy and diagnostic devices. Current multiphoton imaging devices must be used in an absolutely dark room, which precludes use of these devices as diagnostic instruments. Provectus' technologies allow these devices to be used in ambient light by adding patented signal processing technology to existing devices. This advance is expected to facilitate an ongoing transition of the device from the research lab to the clinic.
- (3) Devices that cut tissue for precise surgical applications, including laser vision correction. The Company's photonics technologies produce a very high peak laser power that yields precise tissue cutting with minimal damage to surrounding tissue.



### PROVECTUS BIOTECH, INC.

Provectus' biotechnology subsidiary is based on patented, cost-effective methods used to improve the yield or performance of recombinant DNA products (including enzymes, antigens, drugs, or other proteins) and vaccines. This may be achieved by a simple modification of the production process or through a one-time genetic modification of the cells that produce these products.

In addition, Provectus has an innovative "virus hunter" method used to isolate and identify dangerous new viruses. This technology may play a crucial role in discovering the underlying cause of certain cancers and other serious diseases, and ultimately in producing preventative vaccines. For instance, the recent demonstration that vaccination against human papillomavirus (HPV) may prevent cervical cancer highlights the possibility that many cancers may be caused by viruses. Provectus' technology may be used by pharmaceutical companies to discover the cause and develop preventative vaccines against cancers of the breast, prostate, and other parts of the body.

Provectus holds four biotechnology patents (refer to page 8) and intends to license this portfolio to major partners in the pharmaceutical industry. To date, Schering-Plough has purchased a non-exclusive license from Provectus to enhance production and performance of veterinary vaccines.

### Key Attributes

Key attributes of Provectus' biotechnology are summarized in Table 9.

### Table 9

Provectus Pharmaceuticals, Inc.
KEY ATTRIBUTES OF COMPANY'S BIOTECHNOLOGY

Increase yield of vaccines

Increase vaccine immunogenicity (ability to stimulate an immune response)

Increase yield and performance of products produced by genetic engineering

Potentially isolate as-yet-undiscovered viruses

Potentially create new diagnostic tests for cancers

Potentially develop vaccines against virus-induced cancers



### PURE-IFIC, CORP.

The over-the-counter (OTC) products from Provectus' Pure-ific subsidiary are designed to be safer and more specific than competing products. The Company's technologies offer practical solutions for common maladies, using ingredients that have limited or no side effects. Provectus' OTC products typically use compounds with potent antibacterial and antifungal activity as building blocks and then combine these building blocks with anti-inflammatory and moisture-absorbing agents. Products with these properties can be used for treating many dermatologic conditions, including hand irritation associated with the use of disposable gloves; eczema; and mild to moderate acne. Where appropriate, the Company has filed patent applications and has sought other intellectual property protection for its unique formulations.

### Pure-ific™

Figure 8
Provectus Pharmaceuticals, Inc.
PURE-IFIC™



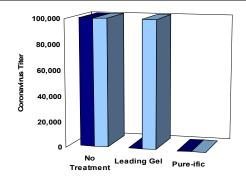
Source: Provectus Pharmaceuticals, Inc.

Pure-ific™, illustrated in Figure 8, is an antibacterial hand and surface spray that helps eliminate germs. Unlike ordinary hand gels, Pure-ific™ is a quick-drying mist. Its formulation as a spray is useful for hands as well as surfaces. The Pure-ific™ line of products includes two sizes of its quick-drying sprays, which immediately eradicate up to 99.9% of germs on skin, preventing regrowth for six hours.

The product's efficacy is illustrated both in Figure 9 (Control of Virus Contamination Levels on Treated Surfaces) and Figure 10 (Bacterial Growth). The Company has determined the effectiveness of Pure-ific™ based on its internal testing, as well as testing performed by Paratus Laboratories H.B., an independent research lab.

Pure-ific™ products help prevent the spread of germs, which complements the other OTC products from Provectus designed to treat irritated skin or skin conditions such as acne, eczema, and fungal infections.

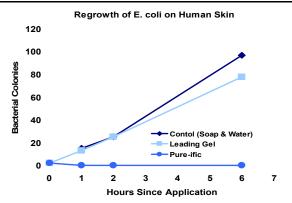
Figure 9
Provectus Pharmaceuticals, Inc.
CONTROL OF VIRUS CONTAMINATION LEVELS ON
TREATED SURFACES



■ Virus Level - Contamination Immediately After Application
□ Virus Level - Contamination 8 hrs After Application

Source: Provectus Pharmaceuticals, Inc.

Figure 10
Provectus Pharmaceuticals, Inc.
BACTERIAL GROWTH





### Marketing

During 2003 and 2004, the Company identified and engaged sales and brokerage forces for Pure-ific™. Provectus emphasized establishing sales in independent pharmacies and mass markets via chain stores. A supply chain for Pure-ific™ was established in tandem with a contract warehouse/fulfillment center. In addition, a website for Pure-ific™ was developed with the ability to support on-line sales. The Company expects to expand the Pure-ific™ product line to include additional applications. Modest amounts of the product were sold during 2004.

### Market Opportunity

Hand sanitizers are believed to comprise a greater than \$100 million market (Source: Company Profile Report: GOJO Industries Inc, D&B, April 22, 2004). Antibacterial sprays, such as Lysol® by Reckitt Benckiser Inc. (RKBKF.PK), represent a \$1.2 billion market. AmerisourceBergen Corporation (ABC-NYSE), the leading distributor of pharmaceutical products and services to independent and chain pharmacies, hospitals, physicians' offices, alternate care, and mail order facilities, is beginning to sell Pure-ific™ hand spray to its customers. In addition, the product is expected to be available shortly at select regional stores of national discount retailers and through the Web site www.pureific.com. Target customers include parents, teachers, daycare workers, office workers, travelers, and others concerned with good health and sanitation.

### GloveAid™

GloveAid<sup>™</sup>, illustrated in Figure 11, is a hand cream designed to reduce the discomfort of wearing disposable gloves. It also has applications for use in sports. Disposable gloves are used regularly in many occupations, such as those listed in Table 10, with The Occupational Safety and Health Administration (OSHA) mandating the use of disposable gloves by medical workers.

Accompanying the increased long-term use of disposable gloves is a mounting incidence of chronic skin irritation that has been characterized as an allergic-like reaction to the glove materials. Currently, physicians treat the condition using steroids and other immunosuppressive therapies. To address this market, the Company has developed GloveAid™, a hand cream with both antiperspirant and antibacterial properties, to increase the comfort of users' hands during and after the wearing of disposable gloves.

To avoid possible regulatory bars, the Company markets GloveAid™ as a means to increase users' comfort, not as a long-term therapy for treatment of chronic skin irritation. However, as the Company obtains data on people with chronic skin irritation, Provectus may seek regulatory approval GloveAid™ in order to market it as a therapy for chronic skin problems associated with wearing disposable gloves.

Figure 11
Provectus Pharmaceuticals, Inc.
GLOVEAID™



Source: Provectus Pharmaceuticals, Inc.

Table 10

### OCCUPATIONS THAT REGULARLY USE DISPOSABLE GLOVES

Airport security

Food handling and preparation

Sanitation workers

Postal and package delivery handlers and sorters

Laboratory researchers

Healthcare workers (hospital and blood bank personnel)

Police, fire, and emergency-response workers



### Market Opportunity

The worldwide market for disposable gloves is more than \$3 billion (Source: "Anxiety Spreads Love of Gloves," USA Today, February 28, 2002; "Kimberly-Clark Completes Acquisition of Safeskin Corporation," company press release, February 8, 2000). There are greater than 25 billion gloves sold annually in the U.S. every year. As usage continues to mount, it is anticipated that corresponding amounts will be spent on hand-care products. During 2003, Provectus conducted a pilot-scale run at the manufacturer of GloveAid™.

### Second-stage OTC products

Second-stage products are expected to target acne, eczema, and mild to moderate psoriasis. The Company also plans to develop specialized hand and foot antiperspirants for athletic use. Similar to GloveAid™, these products are designed to alter the skin environment to control microbial growth.

#### Pure-Stick™

Figure 12
Provectus Pharmaceuticals, Inc.
PURE-STICK™



Source: Provectus Pharmaceuticals, Inc.

Pure-Stick™, illustrated in Figure 12, is a topical acne treatment. Acne results from an overproduction of sebum and other fluids in the skin, which can plug sweat glands and ducts, providing an ideal environment for proliferation of normally benign bacteria. Pure-Stick™ is a non-toxic, topical agent that checks the production of sebum and sweat while damping skin pathogens associated with acne. Pure-Stick™ can be used both as a remedy and a preventative for acne.

### Market Opportunity

Acne affects approximately 17 million people in the U.S. (Source: (Berson et al., "Current concepts in the treatment of

acne: report from a clinical roundtable," Cutis. 72 (2003) 5-13). Frost & Sullivan have estimated the U.S. prescription acne care market at approximately \$1.3 billion in 2003 (Source: "U.S. Prescription Dermatology Pharms—Anti-Acne Mkt," Frost & Sullivan, October 31, 1996). The Company believes that the diverse and highly fragmented OTC acne care market is approximately equivalent in size, representing an opportunity in excess of \$1.3 billion annually.



## Competition

There is intense competition in the markets targeted by Provectus Pharmaceuticals, Inc.

### Oncology

In the area of oncology, if Provectus' products should reach the market, they would compete with larger companies such as Genentech Inc. (DNA-NYSE), Novartis AG (NVS-NYSE), and Bristol-Myers Squibb Company (BMY-NYSE), among others. While there is no comprehensive market analysis available for pharmaceutical products addressing treatment of melanoma and liver, breast and prostate cancers, it is possible to survey the potential market for Provecta<sup>™</sup> using similar oncology markets.

### Genentech Inc.

Genentech is a biotechnology company specializing in the discovery, development, manufacture, and commercialization of biotherapeutics for cancer, heart attack, allergic asthma, psoriasis, stroke, growth hormone deficiency, and cystic fibrosis. The Company's key products include blockbuster oncology agents Avastin and Rituxan. Avastin (approved in the U.S. in February 2004 as a first-line therapy for colorectal cancer (CRC) is expected to post sales in excess of \$780 million in 2005 (Source: Goldman Sachs). The wholesale cost of Avastin has been set at \$2,200 per vial, which translates to \$40,000 per patient regimen. According to the American Cancer Society, there are approximately 147,000 new cases of CRC per year in the U.S. Thus, sales of \$780 million represent capture of 13% of the CRC market. Rituxan is used to treat patients with non-Hodgkin Lymphoma (nHL). Sales were estimated at \$1.6 billion in the U.S. in 2004 (Source: Goldman Sachs). According to the American Cancer Society, there are approximately 53,400 new cases of nHL per year in the U.S., which implies a wholesale price of about \$20,600 per patient.

### Novartis AG

Novartis AG is an integrated pharmaceutical company with products addressing a number of therapeutic areas, including cardiovascular, metabolism, neuroscience, respiratory, dermatology, oncology, immunology, and infectious diseases. The company's blockbuster oncology agent, Gleevec, is used to treat patients with chronic myeloid leukemia (CML). Sales were estimated at \$1.5 billion in 2004 (Source: Goldman Sachs). According to the American Cancer Society, there are 30,600 new cases of leukemia per year in the U.S., which implies a wholesale price of about \$20,000 per patient.

### Bristol-Myers Squibb Company

Bristol-Myers Squibb Company is an integrated pharmaceutical company engaged in the discovery, development, license, manufacture, marketing, distribution, and sale of pharmaceutical and other healthcare products, including branded pharmaceutical products for cardiovascular disease, virology, infectious diseases, and oncology. Taxol (which is off-patent) has been a long-running blockbuster for Bristol-Myers, posting sales of \$934 million in 2003, and is used to treat breast cancer (an estimated 217,000 new cases in U.S. in 2004). The average U.S. Medicare reimbursement price/dose for Taxol is approximately \$1,800.

### **Psoriasis**

Competitive products to XantryI<sup>™</sup> treat psoriasis with potent immunosuppresants that have potentially severe side effects. Among the companies with products in development include Genentech in Phase IV with Raptiva; Protein Design Labs Inc. (PDLI-NASDAQ), in Phase II with Daclizamub; and Amgen Inc. (AMGN-NASDAQ), in Phase III with Enbrel. A more comprehensive accounting of these and other products within this field, according to the National Psoriasis Foundation, are illustrated in Table 11.



# Table 11 Provectus Pharmaceuticals, Inc. DRUGS IN DEVELOPMENT FOR PSORIASIS AND PSORIATIC ARTHRITIS

Name of Drug	Company	Mechanism of Action	Status
Amevive (alefacept)	Biogen Idec	systemic biologic reduces T lymphocytes (CD2)	Phase II for psoriatic arthritis
Avandia (rosiglitazone maleate)	GlaxoSmithKline	oral antidiabetic agent	Phase III for psoriasis
ATL1101	Antisense Therapeutics, LTD.	IGF-1 receptor blocking cream	Pre-clinical for psoriasis
Becocalcidiol	QUATRx Pharmaceuticals Co.	topical vitamin D derivative	Phase II for psoriasis
Bimosiamose (bimosiamose microemulsion)	Revotar BioPharmaceuticals AG	endothelin A receptor antagonist	Phase II for psoriasis
CRx-140	CombinatoRx	combination of loratidine and cyclosporine, an antihistamine and immunosuppressant	Phase II for psoriasis
Ecalcidene	Barrier Therapeutics	vitamin D(3) derivative	pre-clinical for psoriasis
Elidel (pimecrolimus)	Novartis Pharmaceuticals Corp.	oral anti-inflammatory	Phase II for psoriasis
Enbrel (etanercept)	Amgen & Wyeth	TNF-alpha inhibitor	Phase IV for pediatric psoriasis
Humira (adalimumab)	Abbott Immunology	monoclonal antibody	Filed for approval 12/04 for psoriatic arthritis; Phase II for psoriasis
IR502	Immune Response Corp.	causes immune system to shut down activated T cells	Phase II complete for psoriasis
ISA247	Isotechnika	systemic immunosuppressant	Phase II complete; Phase III in Canada for psoriasis
Novasome A/B (PTH (1-34))	IGI	regulates epidermal growth and differentiation	Phase I complete for psoriasis
Paxceed (paclitaxel)	Angoitech Pharmaceuticals	topical angiogenesis inhibitor	Phase II complete for psoriasis
Panretin (alitretinoin) (oral)	Ligand Pharmaceuticals	vitamin A derivative	Phase II complete for psoriasis
Panretin (alitretinoin) (topical)	Ligand Pharmaceuticals	topical gel, vitamin A derivative	Phase IV complete for psoriasis
PhotoPoint	Miravant Medical Technologies	photodynamic therapy for plaque psoriasis	Phase II for psoriasis
Psoraxine (AS210) Rambazole	Astralis, LTD. Barrier Therapeutics	injectable immuno-therapeutic agent topical retinoic acid metabolism blocking agents	Phase II for psoriasis Phase I for psoriasis
Raptiva (efalizumab)	Genentech, Inc.	blocks activation and migration of T cells	Phase IV for safety, pregnancy for psoriasis
Remicade (infliximab)	Centocor, Inc.	TNF-alpha inhibitor	approved 5/05 for psoriatic arthritis; Phase III for psoriasis
Oral tazarotene	Allergan, Inc.	oral version of topical vitamin A derivative	Phase III complete; non- approvable letter 9/04 for psoriasis
Tadekinig-alpha (r-IL-18 BP)	Serono, S.A.	II-18 inhibitor	Phase II for psoriasis
Vitaxin	Medimmune	monoclonal antibody	Phase II halted for psoriasis
VX-765	Vertex Pharmaceuticals	cytokine inhibitor	Phase II for psoriasis
Xantryl	Provectus Pharmaceuticals	UV light-activated topical	Phase I complete for psoriasis
XP-828L	Advitech	bioactive products derived from milk proteins	DSHEA clinical trial for psoriasis (Dietary Supplement Health Education Act)
Zenapax (daclizumab)	Protein Design Labs	SMART Anti-Tac Antibody	Phase II complete for psoriasis
Source: National Psoriasis Foundation	n, May 2005.		F-300.0



### **OTC Competitors**

The Company's currently marketed products are subject to competition from products with similar qualities. Provectus faces competition in market areas shared by traditional skincare cosmetic companies, though the Company distinguishes itself by basing its products on unique, proprietary formulations and approaches. Provectus is not aware of any products in its targeted OTC skincare markets that are similar to the GloveAid™. However, the OTC product, Pure-ific™, competes in the market with other hand sanitizing products, including, in particular, the following hand sanitizers:

- Purell<sup>®</sup>, which is manufactured by GOJO Industries;
- Avagard<sup>™</sup> D, which is manufactured by 3M (MMM-NYSE); and
- a large number of generic and private-label equivalents to these market leaders.

GloveAid™ represents a new product category that has no direct competitors; however, other types of products, such as AloeTouch disposable gloves, manufactured by Medline Industries, Inc. of Mundelein, Illinois, target the same market niche.



# Strategic Alliances

Provectus is pursuing partnerships for the development of its products. The Company's core technologies have attracted the attention of major pharmaceutical and biomedical technology companies, including those illustrated in Figure 13. Additionally, the Company is currently pursuing partnerships with other companies to assist in bringing its technologies to market and/or to market current products.

# Figure 13 Provectus Pharmaceuticals, Inc. RELATIONSHIPS WITH OTHER COMPANIES







Source: Provectus Pharmaceuticals, Inc.

### Schering-Plough Corporation

Schering-Plough Corporation operates in the fields of allergic and inflammatory disorders, infectious diseases and inflammation, cancer, and cardiovascular disease. Pursuing a strategy to license its biotechnology portfolio rather than develop it internally, Provectus signed an agreement with Schering-Plough to use its biotechnologies to enhance the production and performance of veterinary vaccines.

Varian Medical Systems, Inc.

Varian Medical Systems has a division in oncology that develops products for treating cancer with radiation, including linear accelerators and treatment simulation. Varian Medical Systems funded a two-year, \$120,000 research award at The Prostate Cancer Foundation that was granted to the School of Veterinary Medicine and The Comprehensive Cancer Center of the University of Wisconsin at Madison for a cancer study using the Provectus drug, Provecta<sup>™</sup>.

Carl Zeiss, Inc.

Carl Zeiss is a global leader in the optical and opto-electronic industries. Provectus developed a variant of the imaging technology for Zeiss, which is assessing its use in the laboratory for biomedical microscopy.



# **Potential Milestones in Next 12-24 Months**

- Oncology (Melanoma). Complete Phase I/II clinical trials for Provecta™ in melanoma, which began in August 2005 (for a duration of six months)
- Oncology (Breast Cancer). Begin Phase I/II clinical trials for Provecta<sup>™</sup> in breast cancer, which are scheduled to begin in fall 2005 (with results available almost immediately after launch)
- Psoriasis. Launch Phase II/III clinical trials for XantryI™ in early 2006
- Continue growth in current product revenues and royalties, as well as in-licensing activities for the pipeline of drugs and devices currently in development



## **Key Points to Consider**

- Provectus is targeting the areas of oncology and dermatology with prescription drugs in development, which is complemented by a line of OTC products and medical devices. The Company develops unique therapies, strengthened by a solid foundation of intellectual property and patent rights. The Company holds 12 issued patents and 3 pending patents from the U.S. Patent and Trademark Office (USPTO), with 19 U.S. patents under examination.
- The Company's growth potential comes from its multi-channel revenue generation model, specifically in oncology and dermatology. Cancer and skin disorder treatments are a multi-billion dollar industry. Products in development from Provectus are noteworthy for studies supporting their high efficacy, low toxicity, affordability, and lack of adverse side effects.
- When injected into tumor tissue, Provecta<sup>™</sup>, Provectus' oncology drug candidate, concentrates in the tumor at cytotoxic levels while quickly dissipating from healthy tissue. This makes it safer and more effective than conventional therapies, such as chemotherapy and radiation. Simultaneously, treatment with Provecta<sup>™</sup> may trigger an immune response that can eliminate tumor tissue that has spread from the treatment site (metastatic tumors). Provecta<sup>™</sup> can also be combined with radiation, increasing the effects of radiation on tumor tissue and potentially enabling less radiation to be used, thereby subjecting patients to fewer side effects.
  - In August 2005, the Company announced that the first group of subjects had completed treatment in a Phase I clinical trial for malignant melanoma (the most deadly type of skin cancer), and that the treatment was well tolerated at the initial lower dosage level. The study is being conducted at two dosage levels with both dosage levels having the potential to demonstrate safety, preliminary efficacy, and the "bystander effect"—potential effects on nearby untreated tumors.
- Like Provecta<sup>™</sup>, Provectus' other pharmaceutical candidate in development, Xantryl<sup>™</sup>, a topical dermatology drug in development to treat psoriasis and other disorders such as eczema, acne, and actinic keratosis (AK), is only active in abnormal or diseased tissues, potentially making it a safer alternative than existing products. Xantryl<sup>™</sup> is delivered directly to diseased tissue through topical application to the skin and may be activated with ambient light, reducing the potential for side effects in healthy tissue.
  - Xantryl™ successfully completed Phase I clinical studies, and is expected to begin Phase II early next year.
- The Company's therapeutic device technologies focus on three main areas: (1) the treatment of ocular melanomas; (2) the improvement of multiphoton microscopy and diagnostic devices; and (3) devices that cut tissue for precise surgical applications, such as laser vision correction.
- Provectus has commercialized the Pure-ific™ line of products, including two sizes of its quick-drying spray, Pure-ific™, which immediately eradicates up to 99.9% of germs on skin, preventing regrowth for six hours. Additionally, GloveAid™ is marketed as a hand cream designed to reduce the discomfort of wearing disposable gloves. A second-stage product, Pure-Stick™, is a non-toxic, topical agent to treat acne.
- As of July 1, 2005, the Company held approximately \$600,000 in cash. At its current cash expenditure rate, the Company believes that this amount will be sufficient to meet its needs. Provectus has already begun to increase its expenditure rate by accelerating some of its research programs for new research initiatives. In addition, Provectus is seeking to improve its cash flow by increasing sales of OTC products.



# **Historical Financial Results**

Tables 12, 13, and 14 (pages 33, 34, and 35) provide a summary of the key historical financial statements of Provectus for the years ended 2004 and 2003, as well as for the cumulative amounts from inception (January 17, 2002) to the year ended 2004 (December 31, 2004). These include the Consolidated Statements of Operations, Consolidated Balance Sheets, and Consolidated Statements of Cash Flows.

# Table 12 Provectus Pharmaceuticals, Inc. CONSOLIDATED STATEMENTS OF OPERATIONS

Years Ended 2004 and 2003, as well as Cumulative Amounts Since Inception (January 17, 2002 to December 31, 2004)

	12/31/2004	12/31/2003	Cu	mulative
Revenues:				
OTC Product Revenue	\$ 18,728	_	\$	18,728
Medical Device Revenue	13,125	_		13,125
Total revenues	31,853	_		31,853
Costs of Sales:	10,781			10,781
Gross Profit	21,072	_		21,072
Operating Expenses:				
Research and development	1,291,817	724,924		2,067,455
General and administrative	1,690,841	1,582,250		10,196,037
Amortization	671,120	671,120		1,420,537
Total operating loss	(3,632,706)	(2,978,294)		(13,662,957)
Gain on sale of equipment	_	55,000		55,000
Net loss on extinguishment of debt	(101,412)	_		(101,412)
Interest expense	(610,407)	(232,019)		(856,604)
Net Loss Applicable to Common Stockholders	\$ (4,344,525)	\$ (3,155,313)	\$	(14,565,973)
Basic and Diluted Loss Per Common Share	(0.31)	(0.33)		_
Weighted Average Number of Common Shares outstanding, basic and diluted	14,122,559	9,706,064		_



# Table 13 Provectus Pharmaceuticals, Inc. CONSOLIDATED BALANCE SHEETS

	12/31/2004	12/31/2003
ASSETS		
Current assets:		
Cash	\$ 10,774	\$ 87,875
Stock subscription receivable	_	445
Inventory	94,142	72,578
Prepaid expenses and other current assets	20,582	26,227
Prepaid consulting expense	205,427	420,817
Prepaid commitment fee, net of amortization of \$38,326	272,540	
Total current assets	603,465	771,642
Equipment and Furnishings, less accumulated depreciation of \$366,571 and \$244,760	_	121,415
Patents, net of amortization of \$1,420,537 and \$749,417	10,294,908	10,966,028
Deferred loan costs, net of amortization of \$35,922 and \$19,569	270,578	150,961
Other assets	27,000	27,000
Total assets	\$ 11,195,951	\$ 12,037,046
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable - trade	\$ 154,214	\$ 100,640
Accrued compensation	156,377	352,500
Accrued expenses	6,240	57,549
Accrued interest	43,670	100,021
Short-term convertible debt, net of debt discount of \$-0- and \$442,623	_	57,377
Gryffindor convertible debt, net of debt discount of \$95,157 and \$57,052	1,090,802	968,907
Total current liabilities	1,451,303	1,636,994
Loan from stockholder	149,000	149,000
Cornell convertible debt, net of debt discount of \$316,053 and \$0	433,947	_
Stockholders' equity		
Common stock, par value \$0.001: per share; 100,000,000 shares authorized; 16,133,876		
and 10,867,509 shares issued and outstanding, respectively	16,134	10,868
Paid-in capital	23,711,540	20,461,632
Deficit accumulated during the development stage	(14,565,973)	(10,221,448)
Additional paid-in capital	111,691	110,991
Total stockholders' equity (deficit)	9,161,701	10,251,052
Total liabilities	\$ 11,195,951	\$ 12,037,046



### Table 14

### Provectus Pharmaceuticals, Inc.

### CONSOLIDATED STATEMENTS OF CASH FLOWS

Years Ended 2004 and 2003, as well as Cumulative Amounts Since Inception (January 17, 2002 to December 31, 2004)

	12/31/2004	12/31/2003	Cumulative
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	\$(4,344,525)	\$(3,155,313)	\$(14,565,973
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	121,811	228,315	389,572
Amortization of patents	671,120	671,120	1,420,537
Amortization of original issue discount	360,663	120,669	487,575
Amortization of commitment fee	38,326	· <u>—</u>	38,326
Amortization of prepaid consultant expense	606,888	245,962	852,850
Amortization of deferred loan costs	120,953	19,569	140,522
Loss on extinguishment of debt	101,412	· —	101,412
Compensation through issuance of stock options	15,612	34,659	50,27
Compensation through issuance of stock	· _	· —	932,000
Issuance of stock for services	76,558	_	5,580,558
Issuance of warrants for services	22,481	_	22,481
Gain on sale of fixed asset	_	(55,000)	(55,000
Increase (decrease) in assets:		, ,	,
Prepaid expenses	5,645	9,254	(20,582
Inventory	(21,564)	(72,578)	(94,142
Increase (decrease) in liabilities:	,	, ,	,
Accounts payable	53,574	1,766	150,569
Accrued expenses	(143,783)	432,289	366,287
NET CASH USED IN OPERATING ACTIVITIES:	(2,314,829)	(1,519,288)	(4,202,737
Cash flows from investing activities:	,	, ,	• • • • • • • • • • • • • • • • • • • •
Proceeds from sale of fixed asset	_	180,000	180,000
Capital expenditures	(396)	(3,301)	(3,697
NET CASH (USED IN) PROVIDED BY INVESTING ACTIVITIES:	(396)	176,699	176,303
Cash flows from financing activities:			
Proceeds from loans from stockholder	_	40,000	149,000
Proceeds from convertible debt	750,000	525,959	2,275,959
Proceeds from sale of common stock	2,169,873	292,472	2,487,345
Proceeds from exercise of warrants	5,000	_	5,453
Cash paid to retire convertible debt	(500,000)	_	(500,000
Cash paid for deferred loan costs	(162,500)	(69,530)	(232,030
Premium paid on extinquishment of debt	(100,519)	· · · <u>·</u>	(100,519
Purchase and retirement of common stock	· · ·	_	(48,000
NET CASH PROVIDED BY FINANCING ACTIVITIES:	2,161,854	788,901	4,037,208
Net Change in Cash	\$ (153,371)	\$ (553,688)	\$ 10,774
Cash, at beginning of period	\$ 164,145	\$ 717,833	_
Cash, at end of period	\$ 10,774	\$ 164,145	\$ 10,774



### **Risks**

Some of the information in this Executive Informational Overview<sup>™</sup> (EIO<sup>™</sup>) relates to future events or future business and financial performance. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in the statements by Provectus on Forms 10-KSB, 10-QSB, 8-K, as well as other forms filed from time to time. The content of this EIO<sup>™</sup> with respect to Provectus has been compiled primarily from information available to the public released by the Company through news releases, in Annual Reports, and through SEC filings. Provectus is solely responsible for the accuracy of that information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Provectus. Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding. For more complete information about Provectus, please refer to the Company's Website at <a href="https://www.pvct.com">www.pvct.com</a>.

### Competition

The pharmaceutical industry is fiercely competitive. Many companies are also developing alternative therapies to treat cancer and dermatological conditions and, in this regard, are competitors. The Company's competitors may include major, multinational pharmaceutical and chemical companies, as well as universities and other research institutions. These competitors may have greater financial and other resources, larger research and development staffs, and more effective marketing and manufacturing organizations than Provectus. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. In addition, academic and government institutions may enter into exclusive licensing agreements with commercial enterprises, including the Company's competitors, to market products based on technology developed at such institutions. These companies and institutions compete with Provectus in recruiting and retaining qualified scientific and management personnel. The Company's competitors may succeed in developing or licensing technologies and products that are more effective and less costly than the Company's, or succeed in obtaining FDA or other regulatory approvals for candidates before it does. A more comprehensive discussion on the Company's competitors is provided on pages 27-29.

### **Government Regulation**

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of the Company's products are extensively regulated by governmental authorities in the U.S. and other countries. In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject the Company to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution.

### **Intellectual Property**

Intellectual property (IP) is an important part of the Company's core business. Provectus has been issued 12 patents from the U.S. Patent and Trademark Office, where it also has 3 patents pending. If Provectus is unable to secure or enforce patent rights, trademarks, trade secrets, or other intellectual property, its business could be harmed. If the Company infringes on the intellectual property of others, its business could be harmed. Provectus must take care to update and enhance its technologies to keep them from becoming obsolete.

### **Dependence on Personnel**

The Company's success is dependent, in part, upon its ability to attract and retain highly qualified scientific and management personnel. Provectus faces competition for such personnel from other companies, academic institutions, government entities, and other organizations. There can be no assurance that the Company will retain its current personnel and will be able to continue to attract qualified employees. In addition to their responsibilities for management of the overall business strategy, Drs. Dees, Scott, and Wachter (biographies on pages 9-10) are the chief researchers in the fields in which the Company



participates. Also, as of December 31, 2004, the Company owed \$156,377 in accrued but unpaid compensation to its employees. The loss of any of these key employees could have a material adverse effect on its operations and its ability to execute the business plan.

### **History of Operating Losses**

The Company's technologies are in early stages of development. Provectus has generated minimal initial revenues from sales and operations in 2004, but does not expect to generate sufficient revenues to enable it to be profitable for several calendar quarters. The Company will need additional capital to conduct its operations and develop its products, and its ability to obtain the necessary funding is uncertain.

As of December 31, 2004, Provectus had \$2,084,959 in debt, net of a debt discount of \$411,210, and \$43,671 of accrued interest on the balance sheet, consisting of \$1,185,959 in principal and \$9,224 in accrued but unpaid interest owed to Gryffindor pursuant to the Note; \$750,000 in principal and \$19,011 in accrued interest owed to the holders of its debentures, which has been authorized to be paid on March 30, 2005 and \$149,000 in principal and \$15,436 in accrued interest owed to Dr. Wachter. The amounts due to Gryffindor are due in November 2005, the amounts due in equal installments to the holders of its debentures are due in July and October 2007, and the amounts due to Dr. Wachter are due in 2009. Because of the convertible nature of the debt owed to Gryffindor and to the holders of the convertible debentures, the Company may not have to repay this debt if the debt is converted into shares of the common stock, but there are no assurances this will occur. Furthermore, because the Company is currently generating limited revenue, it may be unable to pay its debts when they become due.

### **Uncertain Development**

The pharmaceutical drug and medical device products that Provectus is developing will require significant additional research, formulation, and manufacture development, and pre-clinical and extensive clinical testing prior to regulatory licensure and commercialization. Pharmaceutical and medical device products that appear to be promising at early stages of development may not reach the market or be marketed successfully for a number of reasons, including poor trial results, limited efficacy, regulatory limits, high cost of manufacture, lack of market acceptance, and disputes with other copyright holders. Provectus does not expect any pharmaceutical products or medical device products now in development to be commercially available for at least several years, if at all.

### **Cash Flow**

As of July 1, 2005, the Company held approximately \$600,000 in cash. At its current cash expenditure rate, the Company believes that this amount will be sufficient to meet its needs. Provectus has already begun to increase its expenditure rate by accelerating some of its research programs for new research initiatives. In addition, the Company is seeking to improve its cash flow by increasing sales of OTC products. However, there can be no assurance that the Company will be successful in increasing sales of its OTC products. Moreover, even if successful in improving its current cash flow position, the Company will nonetheless require additional funds to meet its long-term needs. These funds could come from the proceeds of private placements or public offerings of debt or equity securities.



### **Recent Events**

**08/24/2005**—Announced second quarter financial results for the quarter ended June 30, 2005. Product revenue increased by \$837 in the three months ended June 30, 2005 to \$1,672 from \$835 in the three months ended June 30, 2004. The increase in OTC product revenue resulted primarily from sales of Pure-ific™ in retail stores. OTC product revenue increased by \$1,455 in the six months ended June 30, 2005 to \$4,066 from \$2,611 in the six months ended June 30, 2004. The increase in OTC product revenue resulted primarily from sales of Pure-ific™ in retail stores. Medical device revenue was unchanged in the three months ended June 30, 2005 from the three months ended June 30, 2004. Medical device revenue decreased by \$12,141 in the six months ended June 30, 2005 to \$984 from \$13,125 in the six months ended June 30, 2004. The decrease in medical device revenue resulted primarily due to a large beta unit sale in the six months ended June 30, 2004 that was not repeated in the six months ended June 30, 2005.

**08/17/2005**—Announced that the first group of subjects have completed treatment in its Phase I clinical trial of Provecta<sup>™</sup>, and that the treatment was well tolerated at the initial lower dose level. The study is being conducted at two dosage levels with both dosage levels having the potential for showing safety, preliminary efficacy, and the "bystander effect." The authorized dosage will now be increased to the maximum level for treatment of the remaining subjects.

**08/08/2005**—Announced that the first patients have completed treatment in its Phase I clinical trial of Provecta<sup>™</sup>. The study is being conducted at two of the world's leading melanoma treatment and research centers, both located in New South Wales, Australia, a country where the incidence of melanoma is more than twice that of the U.S. Each patient enrolled in the study is having one to three tumors treated with a single injection of PV-10 and the local response to the treatment is then being observed for a period of 12 to 24 weeks. It is anticipated that the full study will be finished early next year.

**08/01/2005**—Provectus' CEO, Craig Dees, issued an open letter to shareholders and interested members of the investment community in order to update all parties on the Company's operational and clinical progress.

**07/21/2005**—Announced that it has obtained final clearance to begin the first Phase I clinical trial of Provecta<sup>™</sup>. The study is designed to evaluate the safety and preliminary efficacy of Provecta<sup>™</sup> in 20 subjects with Stage III metastatic melanoma (the most aggressive form of skin cancer). Provecta<sup>™</sup> will be injected into one to three tumors in each subject.

**07/18/2005**—Announced it has received a notice of allowance for a patent application covering the Company's anti-cancer pharmaceutical agent Provecta<sup>™</sup>. The notice of allowance from the U.S. Patent and Trademark Office indicates that the application is in condition for issuance and will issue as a U.S. patent within several months.

**06/14/2005**—Announced that Kevin Richardson, a cancer activist and member of the popular band, the Backstreet Boys, became a corporate spokesperson for Provectus. Richardson became involved with the Company through his introduction to Peter Culpepper, CFO of Provectus, whose daughter Victoria, a young cancer survivor, was the Honorary Survivor at the Relay For Life fundraising event in East Tennessee.

**06/07/2005**—Announced that CEO Craig Dees was to address the Financial Analyst Society of San Diego on June 9. The lunch meeting provided members of the San Diego investment community the opportunity to hear the Provectus story and to ask questions of Dr. Dees relating to the Company's ongoing clinical work for treating cancer and serious skin conditions.

**04/27/2005**—Announced the addition of David M. Darst to the Company's Corporate Advisory Board. Darst is a co-founder of Potentia Pharmaceuticals, a biotechnology company developing therapeutics for macular degeneration.



**04/12/2005**—Announced it had begun the process to start Phase II trials for Xantryl™ to treat psoriasis and later eczema. The Company is expected to begin clinical studies for psoriasis in late 2005 and eczema in 2006. It had successfully completed pre-clinical and Phase I studies in Denmark and the U.S. for the treatment of psoriasis with Xantryl™.

**04/04/2005**—Announced that it raised \$3.15 million in debt financing via a convertible debenture placed with an investor group led by Network 1 Financial Securities, Inc. and DC Opportunity Fund Ltd. The new debenture instruments are convertible to common stock at a fixed price of \$0.75 per share. As an additional consideration, the new debenture holders will receive five-year warrants to purchase 4.2 million shares of Provectus Pharmaceuticals common stock at an exercise price of \$1.06 per share.

**03/14/2005**—Announced that it had selected Allen & Caron Inc, based in Irvine, CA, as its investor relations agency.

**02/01/2005**—Announced that it had entered into a strategic sales, advertising, and marketing agreement for its over-the-counter (OTC) products with Legacy Marketing, Inc., a brand management and marketing organization based in Frankfort, III. Provectus' OTC products include Pure-ific™ Antibacterial Hand Spray, GloveAid™ hand cream, and Pure-Stick™ anti-acne treatment.

**01/25/2005**—Announced that CEO Craig Dees, was to address the Chartered Financial Analyst Society of Cleveland on January 26.

**01/11/2005**—CEO Craig Dees, issued a letter to the Company's shareholders. It focused on the potential of its over-the-counter (OTC) product, Provecta<sup>™</sup>, a cancer drug that completed pre-clinical studies.

**12/14/2004**—Announced it had received a notice of allowability for what was anticipated to be its fourteenth U.S. patent, as well as the third patent for its pharmaceutical products.

**12/09/2004**—Announced that it had completed a private placement transaction with 14 accredited investors, as reported on the Company's 8K filed on November 16, 2004.

**11/09/2004**—Announced that new chain stores had agreed to sell the Company's first OTC product, Pure-ific™ Antibacterial Hand Spray.

**10/15/2004**—Announced CEO Craig Dees, was to be one of the guest lecturers at Auburn University's College of Veterinary Medicine on October 22, as part of the Joy Goodwin Lecture Series. Dees' lecture were to focus on recent developments at Provectus, including the use of pharmacological agents designed to selectively target and destroy disease cells without harming surrounding healthy tissue, thereby reducing potential side effects.

**10/11/2004**—Announced it had achieved FDA clearance of its Investigational New Drug (IND) application for Provecta™. The application was submitted in late August.

**10/05/2004—**CEO Craig Dees, issued a letter to the Company's shareholders. It detailed its OTC products and future plans for these products.

**09/28/2004—**Announced it had received a notice of allowance for what was anticipated to be the Company's thirteenth U.S. patent, as well as its fourth patent for a therapeutic medical device.

**08/25/2004**—Announced it had filed an Investigational New Drug (IND) application to the U.S. Food & Drug Administration for Provecta™.

**08/17/2004**—Announced it had obtained the necessary financing to support its planned operations and research activities. This financing alleviated the doubt concerning its ability to operate in the future, as discussed in the Company's second quarter 2004 financial statements released in its form 10-QSB.

**08/02/2004**—Announced that AmerisourceBergen will sell the Company's first OTC product, Pure-ific™ Antibacterial Hand Spray.



07/28/2004—Announced execution of \$20.75 million in equity financing with Cornell Capital Partners, LP.

**06/29/2004**—Announced it had completed a fixed-price financing of \$1 million for the purchase of restricted common shares. The total financing to the Company was to be \$2.3 million if all warrants are exercised.

**05/24/2004**—Announced it had learned the Company was to be listed, without authorization, on the Berlin Stock Exchange, along with more than 200 U.S. publicly traded companies. The Company's attorneys had issued a demand letter to the Berlin Stock Exchange requesting immediate removal from the exchange's stock listing process.

**05/06/2004**—Announced that members of Provectus would attend the National Investment Banking Association (NIBA) conference in Chicago on May 13-14, 2004. The event brings institutional investors, brokers, and investment bankers together with presenting public and pre-IPO companies.

**04/28/2004**—Announced that Paul M. Goldfarb, M.D., had been appointed to the Company's newly formed Corporate Advisory Board.

**04/28/2004**—Announced it had shipped a prototype signal processor for laboratory microscopes used in biomedical research. The prototype utilizes the Company's proprietary advanced signal processing technologies described in its U.S. Patents 6,519,076 and 6,525,862. The unit was shipped to Carl Zeiss MicroImaging, Inc. If Zeiss determines that it can commercialize this technology, then the Company would expect to enter into negotiation of a license agreement covering the underlying intellectual property.

**04/01/2004**—Announced that The Prostate Cancer Foundation had made a donor-directed research award to the School of Veterinary Medicine and The Comprehensive Cancer Center of the University of Wisconsin-Madison for a cancer study using Provectus' drug Provecta™. The two-year, \$120,000 research award was funded by Varian Medical Systems, Inc.

**02/19/2004**—Announced that Peter Culpepper, CPA, MBA, had been appointed to serve as CFO of the Company. Provectus' former CFO, Dan Hamilton, had left to pursue other professional interests.

**01/27/2004**—Announced it was preparing an IND application for Provecta<sup>™</sup>, a drug therapy intended for breast and liver cancer.

**01/23/2004**—Announced that it had engaged Elite Financial Communications Group, LLC, a financial communications, investor relations, and strategic resourcing firm, to launch a comprehensive marketing campaign to increase investor awareness and market support for the Company among individual and professional investors, industry and securities analysts, and the media.

**01/15/2004**—Announced that The Research Works, Inc., an equity research boutique, initiated coverage and published a report on the Company. The report is available online through Stocks on the Web, the web-publishing division of The Research Works, at <a href="https://www.stocksontheweb.com/pvct.htm">www.stocksontheweb.com/pvct.htm</a>.

**01/07/2004**—Announced that the Company is working to correct inaccurate reporting of proposed sales of shares by the Company directors.



## Glossary of Lesser-Known Terms

**Ablation**—To remove or destroy the function of a body part (such as a tumor) by a surgical procedure or use of a noxious substance.

**Acne—**An inflammatory disease of the sebaceous glands and hair follicles of the skin that is marked by the eruption of pimples or pustules, especially on the face.

Actinic keratosis (AK)—An overgrowth of skin layers thought to result from extended exposure to the sun.

**Ambient**—Describes the surrounding environment (especially temperature and pressure) of an object or experiment, in particular an environment which affects the object or experiment but is not affected by it.

Chemotherapy—Treatment of cancer through the use of cytoxic anti-cancer drugs.

Cytotoxic—Of, relating to, or producing a toxic effect on cells.

**Eczema—**A noncontagious inflammation of the skin, characterized chiefly by redness, itching, and the outbreak of lesions that may discharge serous matter and become encrusted and scaly.

Enucleation—To remove (a tumor or eye, for example) whole from an enveloping cover or sac.

**GloveAid**<sup>™</sup>—A hand cream with both antiperspirant and antibacterial properties developed by Provectus.

**Homografts**—A graft of tissue obtained from a donor of the same species as, but with a different genetic make-up from the recipient, as a tissue transplant between two humans. Also called allograft.

**Immunotherapy**—Treatment of disease by inducing or suppressing an immune response.

**Investigational New Drug (IND)**—An application containing laboratory study results of the drug candidate is submitted to the FDA to request permission to conduct studies in humans.

**Melanoma**—A malignant tumor that develops from melanocytes, which are melanin-producing cells in the skin.

**Metastasis—**To spread from one part of the body to another. Cells in the secondary tumors may be dissimilar to those in the primary tumor.

**Micrometastesis—**The spread of cancer cells from the primary site with the secondary tumors too small to be clinically detected.

**Photoactivation**—The use of concentrated light sources to affect a chemical reaction.

**Provecta**<sup>™</sup>—An injectable oncology drug developed by Provectus.

**Psoriasis—**A noncontagious inflammatory skin disease characterized by chronic reddish patches covered with silvery scales.

Pure-ific<sup>™</sup>—An antibacterial hand and surface spray developed by Provectus.

**Pure-Stick™**—A non-toxic, topical agent that checks the production of sebum and sweat while damping skin pathogens associated with acne. Can be used both as a remedy and a preventative for acne; developed by Provectus.

**Psoralen and ultraviolet A light (PUVA)**—A treatment for psoriasis combining the oral administration of psoralen with subsequent exposure to long wavelength ultraviolet light.



**PV-10**—Provectus code name for Rose Bengal (RB); used in therapeutic products for cancer and dermatology. See Rose Bengal (RB).

Radiation therapy—The use of high-energy radiation to kill cancer cells and shrink tumors.

**Rose bengal (RB)**—The active ingredient in Provecta<sup>™</sup> and Xantryl<sup>™</sup>, a synthetic small molecule agent that is highly stable at room temperature and long-lasting.

**Xantryl**<sup>™</sup>—A topical dermatology drug developed by Provectus.

**Xenograft**—A type of tissue graft in which the donor and recipient are of different species. Also called heterograft.



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