PROVECTUS PHARMACEUTICALS INC
Form 10KSB
March 30, 2006

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-KSB

(Mark One)

xAnnual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended December 31, 2005; OR

o Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the transition period from _____ to _____

Commission file number: 0-9410

Provectus Pharmaceuticals, Inc.
(Name of Small Business Issuer in Its Charter)

Nevada	**90-0031917**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)
7327 Oak Ridge Highway, Suite A, Knoxville, Tennessee	**37931**
(Address of Principal Executive Offices)	(Zip Code)

865/769-4011
(Issuer's Telephone Number, Including Area Code)

Securities registered under Section 12(b) of the Exchange Act:
None
_____
(Title of Class)

Securities registered under Section 12(g) of the Exchange Act:
Common shares, par value $.001 per share
_____
(Title of Class)

Check whether the issuer is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. o
Note - Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d)

of the Exchange Act from their obligations under those Sections.

Check whether the issuer: (1) filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes xNo o
Check if there is no disclosure of delinquent filers in response to Item 405 of Regulation S-B contained in this form, and no disclosure will be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-KSB or any amendment to this Form 10-KSB. x

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

The issuer’s revenues for the most recent fiscal year were $6,536.

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of February 13, 2006, was $31,212,267 (computed on the basis of $0.88 per share).

The number of shares outstanding of the issuer's stock, $0.001 par value per share, as of February 13, 2006 was 35,468,485.

Documents incorporated by reference in Part III hereof: Proxy Statement for 2006 Annual Meeting of Stockholders.

Transitional Small Business Disclosure Format (check one): Yes o No x

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PART I

Item 1. Description of Business.

History

Provectus Pharmaceuticals, Inc., formerly known as "Provectus Pharmaceutical, Inc." and "SPM Group, Inc.," was incorporated under Colorado law on May 1, 1978. SPM Group ceased operations in 1991, and became a development-stage company effective January 1, 1992, with the new corporate purpose of seeking out acquisitions of properties, businesses, or merger candidates, without limitation as to the nature of the business operations or geographic location of the acquisition candidate.

On April 1, 2002, SPM Group changed its name to "Provectus Pharmaceutical, Inc." and reincorporated in Nevada in preparation for a transaction with Provectus Pharmaceuticals, Inc., a privately-held Tennessee corporation, which we refer 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 a wholly owned subsidiary of Provectus. For accounting purposes, we treat this transaction as a recapitalization of PPI.

On November 19, 2002, we acquired Valley Pharmaceuticals, Inc., a privately-held Tennessee corporation formerly known as Photogen, Inc., by merging our subsidiary PPI with and into Valley and naming the surviving corporation "Xantech Pharmaceuticals, Inc." Valley had minimal operations and had no revenues prior to the transaction with the Company. By acquiring Valley, we acquired our most important intellectual property, including issued U.S. patents and patentable inventions, with which we intend to develop:

- prescription drugs, medical and other devices (including laser devices) and over-the-counter pharmaceutical products in the fields of dermatology and oncology; and

- technologies for the preparation of human and animal vaccines, diagnosis of infectious diseases and enhanced production of genetically engineered drugs.

Prior to the acquisition of Valley, we were considered to be, and continue to be, in the development stage and had not generated any revenues from the assets we acquired.

On December 5, 2002, we acquired the assets of Pure-ific L.L.C., a Utah limited liability company, and created a wholly owned subsidiary, Pure-ific Corporation, to operate that business. We acquired the product formulations for Pure-ific personal sanitizing sprays, along with the "Pure-ific" trademarks. We intend to continue product development and begin to market a line of personal sanitizing sprays and related products to be sold over the counter under the "Pure-ific" brand name.

Description Of Business

Overview

Provectus, and its five wholly owned subsidiaries:

- o Xantech Pharmaceuticals, Inc.
- o Pure-ific Corporation
- o Provectus Biotech, Inc.
- o Provectus Devicetech, Inc.
- o Provectus Pharmatech, Inc.

(which we refer to as our subsidiaries) develop, license and market and plan to sell products in three sectors of the healthcare industry:

- o Over-the-counter products, which we refer to in this report as "OTC products;"
- o Prescription drugs; and
- o Medical device systems

We manage Provectus and our subsidiaries on an integrated basis and when we refer to "we" or "us" or "the Company" in this Annual Report on Form 10-KSB, we refer to all six corporations considered as a single unit. Our principal executive offices are located at 7327 Oak Ridge Highway, Suite A, Knoxville, Tennessee 37931, telephone 865/769-4011.

Through discovery and use of state-of-the-art scientific and medical technologies, the founders of our pharmaceutical business have developed a portfolio of patented, patentable, and proprietary technologies that support multiple products in the prescription drug, medical device and OTC products categories (including patented technologies for: (a) treatment of cancer; (b) novel therapeutic medical devices; (c) enhancing contrast in medical imaging; (d) improving signal processing during biomedical imaging; and (e) enhancing production of biotechnology products). Our prescription drug products encompass the areas of dermatology and oncology and involve several types of small molecule-based drugs. Our medical device systems include therapeutic and cosmetic lasers, while our OTC products address markets primarily involving skincare applications. Because our prescription drug candidates and medical device systems are in the early stages of development, they are not yet on the market and there is no assurance that they will advance to the point of commercialization.

Our first commercially available products are directed into the OTC market, as these products pose minimal or no regulatory compliance barriers to market introduction. For example, the active pharmaceutical ingredient (API) in our ethical products is already approved for other medical uses by the FDA and has a long history of safety for use in humans. This use of known APIs for novel uses and in novel formulations minimizes potential adverse concerns from the FDA, since considerable safety data on the API is available (either in the public domain or via license or other agreements with third parties holding such information). In similar fashion, our OTC products are based on established APIs and, when possible, utilize formulations (such as aerosol or cream formulations) that have an established precedent. (For more information on compliance issues, see "Federal Regulation of Therapeutic Products" below.) In this fashion, we believe that we can diminish the risk of regulatory bars to the introduction of safe, consumer-friendly products and minimize the time required to begin generating revenues from product sales. At the same time, we continue to develop higher-margin prescription pharmaceuticals and medical devices, which have longer development and regulatory approval cycles.

Over-the-Counter Pharmaceuticals

Our OTC products are designed to be safer and more specific than competing products. Our technologies offer practical solutions for a number of intractable maladies, using ingredients that have limited or no side effects compared with existing products. To develop our OTC products, we typically use compounds with potent antibacterial and antifungal activity as building blocks and combine these building blocks with anti-inflammatory and moisture-absorbing agents. Products with these properties can be used for treatment of a large number of skin afflictions, including:

- o hand irritation associated with use of disposable gloves
- o eczema
- o mild to moderate acne

Where appropriate, we have filed or will file patent applications and will seek other intellectual property protection to protect our unique formulations for relevant applications.

GloveAid

Personnel in many occupations and industries now use disposable gloves daily in the performance of their jobs, including:

- o Airport security personnel;
- o Food handling and preparation personnel;

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- o Sanitation workers;
- o Postal and package delivery handlers and sorters;
- o Laboratory researchers;
- o Health care workers such as hospital and blood bank personnel; and
- o Police, fire and emergency response personnel.

Accompanying the increased use of disposable gloves is a mounting incidence of chronic skin irritation. To address this market, we have 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. During 2003, we ran a pilot scale run at the manufacturer of GloveAid. We now intend to license this product to a third party with experience in the institutional sales market.

Pure-ific

Our Pure-ific line of products includes two quick-drying sprays, Pure-ific and Pure-ific Kids, that immediately kill up to 99.9% of germs on skin and prevent regrowth for 6 hours. We have determined the effectiveness of Pure-ific based on our internal testing and testing performed by Paratus Laboratories H.B., an independent research lab. Pure-ific products help prevent the spread of germs and thus complement our other OTC products designed to treat irritated skin or skin conditions such as acne, eczema, dandruff and fungal infections. Our Pure-ific sprays have been designed with convenience in mind and are targeted towards mothers, travelers, and anyone concerned about the spread of sickness-causing germs. During 2003 and 2004, we identified and engaged sales and brokerage forces for Pure-ific. We emphasized getting sales in independent pharmacies and mass (chain store) markets. The supply chain for Pure-ific was established with the ability to support large-scale sales and a starting inventory was manufactured and stored in a contract warehouse/fulfillment center. In addition, a website for Pure-ific was developed with the ability for supporting online sales of the antibacterial hand spray. During 2005, most of our sales were generated from customers accessing our website for Pure-ific and making purchases online. We now intend to license the Pure-ific product and sell the underlying assets.

Acne

A number of dermatological conditions, including acne and other blemishes result from a superficial infection which triggers an overwhelming immune response. We anticipate developing OTC products similar to the GloveAid line for the treatment of mild to moderate cases of acne and other blemishes. Wherever possible, we intend to formulate these products to minimize or avoid significant regulatory bars that might adversely impact time to market.

Prescription Drugs

We are developing a number of prescription drugs which we expect will provide minimally invasive treatment of chronic severe skin afflictions such as psoriasis, eczema, and acne; and several life-threatening cancers such as those of the liver, breast and prostate. We believe that our products will be safer and more specific than currently existing products. Use of topical or other direct delivery formulations allows these potent products to be conveniently and effectively delivered only to diseased tissues, thereby enhancing both safety and effectiveness. The ease of use and superior performance of these products may eventually lead to extension into OTC applications currently serviced by less safe, more expensive alternatives. All of these products are in the pre-clinical or clinical trial stage.

Dermatology

Our most advanced prescription drug candidate for treatment of topical diseases on the skin is Xantryl, a topical gel. PV-10, the active ingredient in Xantryl, is "photoactive": it reacts to light of certain wavelengths, increasing its therapeutic effects. PV-10 also concentrates in diseased or damaged tissue but quickly dissipates from 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 PV-10, we can deliver a higher therapeutic effect at lower dosages of active ingredient, thus minimizing potential side effects including damage to nearby healthy tissues. PV-10 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, we have 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.

Acute psoriasis. Psoriasis is a common chronic disorder of the skin characterized by dry scaling patches, called "plaques," for which current treatments are few and those that are available have potentially serious side effects. According to Roenigk and Maibach (Psoriasis, Third Edition, 1998), there are approximately five million people in the United States who suffer from psoriasis, with an estimated 160,000 to 250,000 new psoriasis cases each year. There is no known cure for the disease at this time. According to the National Psoriasis Foundation, the majority of psoriasis sufferers, those with mild to moderate cases, are treated with topical steroids that can have unpleasant side effects; none of the other treatments for moderate cases of psoriasis have proven completely effective. The 25-30% of psoriasis patients who suffer from more severe cases generally are treated with more intensive drug therapies or 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.

We believe 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; moreover, the therapy has shown promise in comprehensive Phase 1 clinical trials. The objective of a Phase 1 clinical trial is to determine if there are safety concerns with the therapy. In these studies, involving more than 50 test subjects, Xantryl was applied topically to psoriatic plaques and then illuminated with green light. In our first study, a single-dose treatment yielded an average reduction in plaque thickness of 59% after 30 days, with further response noted at the final follow-up examination 90 days later. Further, no pain, significant side effects, or evidence of “rebound” (increased severity of a psoriatic plaque after the initial reduction in thickness) were 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. We are continuing the required Food and Drug Administration reporting to support the active Investigational New Drug application for Xantryl’s Phase 2 clinical trials on psoriasis. The required reporting includes the publication of results regarding the multiple treatment scenario of the active ingredient in Xantryl. We expect to conduct Phase 2 studies in the near future, in which we expect to assess the potential for remission of the disease using a regimen of weekly treatments similar to those used for PUVA.

Actinic Keratosis. According to Schwartz and Stoll (Fitzpatrick's Dermatology in General Medicine, 1999), actinic keratosis, or "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 over 50% of elderly fair-skinned persons living in sunny climates. These experts note 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 comprising excision, cryotherapy, and ablation with topical 5-fluorouracil) are often painful and frequently yield unacceptable cosmetic outcomes due to scarring. Building on our experience with psoriasis, we are assessing the use of Xantryl with green-light activation as a possible improvement in treatment of early and more advanced stages of AK. We completed an initial Phase 1 clinical trial of the therapy for this indication in 2001 with the predecessor company that was acquired in 2002. 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. We have decided to prioritize further clinical development of Xantryl

for treatment of psoriasis and eczema rather than AK at this time since the market is much larger for psoriasis and eczema.

Severe Acne. According to Berson et al. (Cutis. 72 (2003) 5-13), acne vulgaris affects approximately 17 million individuals in the U.S., causing pain, disfigurement, and social isolation. Moderate to severe forms of the disease have proven responsive to several photodynamic regimens, and we anticipate that Xantryl can be used as an advanced treatment for this disease. Pre-clinical studies show that the active ingredient in Xantryl readily kills bacteria associated with acne. This finding, coupled with our clinical experience in psoriasis and actinic keratosis, suggests that therapy with Xantryl will exhibit no significant side effects and will afford improved performance relative to other therapeutic alternatives. If correct, this would be a major advance over currently available products for severe acne.

As noted above, we are researching multiple uses for Xantryl with green-light activation. Multiple-indication use by a common pool of physicians - dermatologists, in this case - should reduce market resistance to this new therapy.

Oncology

Oncology is another major market where our planned products may afford competitive advantage compared to currently available options. We are developing Provecta, a sterile injectible form of PV-10, for direct injection into tumors. Because PV-10 is retained in diseased or damaged tissue but quickly dissipates from healthy tissue, we believe we can develop therapies that confine treatment to cancerous tissue and reduce collateral impact on healthy tissue. During 2003 and 2004, we worked toward completion of the extensive scientific and medical materials necessary for filing an Investigational New Drug (IND) application for Provecta in anticipation of beginning Phase 1 clinical trials for breast and liver cancer. This IND was filed and cleared by the FDA in 2004 setting the stage for two Phase 1 clinical trials; namely, treating metastatic melanoma and recurrent breast carcinoma. We started both of these Phase 1 clinical trials in 2005.

Liver Cancer. 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 a localized injection of ethanol (alcohol), cryosurgery, radiofrequency ablation, or ionizing radiation such as X-rays. Where effective, these therapies have many side effects; selecting therapies with fewer side effects tends to reduce overall effectiveness. Combined, ablative therapies have a five-year survival rate of 33% - meaning that only 33% of those liver cancer patients whose cancers are treated using these therapies survive for five years after their initial diagnoses. In pre-clinical studies we have 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, this approach appears to produce no significant side effects. Based on these encouraging preclinical results, we are assessing strategies for initiation of clinical trials of Provecta for treatment of liver cancer.

Breast Cancer. Breast cancer afflicts over 200,000 U.S. citizens annually, leading to over 40,000 deaths. Surgical resection, chemotherapy, radiation therapy, and immunotherapy comprise the standard treatments for the majority of cases, resulting in serious side effects that in many cases are permanent. Moreover, current treatments are relatively ineffective against metastases, which in many cases are the eventual cause of patient mortality. Pre-clinical studies using human breast tumors implanted in mice have shown that direct injection of Provecta into these tumors ablates the tumors, and, as in 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 diagnosis of 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 clearly has the potential of becoming a primary treatment. We are evaluating options for expanding clinical studies of direct injection of Provecta into breast tumors while conducting Phase 1 clinical studies of our indication for Provecta in recurrent breast carcinoma.

Prostate Cancer. Cancer of the prostate afflicts approximately 190,000 U.S. men annually, leading to over 30,000 deaths. As with breast cancer, surgical resection, chemotherapy, radiation therapy, and immunotherapy comprise the standard treatments for the majority of cases, and can result in serious, permanent side effects. We believe that 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, are becoming routine procedures for diagnosis and treatment of these cancers, we believe that localized destruction of suspected tumors through direct injection of Provecta can become a primary treatment. We are evaluating options for initiating clinical studies of direct injection of Provecta into prostate tumors, and expect to formulate final plans based on results from clinical studies of our indications for Provecta in the treatment of liver and breast cancer.

Metastatic Melanoma. Melanoma is expected to strike 62,000 people in the U.S. this year, leading to 7,600 deaths. The incidence of melanoma in Australia, where our Phase 1 clinical study is currently underway, is 4X that of the U.S. There have been no significant advances in the treatment of melanoma for approximately 30 years. We are evaluating options for expanding clinical studies of direct injection of Provecta into melanoma lesions while conducting Phase 1 clinical studies of our indication for Provecta in Stage 3 metastatic melanoma.

Medical Devices

We are developing medical devices to address two major markets:

o cosmetic treatments, such as reduction of wrinkles and elimination of spider veins and other cosmetic blemishes; and

o therapeutic uses, including photoactivation of Xantryl other prescription drugs and non-surgical destruction of certain skin cancers.

We expect to develop medical devices through partnerships with third-party device manufacturers or, if appropriate opportunities arise, through acquisition of one or more device manufacturers.

Photoactivation. Our clinical tests of Xantryl for dermatology have, up to the present, utilized a number of commercially available lasers for activation of the drug. This approach has several advantages, including the leveraging of an extensive base of installed devices present throughout the pool of potential physician-adopters for Xantryl; 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 dermatological treatment, is potentially too cumbersome and costly for routine treatment of the large population of patients with psoriasis, we have begun investigating potential 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. We anticipate that such photoactivation hardware would be developed, manufactured, and supported in conjunction with one or more third-party device manufacturer.

Melanoma. A high priority in our medical devices field is the development of a laser-based product for treatment of melanoma. We have conducted extensive research on ocular melanoma at the Massachusetts Eye and Ear Infirmary (a teaching affiliate of Harvard Medical School) using a new laser treatment that may offer significant advantage over current treatment options. A single quick non-invasive treatment of ocular melanoma tumors in a rabbit model resulted in elimination of over 90% of tumors, and may afford significant advantage over invasive alternatives, such as surgical excision, enucleation, or radiotherapy implantation. Ocular melanoma is rare, with approximately 2,000 new cases annually in the U.S. However, we believed that our extremely successful results could be extrapolated to treatment of primary melanomas of the skin, which have an incidence of over 52,000 new cases annually in the U.S. and a 13% five-year survival rate after metastasis of the tumor. We have performed similar laser treatments on large

(averaging approximately 3 millimeters thick) cutaneous melanoma tumors implanted in mice, and have been able to eradicate over 90% of these pigmented skin tumors with a single treatment. Moreover, we have 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, we believe that a device for laser treatment of primary melanomas of the skin and eye is nearly ready for human studies. We anticipate partnering with a medical device manufacturer to bring it to market in reliance on a 510(k) notification. For more information about the 510(k) notification process, see "Federal Regulation of Therapeutic Products" below.

Research and Development

We continue to actively develop projects that are product directed and are attempting to conserve available capital and achieve full capitalization of our company through equity and convertible debt offerings, generation of product revenues, and other means. All ongoing research and development activities are directed toward maximizing shareholder value and advancing our corporate objectives in conjunction with our OTC product licensure, our current product development and maintaining our intellectual property portfolio.

Production

We have determined that the most efficient use of our capital in further developing our OTC products is to license the products and sell the underlying assets for upfront consideration.

Sales

Our first commercially available products are directed into the OTC market, as these products pose minimal or no regulatory compliance barriers to market introduction. In this fashion, we believe that we can diminish the risk of regulatory bars to the introduction of products and minimize the time required to begin generating revenues from product sales. At the same time, we continue to develop higher-margin prescription pharmaceuticals and medical devices, which have longer development and regulatory approval cycles.

We have commenced limited sales of Pure-ific, our antibacterial hand spray. We sold small amounts of this product during 2004 and 2005. We will continue to seek additional markets for our products through existing distributorships that market and distribute medical products, ethical pharmaceuticals, and OTC products for the professional and consumer marketplaces through licensure and partnership arrangements, and through potential merger and acquisition candidates.

In addition to developing and selling products ourselves on a limited basis, we are negotiating actively with a number of potential licensees for several of our intellectual properties, including patents and related technologies. To date, we have not yet entered into any licensing agreements; however, we anticipate consummating one or more such licenses in the future.

Intellectual Property

Patents

We hold a number of U.S. patents covering the technologies we have developed and are continuing to develop for the production of prescription drugs, medical devices and OTC pharmaceuticals, including those identified in the following table:

U.S. Patent No.	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
6,986,740	Ultrasound contrast using halogenated xanthenes	January 17, 2006	TBD
6,991,771	Improved intracorporeal medicaments for High energy phototherapeutic treatment of disease	January 31, 2006	TBD

We continue to pursue patent applications on numerous other developments we believe to be patentable. We consider our issued patents, our pending patent applications and any patentable inventions which we may develop to be extremely valuable assets of our business.

Trademarks

We own the following trademarks used in this document: Xantryl(TM), Provecta(TM), GloveAid(TM), and Pure-ific(TM) (including Pure-ific(TM) and Pure-ific(TM) Kids). We also own the registered trademark PulseView(R). Trademark rights are perpetual provided that we continue to keep the mark in use. We consider these marks, and the associated name recognition, to be valuable to our business.

Material Transfer Agreement

We have entered into a Material Transfer Agreement dated as of July 31, 2003 with Schering-Plough Animal Health Corporation, which we refer to as "SPAH", the animal-health subsidiary of Schering-Plough Corporation, a major international pharmaceutical company. This Material Transfer Agreement is still in effect through 2005. We refer to this agreement in this report as the "Material Transfer Agreement." Under the Material Transfer Agreement, we will provide SPAH with access to some of our patented technologies to permit SPAH to evaluate those technologies for use in animal-health applications. If SPAH determines that it can commercialize our technologies, then the Material Transfer Agreement obligates us and SPAH to enter into a license agreement providing for us to license those technologies to SPAH in exchange for progress payments upon the achievement of goals. The Material Transfer Agreement covers four U.S. patents that cover biological material manufacturing technologies (i.e., biotech related). The Material Transfer Agreement continues indefinitely, unless SPAH terminates it by giving us notice or determines that it does not wish to secure from us a license for our technologies. The Material Transfer Agreement can also be terminated by either of us in the event the other party breaches the agreement and does not cure the breach within 30 days of notice from the other party. We can give you no assurance that SPAH will determine that it can commercialize our technologies or that the goals required for us to obtain progress payments from SPAH will be achieved.

Competition

In general, the pharmaceutical industry is intensely competitive, characterized by rapid advances in products and technology. A number of companies have developed and continue to develop products that address the areas we have targeted. Some of these companies are major pharmaceutical companies that are international in scope and very large in size, while others are niche players that may be less familiar but have been successful in one or more areas we are targeting. Existing or future pharmaceutical, device, or other competitors may develop products that accomplish similar functions to our technologies in ways that are less expensive, receive faster regulatory approval, or receive greater market acceptance than our products. Many of our competitors have been in existence for considerably longer than we have, have greater capital resources, broader internal structure for research, development, manufacturing and marketing, and are in many ways further along in their respective product cycles.

At present, our most direct competitors are smaller companies that are exploiting niches similar to ours. In the field of photodynamic therapy, one competitor, QLT, Inc., has received FDA approval for use of its agent Photofrin(R) for treatment of several niche cancer indications, and has a second product, Visudyne(R), approved for treatment of certain forms of macular degeneration. Another competitor in this field, Dusa Pharmaceuticals, Inc. recently received FDA approval of its photodynamic product Levulan(R) Kerastik(R) for treatment of actinic keratosis. We believe that QLT and Dusa, among other competitors, have established a working commercial model in dermatology and oncology, and that we can benefit from this model by offering products that, when compared to our competitors' products, afford superior safety and performance, greatly reduced side effects, improved ease of use, and lower cost, compared to those of our competitors.

While it is possible that eventually we may compete directly with major pharmaceutical companies, we believe it is more likely that we will enter into joint development, marketing, or other licensure arrangements with such

competitors.

We also have a number of market areas in common with traditional skincare cosmetics companies, but in contrast to these companies, our products are based on unique, proprietary formulations and approaches. For example, we are unaware of any products in our targeted OTC skincare markets that our similar to our GloveAid and Pure-ific products. Further, proprietary protection of our products may help limit or prevent market erosion until our patents expire.

Federal Regulation of Therapeutic Products

All of the prescription drugs and medical devices we currently contemplate developing will require approval by the FDA prior to sales within the United States and by comparable foreign agencies prior to sales outside the United States. The FDA and comparable regulatory agencies impose substantial requirements on the manufacturing and marketing of pharmaceutical products and medical devices. These agencies and other entities extensively regulate, among other things, research and development activities and the testing, manufacturing, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our proposed products. While we attempt to minimize and avoid significant regulatory bars when formulating our products, some degree of regulation from these regulatory agencies is unavoidable. Some of the things we do to attempt to minimize and avoid significant regulatory bars include the following:

- o Using chemicals and combinations already allowed by the FDA;
- o Carefully making product performance claims to avoid the need for regulatory approval;
- o Using drugs that have been previously approved by the FDA and that have a long history of safe use;
- o Using chemical compounds with known safety profiles; and

o In many cases, developing OTC products which face less regulation than prescription pharmaceutical products.

The regulatory process required by the FDA, through which our drug or device products must pass successfully before they may be marketed in the U.S., generally involves the following:

o Preclinical laboratory and animal testing;

o Submission of an application that must become effective before clinical trials may begin;

o Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for its intended indication; and

o FDA approval of the application to market a given product for a given indication.

For pharmaceutical products, preclinical tests include laboratory evaluation of the product, its chemistry, formulation and stability, as well as animal studies to assess the potential safety and efficacy of the product. Where appropriate (for example, for human disease indications for which there exist inadequate animal models), we will attempt to obtain preliminary data concerning safety and efficacy of proposed products using carefully designed human pilot studies. We will require sponsored work to be conducted in compliance with pertinent local and international regulatory requirements, including those providing for Institutional Review Board approval, national governing agency approval and patient informed consent, using protocols consistent with ethical principles stated in the Declaration of Helsinki and other internationally recognized standards. We expect any pilot studies to be conducted outside the United States; but if any are conducted in the United States, they will comply with applicable FDA regulations. Data obtained through pilot studies will allow us to make more informed decisions concerning possible expansion into traditional FDA-regulated clinical trials.

If the FDA is satisfied with the results and data from preclinical tests, it will authorize human clinical trials. Human clinical trials typically are conducted in three sequential phases which may overlap. Each of the three phases involves testing and study of specific aspects of the effects of the pharmaceutical on human subjects, including testing for safety, dosage tolerance, side effects, absorption, metabolism, distribution, excretion and clinical efficacy.

Phase 1 clinical trials include the initial introduction of an investigational new drug into humans. These studies are closely monitored and may be conducted in patients, but are usually conducted in healthy volunteer subjects. These studies are designed to determine the metabolic and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. While the FDA can cause us to end clinical trials at any phase due to safety concerns, Phase 1 clinical trials are primarily concerned with safety issues. We also attempt to obtain sufficient information about the drug’s pharmacokinetics and pharmacological effects during Phase 1 clinical trial to permit the design of well-controlled, scientifically valid, Phase 2 studies.

Phase 1 studies also evaluate drug metabolism, structure-activity relationships, and the mec