

CALLISTO PHARMACEUTICALS INC
Form 10-K
March 28, 2008

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**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

WASHINGTON, D.C. 20549

FORM 10-K

(Mark one)

ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED: DECEMBER 31, 2007

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 001-32325

CALLISTO PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

13-3894575
(I.R.S. Employer
Identification No.)

420 Lexington Avenue, Suite 1609, New York, New York 10170

(Address of Principal Executive Offices) (Zip Code)

(212) 297-0010

(Issuer's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, \$.0001 par value Securities registered pursuant to section 12(g) of the Act:	American Stock Exchange

Title of class: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

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Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 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 No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not 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-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of "*large accelerated filer*", "*accelerated filer*" and "*smaller reporting company*" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
(do not check if smaller reporting company)

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was \$25,520,017 on June 29, 2007 (based on \$0.69 per share, the closing price on the American Stock Exchange that day).

As of March 25, 2008 the registrant had a total of 47,218,161 shares of Common Stock outstanding.

CALLISTO PHARMACEUTICALS, INC.

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PART I

This Form 10-K contains forward-looking statements that involve risks and uncertainties. Such forward-looking statements are characterized by future or conditional verbs and include, but are not limited to, statements regarding the results of product development efforts, clinical trials and applications for marketing approval of pharmaceutical products, and the scope and success of future operations. Such statements are only predictions and our actual results may differ materially from those anticipated in these forward-looking statements. Factors that may cause such differences include, but are not limited to, those discussed under "Risk Factors" and elsewhere in this Form 10-K for the year ended December 31, 2007, as filed with the Securities and Exchange Commission, including the uncertainties associated with product development, the risk that products that appeared promising in early clinical trials do not demonstrate efficacy in larger-scale clinical trials, the risk that we will not obtain approval to market our products, the risks associated with dependence upon key personnel and the need for additional financing. We do not assume any obligation to update forward-looking statements as circumstances change.

ITEM 1. BUSINESS.

Callisto Pharmaceuticals, Inc. is referred to throughout this report as "Callisto," "we" or "us."

We are a biopharmaceutical company focused primarily on the development of drugs to treat neuroendocrine cancer (including advanced carcinoid cancer), acute leukemia and gastrointestinal disorders and diseases. Our lead drug candidate in the clinic, Atiprimod, is an orally administered drug with antiproliferative and antiangiogenic activity. On November 7, 2006, we announced the initiation of a multi-center open-label Phase II clinical trial of Atiprimod for low-to-intermediate grade neuroendocrine cancers, primarily in advanced carcinoid cancer patients. This trial is based on earlier encouraging clinical results from a Phase I trial of Atiprimod in advanced cancer patients that showed stable disease and disease-related symptom relief in patients with advanced carcinoid cancer. On September 20, 2007, we announced that we had completed enrollment of the 40-patient Phase II clinical trial, and that patients had been on drug as long as 11 months. In October 2007, we announced the opening of a Phase II extension trial to permit those patients who had successfully completed a full year in the Phase II advanced carcinoid cancer trial, which only permitted dosing for up to one year, to continue to receive Atiprimod therapy. We are no longer dosing patients in the Phase I clinical trial of Atiprimod in relapsed or refractory multiple myeloma and have no plans at present to continue evaluating the drug in this disease indication, instead focusing on the clinical development of Atiprimod to treat advanced carcinoid cancer.

Our second drug candidate, L-Annamycin, earlier completed an initial Phase I/IIa clinical trial in relapsed or refractory leukemia patients with a prior sponsor. L-Annamycin is a novel compound from the anthracycline family of proven anti-cancer drugs, which has a novel therapeutic profile, including activity against drug resistant tumors and significantly reduced cardiotoxicity, or damage to the heart. L-Annamycin was in-licensed by us in October 2004 and is presently in two clinical trials: 1) a Phase I/IIa clinical trial in adult relapsed or refractory acute lymphocytic leukemia (ALL) patients at three clinical sites in the U.S.; and 2) a Phase I clinical trial in children and young adults with relapsed or refractory ALL or AML. We recently reached the maximum tolerated dose (MTD) in the adult trial and are currently evaluating its potential at the fixed-dose portion of the trial. We have not yet established the MTD in children. We plan to review future development of this drug once data from the adult trial are available.

In October 2007 we announced a major strategic initiative to develop SP-304 (Guanilib), our guanylyl cyclase C (GC-C) receptor agonist, to treat gastrointestinal disorders, primarily chronic constipation and constipation-predominant irritable bowel syndrome (IBS-C). We plan to file an investigational new drug (IND) application with FDA in the second quarter of 2008, and to initiate a

Phase I clinical trial in volunteers upon FDA approval of our IND application. We also plan to open a Phase Ib trial of SP-304 (Guanilib) in late 2008.

Our plan of operations for the next twelve months is to focus primarily on the Phase II clinical trial development of Atiprimod to treat advanced carcinoid cancer, and on the Phase I clinical trial development of SP-304 (Guanilib) to treat gastrointestinal disorders.

HISTORY

In March 2002, Callisto Pharmaceuticals, Inc. ("Old Callisto"), a non-public company, purchased 99.7% of the outstanding common shares of Webtronics, Inc., ("Webtronics") a public company for \$400,000. Webtronics was incorporated in Florida on February 2, 2001 and had limited operations at December 31, 2002.

On April 30, 2003, pursuant to an Agreement and Plan of Merger dated March 10, 2003, as amended April 4, 2003, Synergy Acquisition Corp., a wholly-owned subsidiary of Webtronics merged into Synergy Pharmaceuticals Inc. ("Synergy") and Callisto Acquisition Corp., a wholly-owned subsidiary of Webtronics merged into Old Callisto (collectively, the "Merger"). As a result of the Merger, Old Callisto and Synergy became wholly-owned subsidiaries of Webtronics. In the Merger Webtronics issued 17,318,994 shares of its common stock in exchange for outstanding Old Callisto common stock and an additional 4,395,684 shares in exchange for outstanding Synergy common stock. Old Callisto changed its name to Callisto Research Labs, LLC ("Callisto Research") and Webtronics changed its name to Callisto Pharmaceuticals, Inc. and changed its state of incorporation from Florida to Delaware. Subsequently, 171,818 shares of common stock issued to former Synergy shareholders were returned to us under the terms of certain indemnification agreements.

ATIPRIMOD TO TREAT ADVANCED CARCINOID CANCER PATIENTS

On August 28, 2002, our wholly-owned subsidiary, Synergy, entered into a worldwide license agreement with AnorMED Inc. ("AnorMED"), a Canadian corporation, to research, develop, sell and commercially exploit the Atiprimod (SKF 106615) patent rights.

On December 31, 2007, Callisto entered into an Amended and Restated License Agreement with AnorMED Corporation (successor in interest to AnorMED Inc.), a wholly-owned subsidiary of Genzyme Corporation ("Genzyme"), pursuant to which Callisto and Genzyme amended the license agreement for Atiprimod to eliminate all maintenance fees and milestone payments and reduce royalties owed to Genzyme to single digits. In return for the reduced future payments to Genzyme, Callisto is paying an upfront fee in 2008.

Atiprimod is one of a class of compounds known as azaspiranes and was originally developed as a potential treatment for rheumatoid arthritis based on encouraging data from a number of animal models of arthritis and autoimmune indications. The development of this drug originated with a partnership between AnorMED and SmithKline Beecham ("SKB") that led to the successful filing of an investigational new drug application, or IND, and completion of three Phase I clinical trials involving a total of 63 patients. The drug successfully completed both single and multiple dose Phase I clinical trials in patients with rheumatoid arthritis. Both trials evaluated the safety and pharmacokinetics (how the body takes up and eliminates drugs) of Atiprimod and showed that the drug is well tolerated. In the third Phase I clinical trial, the drug was found to be well tolerated in an open label extension study performed with 43 patients from the second two studies, with patients on the drug for as long as one year.

PRECLINICAL STUDIES

Atiprimod's specific ability to lower the level of key cell growth factors, known to play an important role in the development of multiple myeloma, is the basis for its potential use as a drug to treat this disease. Atiprimod was previously shown to inhibit the production of the pro-inflammatory mediators IL-6 and TNF(alpha) in a number of animal models of inflammation and autoimmune disease. Atiprimod was also demonstrated using in vitro models of tumor cell growth to inhibit proliferation of a number of human multiple myeloma cell lines. Characterization of the mechanism of Atiprimod's antiproliferative activity in a series of experiments showed that the drug works by inducing apoptosis (programmed cell death) in myeloma cells. In a second series of experiments performed with Atiprimod on co-cultures composed of multiple myeloma cells plus bone marrow stromal cells (used to simulate the human disease), the drug was found to have a profound effect on secretion of the angiogenic (blood vessel related) growth factor VEGF. A separate set of experiments also suggest an additional explanation for the disease-modifying activity of Atiprimod originally observed in chemically-induced arthritic-rat animal studies, and provide a further rationale for the application of this drug to treat multiple myeloma. Using a bone resorption assay (bone degradation experiment) to measure the effect of drug on osteoclast-mediated bone resorption, Atiprimod demonstrated a profound effect on osteoclast, or cells that break down bone, function. The drug appears to be selectively toxic for activated osteoclasts, displaying a negligible effect on bone marrow stromal cells.

COMPLETED CLINICAL STUDIES

Atiprimod successfully completed single and multiple dose Phase I clinical trials in patients with rheumatoid arthritis (RA). In the initial Phase I study, 28 patients were given single escalating doses of drug (0.002 - 1.0 mg/kg), with a 4-month follow-up. Atiprimod was well tolerated, displaying no clinically relevant changes in any laboratory parameters. In particular, liver function tests remained in the normal range. The second Phase I study involved a 28-day multiple-dose-rising study in 35 RA patients. The study evaluated the effect of food on bioavailability, or the concentration of drug in the body, as well as the safety and pharmacokinetics of repeat dosing. Dosages included 0.1, 1.0, 5.0, and 10 mg/day plus a 14-day cohort at 30 mg/day, with 4-month follow-up. All doses were well tolerated and clinical tests were unremarkable. Significantly, reductions in tender and swollen joint counts were noted in a number of subjects during the course of the dosing period. Individuals from the two Phase I safety studies were also involved in a Phase I open-label extension trial at 5 mg/day dosage. Forty-three patients entered the study and remained on the drug as long as 12 months. Clinical laboratory results for all patients were unremarkable, in particular liver enzyme levels remained within the normal range in all patients throughout the study period.

DEVELOPMENT STRATEGY

Atiprimod commenced a Phase I/IIa clinical trial in relapsed or refractory multiple myeloma patients on May 26, 2004. These are patients that have a re-occurrence of active disease, and no longer respond to approved therapies. The Phase I/IIa clinical trial is an open label study, with the primary objective of assessing safety of drug and identifying the maximum tolerated dose. The secondary objectives are to measure the pharmacokinetics, evaluate the response in patients with refractory disease and to identify possible surrogate responses to the drug to better determine the mechanism of drug action. In December 2005, we announced interim results from this trial performed in relapsed or refractory multiple myeloma patients which consisted of 15 patients treated with Atiprimod, including 3 patients at the highest dose level of 180 mg/day. In 2006, we amended this protocol to continue the trial at higher dose levels. The amended trial included the combination of Atiprimod with a drug called ursodiol to enable patients to be dosed at levels of Atiprimod higher than 180 mg/day. In October, 2007 we met the primary objective and reached the MTD in the Atiprimod + ursodiol arm. However, we do not intend to pursue Atiprimod as a single agent in multiple myeloma.

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On March 15, 2005, we announced a second Phase I/IIa clinical trial of Atiprimod in advanced cancer patients. The trial is entitled: "An Open Label Study of the Safety and Efficacy of Atiprimod Treatment for Patients with Advanced Cancer". The primary objective is to assess the safety and determine the maximum tolerated dose of Atiprimod in advanced cancer patients. The secondary objectives are to measure the pharmacokinetics of Atiprimod and evaluate the response in a variety of relapsed solid tumors and hematological malignancies. This study was conducted at the University of Texas M.D. Anderson Cancer Center, and was closed to enrollment in November, 2006. This trial established the potential of Atiprimod to treat advanced carcinoid cancer patients based on encouraging clinical results in a cohort of 5 advanced carcinoid cancer patients within this study.

On November 7, 2006, we announced the initiation of a multi-center, open-label Phase II clinical trial of Atiprimod in neuroendocrine carcinoma, comprised primarily of advanced carcinoid cancer patients. The primary objective of this trial was to evaluate efficacy of Atiprimod in patients with low to intermediate grade neuroendocrine carcinoma who have metastatic or unresectable cancer and who have either symptoms, despite standard therapy (octreotide), or progression of neuroendocrine tumors. Patients, after signing an informed consent, were required to complete two weeks of a symptoms diary to establish their symptoms baseline before commencing Atiprimod dosing. A maximum of 40 evaluable patients were planned for this trial. On September 20, 2007 we announced that we had completed full enrollment of this study, and that patients had been on drug as long as 11 months. There are presently eight clinical sites participating in the study in the U.S., with patients currently enrolled in seven of these sites.

In October 2007, we announced the opening of a Phase II extension trial to permit those patients who had successfully completed a full year on the Phase II advanced carcinoid cancer trial, which only permitted dosing for up to one year, to continue to receive Atiprimod therapy. We plan to release interim data from the advanced carcinoid cancer trials in the first quarter of 2008. We also plan to arrange to meet with the FDA on the design of a registration trial after sufficient clinical data have been collected from the ongoing Phase II trial.

MANUFACTURING OF ATIPRIMOD

A practical, efficient and cost effective method for producing Atiprimod on a commercial scale was originally developed by SKB. In the course of this work, a new dimaleate salt form was developed. A portion of the 7 kilos of Atiprimod drug substance, available from SKB, was used as the source for generating the Atiprimod dimaleate drug product presently being used in the Phase I/IIa clinical study. Several lots of drug substance were re-qualified to meet current FDA approved release specifications. The full package of fully validated analytical methods developed by SKB was transferred to a contract research organization used by us to perform all analytical tests. One large-scale GMP production run of Atiprimod dimaleate led to the successful release of 10 Kg of material available for future Phase II clinical studies.

ORPHAN DRUG STATUS OF ATIPRIMOD

On January 6, 2004, we announced that the Office of Orphan Products Development of the FDA granted orphan drug designation to Atiprimod for the treatment of multiple myeloma. On September 26, 2006, we announced that the Office of Orphan Products Development of the FDA granted orphan drug designation to Atiprimod for the treatment of carcinoid tumors. The FDA grants orphan drug status for drug candidates that are intended to treat rare life-threatening diseases that, at the time of application, affect no more than 200,000 patients in the United States. The drug must have the ability to provide significant patient benefit over currently available treatment or fill an unmet medical need. Orphan drug designation entitles us to seven years of market exclusivity in the United States of America, and ten years of market exclusivity in Europe, upon FDA marketing approval, provided that we continue to meet certain conditions established by the FDA. Once the FDA grants

marketing approval of a new drug, the FDA will not accept or approve other applications to market the same medicinal product for the same therapeutic indication. Other incentives provided by orphan status include certain tax benefits, eligibility for research grants and protocol assistance. Protocol assistance includes regulatory assistance and possible exemptions or reductions of certain regulatory fees.

L-ANNAMYCIN TO TREAT RELAPSED ACUTE LEUKEMIA

On August 12, 2004 we entered into a worldwide exclusive license agreement with The University of Texas M.D. Anderson Cancer Center to develop and commercially exploit the L-Annamycin patent rights. L-Annamycin, an anthracycline drug for leukemia therapy, has a novel therapeutic profile, including activity against drug resistant tumors and significantly reduced toxicity.

PRECLINICAL STUDIES

Nonclinical studies have shown that Annamycin delivered as a liposomal preparation (L-Annamycin) is effective against several different in vivo tumor models (animal experiments), including human tumors which are resistant to other chemotherapy drugs, grafted into animals. Additionally, results from in vitro studies (cell culture experiments) indicate that L-Annamycin and free Annamycin were able to partially overcome tumor resistance to chemotherapy drugs in several tumor cell lines that were resistant to other drugs such as doxorubicin. In nonclinical toxicity studies, myelosuppression (suppression of the body's immune response) was noted in mice at a single intravenous dose of 15.7 mg/kg L-Annamycin. With weekly intravenous doses of 5.2 mg/kg L-Annamycin for 6 weeks, or 3.1 and 4.2 mg/kg L-Annamycin for 10 weeks in mice, the cardiotoxicity (toxicity to heart tissue) of L-Annamycin was substantially less than an equivalent dose of doxorubicin. In dogs, a single 15-minute intravenous infusion of up to 1.42 mg/kg L-Annamycin was well tolerated, with no clinically significant adverse effects, hematological or chemical changes, or pathological changes.

COMPLETED CLINICAL STUDIES

L-Annamycin was evaluated previously by Aronex Pharmaceuticals, Inc. in 3 clinical trials: 1) a Phase I clinical trial in 36 patients with relapsed solid tumors, 2) a Phase II clinical trial in 13 patients with doxorubicin-resistant breast cancer, and 3) a Phase I/IIa trial in 20 patients with relapsed/refractory AML and ALL. In the initial Phase I study, L-Annamycin was administered by a single 1- to 2-h intravenous infusion at 3-week intervals. Thirty-six patients with relapsed solid tumors were treated and 109 treatment courses were administered at doses ranging from 3 to 240 mg/m². No cardiotoxicity was seen on biopsy of heart tissue of four patients studied. The maximum tolerated dose (MTD) for L-Annamycin in solid tumor patients was found to be 190 mg/m². A second Phase II study of L-Annamycin was performed in 13 women with doxorubicin-resistant breast cancer. The median number of prior chemotherapy regimens was two, and six patients had two or more organ sites of involvement. L-Annamycin was administered at 190-250 mg/m² as a single i.v. infusion over 1-2 h every 3 weeks. Of the 13 patients, 12 had clear deterioration and new tumor growth after one or two courses.

The potential of a less cardiotoxic drug that was active against multi-drug resistant tumors led to a third trial in relapsed leukemia patients (both AML and ALL). The trial involved 20 patients with relapsed/refractory AML (n=17) or ALL (n=3). The conclusions drawn from the trial were that L-Annamycin was safe, well tolerated and showed potential clinical activity in patients with acute leukemias, and that further evaluation of this novel anthracycline in patients with hematopoietic, or blood borne, malignancies was clearly warranted.

DEVELOPMENT STRATEGY

We began a Phase I clinical trial at The University of Texas M.D. Anderson Cancer Center in adult relapsed or refractory acute lymphocytic leukemia (ALL) patients on December 1, 2005. Additional sites enrolled in this study include the Roswell Park Cancer Institute (Buffalo, NY) and the Montefiore Medical Center (New York, NY). The single-arm, open-label L-Annamycin trial was designed to enroll patients in a dose escalation Phase I portion followed by 10 patients at a final fixed dose in the Phase II portion once the maximum tolerated dose (MTD) was determined. A major goal of the trial was to confirm the MTD reported from the previous sponsor for use in adult ALL patients. The clinical data from our studies indicate that the MTD reported by the previous sponsor which indicated that patients could be dosed as high as 280 mg/m²/day for 3 consecutive days in ALL patients was too high. We utilized a uniform validated reconstitution method that we believe delivers a more uniform liposomal drug product when infused into patients. This infusion methodology is being utilized across all study sites. We recently established an MTD of 150 mg/m²/day given for 3 consecutive days in the adult trial and are currently evaluating patients in the fixed-dose portion of the trial. We plan to finish dosing of 10 patients at the MTD value and then determine whether the clinical data warrant further clinical evaluation of L-Annamycin in adult acute leukemia patients.

In February, 2007, we opened a Phase I trial of L-Annamycin in pediatric relapsed or refractory ALL or AML patients. Based on the information from the ongoing adult trial, we initiated this trial at 130 mg/m²/day given for three consecutive days. The trial is a multi-center, open-label, single-agent, dose-escalation study that is utilizing POETIC a consortium of ten pediatric cancer centers located in the U.S. and Canada. The trial is presently open at four clinical sites in the U.S. We have not yet established the MTD in children. We plan to review future development of this drug once data from the adult trial are available. Our key employee responsible for coordinating this L-Annamycin program with our pediatric clinical sites, Dr. Donald Picker, former Executive Vice President of Research & Development, resigned from our company in December, 2006. Consequently, work on this clinical program was scaled back.

MANUFACTURING OF ANNAMYCIN

An improved manufacturing method for Annamycin has been developed at Antibioticos S.p.A., our commercial supplier of GMP ("Good Manufacturing Practice") drug substance. GMP material is currently being produced in sufficient quantity for all three anticipated trials outlined in the development strategy section. The analytical methods developed previously have been successfully transferred, and are in the process of being validated by Quantitative Technologies, Inc., our analytical contract research organization, or CRO, for Annamycin development work. The final lyophilized GMP formulated drug product is being manufactured by Pharmaceutical Services, Inc., who previously produced final product for the earlier clinical trials. Currently, Antibioticos S.p.A. is our sole supplier of Annamycin for our clinical trials. Our agreement with Antibioticos provides that Antibioticos will provide 400 grams of GMP drug substance (Annamycin) for our L-Annamycin clinical trials.

ORPHAN DRUG STATUS OF L-ANNAMYCIN

On June 24, 2005, we announced that the Office of Orphan Products Development of the FDA granted orphan drug designation to L-Annamycin for the treatment of acute lymphoblastic leukemia. On June 28, 2005, we announced that the Office of Orphan Products Development of the FDA granted orphan drug designation to L-Annamycin for the treatment of acute myeloid leukemia.

SP-304 (GUANILIB) TO TREAT GASTROINTESTINAL DISORDERS

We announced on October 3, 2007 a major strategic initiative to develop SP-304 (Guanilib), Callisto's guanylyl cyclase C receptor agonist, to treat gastrointestinal disorders, primarily chronic

constipation and constipation-predominant irritable bowel syndrome (IBS-C). SP-304 (Guanilib) was developed by our scientists based on structure-function studies performed in-house. A patent covering composition of matter and therapeutic applications of SP-304 (Guanilib) was granted by the U.S. Patent and Trademark Office on May 9, 2006.

SP-304 (Guanilib) is an analog of uroguanylin, a natural gastro-intestinal hormone produced in the gut that is a key regulator of intestinal function. Uroguanylin works by activating a unique receptor on intestinal cells. The receptor, called the guanylate cyclase C (GC-C) receptor, promotes fluid and ion transport in the gastro-intestinal (GI) tract. Under normal conditions, the receptor is activated by the natural hormones uroguanylin and guanylin. Activation of the receptor leads to the transport of chloride and bicarbonate into the intestine, and water is carried with these ions into the lumen of the intestine, thereby producing a liquid and watery stool, and other pharmacologic effects that could potentially benefit patients with gastrointestinal disorders such as chronic constipation and IBS-C.

PRECLINICAL STUDIES

SP-304 (Guanilib) has been demonstrated to be superior to uroguanylin in its biological activity, protease stability and pH characteristics. SP-304 (Guanilib) acts in an identical manner as the natural hormone as an agonist (i.e. activator) of the GC-C receptor found on the epithelial cells of the colon. Upon activation, the GC-C receptor promotes intracellular synthesis of cGMP, which in turn eventually activates the cystic fibrosis transmembrane conductance regulator (CFTR) within the epithelial cells. Activation of CFTR leads to secretion of salts and water into the intestine, resulting in a liquid and watery intestine content that is more easily transported through the bowel. Recent animal studies performed with SP-304 (Guanilib) have demonstrated the drugs potential to enhance intestinal motility.

SP-304 (Guanilib) has also undergone pre-clinical animal studies as a treatment for gastrointestinal inflammation in a collaborative study involving clinical gastroenterologist Dr. Scott Plevy of the University of North Carolina, Chapel Hill, NC. Recent results from his laboratory showed that SP-304 (Guanilib) was efficacious in animal models of ulcerative colitis.

DEVELOPMENT PLAN

We currently have a major preclinical program underway to support the filing of an investigational new drug (IND) application with FDA in the second quarter of 2008. The plan is to evaluate SP-304 (Guanilib)'s clinical potential first in chronic constipation and IBS-C. The initial Phase I trial is planned to be performed in volunteers in early 2008. The purpose of this trial is to establish the safety of the drug when given as a single oral dose. We also expect to demonstrate that SP-304 (Guanilib) is not systemically absorbed (i.e. taken up in the blood and distributed throughout the body) which means that the compound is likely to be non-toxic in clinical use. We also plan to open a Phase Ib trial of SP-304 (Guanilib) in late 2008.

MANUFACTURING OF SP-304 (GUANILIB)

A practical, efficient and cost effective method for producing SP-304 (Guanilib) on a commercial scale is currently being developed by a CRO, who has produced a 100 gram-scale GMP run of SP-304 (Guanilib), which was released in January 2008.

DEGRASYNS

On January 10, 2006, we entered into a license agreement with the University of Texas M.D. Anderson Cancer Center whereby we were granted the exclusive right to manufacture, have manufactured, use, import, offer to sell and/or sell anti-cancer compounds called tyrphostins (renamed Degrasyns). Degrasyns are a second-generation class of tyrphostins developed by scientists at the University of Texas M.D. Anderson Cancer Center that have a novel anti-cancer mechanism-of-action

that centers on their ability to selectively degrade key proteins that are involved in tumor cell proliferation and survival. The intention in 2007 was to work with key scientists at the University of Texas M.D. Anderson Cancer Center to bring forward a pre-clinical candidate for development in the clinic. Our key employee responsible for this program, Dr. Donald Picker, former Executive Vice President of Research & Development, resigned from our company in December 2006. Consequently, work on this program has been significantly scaled back.

SUPERANTIGEN-BASED BIOTERRORISM DEFENSE

On August 20, 1996, we entered into a license agreement to research, develop, sell and commercially exploit certain Rockefeller University ("Rockefeller") licensed patents covering peptides and antibodies useful in treating toxic shock syndrome and septic shock. In addition, on July 2, 2001, we entered into a license agreement for two additional patents related to the regulation of exoproteins in staphylococcus aureus. On November 14, 2007, we gave 90-day notice to Rockefeller University of termination of the August, 1996 and July, 2001 license agreements, terminating these agreements effective February 14, 2008.

On April 1, 2005 we were awarded a two-year \$885,641 biodefense partnership grant from the National Institute of Allergy and Infectious Diseases ("NIAID") to develop a monoclonal antibody and vaccine against bacterial superantigen toxins. Funding for this program has been extended through March 31, 2008 and as of December 31, 2007 we had approximately \$34,000 of funding remaining. Because the bioterrorism program is not a core activity of ours, we plan to terminate in-house work on this program upon expiration of the research grant on March 31, 2008.

GOVERNMENT REGULATION

Regulation by governmental authorities in the United States of America and other countries will be a significant factor in the production and marketing of any products that may be developed by us. The nature and the extent to which such regulation may apply will vary depending on the nature of any such products. Virtually all of our potential products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous pre-clinical and clinical testing and other approval procedures by the FDA and similar health authorities in foreign countries. Various federal statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of such products. The process of obtaining these approvals and the subsequent compliance with appropriate federal and foreign statutes and regulations requires the expenditure of substantial resources. In order to test in human clinical trials, produce and market products for diagnostic or therapeutic use, a company must comply with mandatory procedures and safety standards established by the FDA and comparable agencies in foreign countries. Before beginning human clinical testing of a potential new drug, a company must file an IND and receive clearance to proceed from the FDA. This application is a summary of the pre-clinical studies that were conducted to characterize the drug, including toxicity and safety studies in animals, as well as an in-depth discussion of the human clinical studies that are being proposed.

The pre-marketing program required for approval of a new drug typically involves a time-consuming and costly three-phase process. In Phase I, trials are conducted with a small number of patients to determine the early safety profile, the pattern of drug distribution and metabolism. In Phase II, trials are conducted with small groups of patients afflicted with a target disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety. In Phase III, large scale, multi-center comparative trials are conducted with patients afflicted with a target disease in order to provide enough data for statistical proof of efficacy and safety required by the FDA and others.

The FDA closely monitors the progress of each of the three phases of clinical testing and may, in its discretion, reevaluate, alter, suspend or terminate the testing based on the data that have been

accumulated to that point and its assessment of the risk/benefit ratio to the patient. Estimates of the total time required for carrying out such clinical testing vary between two and ten years. Upon completion of such clinical testing, a company typically submits a New Drug Application (NDA) or Product License Application (PLA) to the FDA that summarizes the results and observations of the drug during the clinical testing. Based on its review of the NDA or PLA, the FDA will decide whether or not to approve the drug. This review process can be quite lengthy, and approval for the production and marketing of a new pharmaceutical or medical diagnostic product can require a number of years and substantial funding, and there can be no assurance that any approvals will be granted on a timely basis, if at all.

If the product is approved for sale, FDA regulations govern the production process and marketing activities, and a post-marketing testing and surveillance program may be required to monitor continuously a product's usage and effects. Product approvals may be withdrawn if compliance with regulatory standards is not maintained, and other countries, in which any products developed by us are marketed, may impose a similar regulatory process.

COMPETITION

The biopharmaceutical industry is characterized by rapidly evolving technology and intense competition. Our competitors include major pharmaceutical and biotechnology companies focusing on hematological oncology such as Microbia Inc., Hana Biosciences Inc., SGX Pharmaceuticals, Inc., Sunesis Pharmaceuticals, Inc. and Vion Pharmaceuticals, Inc. Most of our competitors have financial, technical and marketing resources significantly greater than our resources. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize products on their own or through joint venture. We are aware of certain development projects for products to prevent or treat certain diseases targeted by us. The existence of these potential products or other products or treatments of which we are not aware, or products or treatments that may be developed in the future, may adversely affect our ability to market the products we develop.

RESEARCH AND DEVELOPMENT EXPENSES

Research and development expenses consist primarily of salaries and other personnel-related expenses, facilities costs, laboratory supplies, license fees and patent legal costs. Research and development expenses were \$6,507,978 for the twelve months ended December 31, 2007, compared to \$6,134,704 and \$6,430,505 for the twelve months ended December 31, 2006 and 2005, respectively.

On April 1, 2005 we were awarded an \$885,641 biodefense partnership grant from the NIAID to develop a monoclonal antibody and vaccine against bacterial superantigen toxins over a two year period. During the twelve months ended December 31, 2007 and 2006 we received \$260,853 and \$352,649, respectively, which has been reported on our Consolidated Statements of Operations as a separate line item entitled "Government Grant". Funding for this program has been extended through April, 2008 and as of December 31, 2007 we had approximately \$34,000 of funding remaining. Because the bioterrorism program is not a core activity of ours, we plan to terminate in-house work on this program upon expiration of the research grant in April, 2008.

PROPRIETARY RIGHTS

We are able to protect our technology from unauthorized use by third parties only to the extent that it is covered by valid and enforceable patents or is effectively maintained as a trade secret. Accordingly, patents or other proprietary rights are an essential element of our business. As of December 31, 2007, we are the assignee or exclusive licensee of 7 pending patent applications and 15 issued patents in the United States, and currently we have approximately 150 issued or pending foreign

patent applications. We seek patent protection of inventions originating from our ongoing research and development activities that are commercially important to our business. Our composition-of-matter and use patent on SP-304 (Guanilib) issued on May 9, 2006. Our composition-of-matter patents for L-Annamycin and Atiprimod expire in 2017 and 2016, respectively. Our formulation patents for L-Annamycin and Atiprimod dimaleate salt both expire in 2016.

We have obtained licenses from various parties that give us rights to technologies that we deem to be necessary or desirable for our research and development. These licenses (both exclusive and non-exclusive) may require us to pay royalties to the parties in addition to upfront or milestone payments, and to expend certain minimum resources to develop these technologies.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

While trade secret protection is an essential element of our business and we have taken security measures to protect our proprietary information and trade secrets, we cannot give assurance that our unpatented proprietary technology will afford us significant commercial protection. We seek to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees and consultants also sign agreements requiring that they assign to us their interests in intellectual property arising from their work for us. All employees sign an agreement not to engage in any conflicting employment or activity during their employment with us and not to disclose or misuse our confidential information. However, it is possible that these agreements may be breached or invalidated, and if so, there may not be an adequate corrective remedy available. Accordingly, we cannot ensure that employees, consultants or third parties will not breach the confidentiality provisions in our contracts, infringe or misappropriate our trade secrets and other proprietary rights or that measures we are taking to protect our proprietary rights will be adequate.

In the future, third parties may file claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend ourselves against such claims, whether they are with or without merit and whether they are resolved in favor of, or against, our licensors or us, we may face costly litigation and the diversion of management's attention and resources. As a result of such disputes, we may have to develop costly non-infringing technology or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all.

LICENSE AGREEMENTS

On January 10, 2006, we entered into a Patent and Technology License Agreement with The University of Texas M.D. Anderson Cancer Center. Pursuant to the license agreement, we were granted the exclusive right to manufacture, have manufactured, use, import, offer to sell and/or sell anti-cancer compounds called tyrphostins (renamed Degrasyns). We paid a nonrefundable license fee of \$200,000 upon execution of this agreement and we are obligated to pay annual license maintenance fees to The University of Texas M.D. Anderson Cancer Center. We are also obligated under this agreement to pay for legal fees and expenses associated with establishing and protecting the patent rights worldwide.

We also agreed to pay The University of Texas M.D. Anderson Cancer Center royalties based on net sales from any licensed products, plus aggregate milestone payments of up to \$1,750,000 based upon achieving certain regulatory submissions and approvals. The term of the agreement is from January 10, 2006 until the end of the term for which the patent rights associated with the licensed technology have expired. If the first pending patent is issued, the agreement is projected to expire in 2025. In addition, at any time after 2 years from January 10, 2006, The University of Texas M.D. Anderson Cancer Center has the right to terminate the license if we fail to provide evidence within 90 days of written notice that we have commercialized or are actively and effectively attempting to commercialize the licensed technology.

On August 12, 2004, we entered into a world-wide license agreement with The University of Texas M.D. Anderson Cancer Center to research, develop, sell and commercially exploit the patent rights for L-Annamycin. Consideration paid for this license amounted to \$31,497 for reimbursement of out-of-pocket costs for filing, enforcing and maintaining the L-Annamycin patent rights and a \$100,000 initial license fee. We also agreed to pay The University of Texas M. D. Anderson Cancer Center royalties based on net sales from any licensed products, plus aggregate milestone payments of up to \$750,000 based upon achieving certain regulatory submissions and approvals. The term of the agreement is from August 12, 2004 until November 2, 2019. Under the terms of the license agreement, we are required to make certain good faith expenditures towards the clinical development of at least one licensed product within the two year period after March 2005. In addition, at any time after 5 years from August 12, 2004, The University of Texas M.D. Anderson Cancer Center has the right to terminate the license if we fail to provide evidence within 90 days of written notice that we have commercialized or we are actively and effectively attempting to commercialize L-Annamycin.

On August 28, 2002, our wholly-owned subsidiary, Synergy, entered into a worldwide license agreement with AnorMED Inc. ("AnorMED"), a Canadian corporation, to research, develop, sell and commercially exploit the Atiprimod (SKF 106615) patent rights.

On December 31, 2007, we entered into an amended and restated license agreement with AnorMED to research, develop, sell and commercially exploit the Atiprimod patent rights. The license agreement provides for us to pay AnorMED royalties on net sales as well as an upfront payment. The license agreement will terminate in 2018.

On August 20, 1996, we entered into a license agreement to research, develop, sell and commercially exploit certain Rockefeller University licensed patents covering peptides and antibodies useful in treating toxic shock syndrome and septic shock. We agreed to work toward commercialization of products related to these patents as evidenced by a minimum expenditure of approximately \$210,000 per year, plus milestone payments and royalties of between 2% and 3% of annual net sales and will pay Rockefeller 30% of any sublicense fee paid by sublicenses. The licensed patents under this agreement are the subject of research that was funded by the NIAID grant awarded to us on April 1, 2005 for \$885,641 over two years. In addition, on July 2, 2001, we entered into a license agreement for two additional patents related to the regulation of exoproteins in staphylococcus aureus. On November 14, 2007, we gave 90-day notice to Rockefeller University of termination of the August, 1996 and July, 2001 License agreements, effective February 14, 2008.

EMPLOYEES

As of March 25, 2008, we had 11 full-time and 2 part-time employees. We believe our employee relations are satisfactory.

AVAILABLE INFORMATION

We operate three wholly owned subsidiary companies Callisto Research Labs, LLC, Synergy Pharmaceuticals Inc. ("Synergy") and Synergy Advanced Pharmaceuticals, Inc. a wholly owned subsidiary of Synergy and we own two inactive subsidiaries, IgX, Ltd (Ireland) and Callisto Pharma, GmbH (Germany). We were incorporated in Delaware in May 2003 and our principal offices are at 420 Lexington Avenue, Suite 1609, New York, NY 10170.

We maintain a site on the world wide web at <http://www.callistopharma.com>; however, information found on our website is not incorporated by reference into this report. We make available free of charge through our website our Securities and Exchange Commission, or SEC, filings, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors and the other information included herein (specifically, but not limited to, Item 9A(T) of this annual report) as well as the information included in other reports and filings made with the SEC before investing in our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations could be harmed. The trading price of our common stock could decline due to any of these risks, and you may lose part or all of your investment.

RISKS RELATED TO OUR BUSINESS

WE ARE AT AN EARLY STAGE OF DEVELOPMENT AS A COMPANY, CURRENTLY HAVE NO SOURCE OF REVENUE AND MAY NEVER BECOME PROFITABLE.

We are a development stage biopharmaceutical company. Currently, we have no products approved for commercial sale and, to date, we have not generated any revenue. Our ability to generate revenue depends heavily on:

demonstration in Phase I and Phase II clinical trials that our product candidates, Atiprimod for the treatment of advanced carcinoid cancer, L-Annamycin for the treatment of relapsed acute leukemia, and SP-304 (Guanilib) for the treatment of gastrointestinal disorders are safe and effective;

the successful development of our other product candidates;

our ability to seek and obtain regulatory approvals, including with respect to the indications we are seeking;

the successful commercialization of our product candidates; and

market acceptance of our products.

All of our existing product candidates will require extensive additional clinical evaluation, regulatory review, significant marketing efforts and substantial investment before they could provide us with any revenue. For example, Atiprimod for the treatment of multiple myeloma entered Phase I/IIa clinical trials in May 2004 and L-Annamycin for the treatment of acute leukemia entered clinical trials in December 2005. Our other product candidates are in preclinical development. As a result, if we do not successfully develop and commercialize Atiprimod or L-Annamycin, we will be unable to generate any revenue for many years, if at all. We do not anticipate that we will generate revenue for several years, at the earliest, or that we will achieve profitability for at least several years after generating material revenue, if at all. If we are unable to generate revenue, we will not become profitable, and we may be unable to continue our operations.

WE HAVE INCURRED SIGNIFICANT LOSSES SINCE INCEPTION AND ANTICIPATE THAT WE WILL INCUR CONTINUED LOSSES FOR THE FORESEEABLE FUTURE.

As of December 31, 2007 we had an accumulated deficit of \$81,331,796. We have incurred losses in each year since our inception in 1996. We incurred net losses available to common stockholders of \$20,887,428, \$15,303,714 and \$11,779,457 for the twelve months ended December 31, 2007, 2006 and 2005, respectively. These losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect to incur significant and increasing operating losses for the next several years as we expand our research and development, continue our clinical trials of Atiprimod for the treatment of multiple myeloma and advanced carcinoid cancer, continue and initiate our clinical trials of L-Annamycin for the treatment of acute leukemias, acquire or license technologies, advance our other product candidates into clinical development, seek regulatory approval and, if we receive FDA approval, commercialize our products. Because of the numerous risks and uncertainties

associated with our product development efforts, we are unable to predict the extent of any future losses or when we will become profitable, if at all. If we are unable to achieve and then maintain profitability, the market value of our common stock will likely decline.

OUR INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM HAS EXPRESSED DOUBT ABOUT OUR ABILITY TO CONTINUE AS A GOING CONCERN, WHICH MAY HINDER OUR ABILITY TO OBTAIN FUTURE FINANCING

Our consolidated financial statements as of December 31, 2007 have been prepared under the assumption that we will continue as a going concern for the year ending December 31, 2007. Our independent registered public accounting firm has issued a report dated March 25, 2008 that included an explanatory paragraph referring to our recurring losses from operations and net capital deficiency and expressing substantial doubt in our ability to continue as a going concern without additional capital becoming available. Our ability to continue as a going concern is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

WE WILL NEED TO RAISE SUBSTANTIAL ADDITIONAL CAPITAL WITHIN THE NEXT YEAR TO FUND OUR OPERATIONS, AND OUR FAILURE TO OBTAIN FUNDING WHEN NEEDED MAY FORCE US TO DELAY, REDUCE OR ELIMINATE OUR PRODUCT DEVELOPMENT PROGRAMS OR COLLABORATION EFFORTS.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to:

complete the clinical development of our two cancer product candidates, Atiprimod for the treatment of advanced carcinoid cancer and L-Annamycin for the treatment of acute leukemia;

initiate and continue clinical development of SP-304 (Guanilib) to treat gastrointestinal disorders.

continue development of our other product candidates and the SP-304 (Guanilib) backup and second-generation program;

finance our general and administrative expenses;

prepare regulatory approval applications and seek approvals for Atiprimod, SP-304 (Guanilib) and L-Annamycin and our other product candidates;

license or acquire additional technologies;

launch and commercialize our product candidates, if any such product candidates receive regulatory approval; and

develop and implement sales, marketing and distribution capabilities.

We expect that our cash used in operating activities will increase significantly for the next several years. For the years ended December 31, 2007, 2006 and 2005 we used approximately \$8.4 million, \$8.3 million and \$8.7 million in operating activities, respectively.

We will be required to raise additional capital within the next year to complete the development and commercialization of our current product candidates and to continue to fund operations at the current cash expenditure levels. Our future funding requirements will depend on many factors, including, but not limited to:

the rate of progress and cost of our clinical trials and other development activities;

any future decisions we may make about the scope and prioritization of the programs we pursue;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the costs and timing of regulatory approval;

the costs of establishing sales, marketing and distribution capabilities;

the effect of competing technological and market developments;

the terms and timing of any collaborative, licensing and other arrangements that we may establish; and

general market conditions for offerings from biopharmaceutical companies.

To date, our sources of cash have been primarily limited to the sale of our equity securities. Net cash provided by financing activities for the twelve months ended December 31, 2007, 2006 and 2005 was approximately \$10.8 million, \$10.8 million and \$4.8 million, respectively. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants that impact our ability to conduct our business. If we are unable to raise additional capital when required or on acceptable terms, we may have to significantly delay, scale back or discontinue the development and/or commercialization of one or more of our product candidates. We also may be required to:

seek collaborators for our product candidates at an earlier stage than otherwise would be desirable and on terms that are less favorable than might otherwise be available; and

relinquish license or otherwise dispose of rights to technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves on unfavorable terms.

IF OUR AGREEMENT WITH THE UNIVERSITY OF TEXAS M.D. ANDERSON CANCER CENTER TERMINATES, OUR BUSINESS WOULD BE ADVERSELY AFFECTED.

Our business is partially dependent on rights we have licensed from The University of Texas M.D. Anderson Cancer Center. Under the terms of The University of Texas M.D. Anderson Cancer Center license agreement for L-Annamycin, at any time after 5 years from August 12, 2004, The University of Texas M.D. Anderson Cancer Center has the right to terminate the license if we fail to provide evidence within 90 days of written notice that we have commercialized or we are actively and effectively attempting to commercialize L-Annamycin. If we fail to fulfill these obligations or other material obligations, The University of Texas M.D. Anderson Cancer Center license agreement may be terminated and our business would be adversely affected.

CLINICAL TRIALS INVOLVE A LENGTHY AND EXPENSIVE PROCESS WITH AN UNCERTAIN OUTCOME, AND RESULTS OF EARLIER STUDIES AND TRIALS MAY NOT BE PREDICTIVE OF FUTURE TRIAL RESULTS.

In order to receive regulatory approval for the commercialization of our product candidates, we must conduct, at our own expense, extensive clinical trials to demonstrate safety and efficacy of these product candidates. Clinical testing is expensive, can take many years to complete and its outcome is uncertain. Failure can occur at any time during the clinical trial process.

The results of preclinical studies and early clinical trials of our product candidates do not necessarily predict the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. The data collected from clinical trials of our product candidates may not be sufficient to

support the submission of a new drug application or to obtain regulatory approval in the United States or elsewhere. Because of the uncertainties associated with drug development and regulatory approval, we cannot determine if or when we will have an approved product for commercialization or achieve sales or profits.

DELAYS IN CLINICAL TESTING COULD RESULT IN INCREASED COSTS TO US AND DELAY OUR ABILITY TO GENERATE REVENUE.

While to date there has been no delays in our clinical trials, enrollment in our Atiprimod Phase I/IIa trial in multiple myeloma was slower than anticipated due to limited availability of relapsed multiple myeloma patients. In the future, we may experience delays in clinical testing of our product candidates. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a trial, in reaching agreement on acceptable clinical trial terms with prospective sites, in obtaining institutional review board approval to conduct a trial at a prospective site, in recruiting patients to participate in a trial or in obtaining sufficient supplies of clinical trial materials. Many factors affect patient enrollment, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, competing clinical trials and new drugs approved for the conditions we are investigating. Prescribing physicians will also have to decide to use our product candidates over existing drugs that have established safety and efficacy profiles. Any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and delay our ability to generate revenue.

WE MAY BE REQUIRED TO SUSPEND OR DISCONTINUE CLINICAL TRIALS DUE TO UNEXPECTED SIDE EFFECTS OR OTHER SAFETY RISKS THAT COULD PRECLUDE APPROVAL OF OUR PRODUCT CANDIDATES.

Our clinical trials may be suspended at any time for a number of reasons. For example, we may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to the clinical trial patients. In addition, regulatory agencies may order the temporary or permanent discontinuation of our clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements or that they present an unacceptable safety risk to the clinical trial patients.

Administering any product candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory authorities denying further development or approval of our product candidates for any or all targeted indications. Ultimately, some or all of our product candidates may prove to be unsafe for human use. Moreover, we could be subject to significant liability if any volunteer or patient suffers, or appears to suffer, adverse health effects as a result of participating in our clinical trials.

IF WE ARE UNABLE TO SATISFY REGULATORY REQUIREMENTS, WE MAY NOT BE ABLE TO COMMERCIALIZE OUR PRODUCT CANDIDATES.

We need FDA approval prior to marketing our product candidates in the United States of America. If we fail to obtain FDA approval to market our product candidates, we will be unable to sell our product candidates in the United States of America and we will not generate any revenue.

This regulatory review and approval process, which includes evaluation of preclinical studies and clinical trials of a product candidate as well as the evaluation of our manufacturing process and our contract manufacturers' facilities, is lengthy, expensive and uncertain. To receive approval, we must,

among other things, demonstrate with substantial evidence from well-controlled clinical trials that the product candidate is both safe and effective for each indication where approval is sought. Satisfaction of these requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. We cannot predict if or when we might submit for regulatory review any of our product candidates currently under development. Any approvals we may obtain may not cover all of the clinical indications for which we are seeking approval. Also, an approval might contain significant limitations in the form of narrow indications, warnings, precautions, or contra-indications with respect to conditions of use.

The FDA has substantial discretion in the approval process and may either refuse to file our application for substantive review or may form the opinion after review of our data that our application is insufficient to allow approval of our product candidates. If the FDA does not file or approve our application, it may require that we conduct additional clinical, preclinical or manufacturing validation studies and submit that data before it will reconsider our application. Depending on the extent of these or any other studies, approval of any applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to make our applications approvable. If any of these outcomes occur, we may be forced to abandon our applications for approval, which might cause us to cease operations.

We will also be subject to a wide variety of foreign regulations governing the development, manufacture and marketing of our products. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must still be obtained prior to manufacturing or marketing the product in those countries. The approval process varies from country to country and the time needed to secure approval may be longer or shorter than that required for FDA approval. We cannot assure you that clinical trials conducted in one country will be accepted by other countries or that approval in one country will result in approval in any other country.

IF OUR PRODUCT CANDIDATES ARE UNABLE TO COMPETE EFFECTIVELY WITH MARKETED DRUGS TARGETING SIMILAR INDICATIONS AS OUR PRODUCT CANDIDATES, OUR COMMERCIAL OPPORTUNITY WILL BE REDUCED OR ELIMINATED.

We face competition from established pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize cancer drugs that are safer, more effective, have fewer side effects or are less expensive than our product candidates. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses complementary to our programs or advantageous to our business.

We expect that our ability to compete effectively will depend upon our ability to:

successfully and rapidly complete clinical trials and submit for and obtain all requisite regulatory approvals in a cost-effective manner;

maintain a proprietary position for our products and manufacturing processes and other related product technology;

attract and retain key personnel;

develop relationships with physicians prescribing these products; and

build an adequate sales and marketing infrastructure for our product candidates.

Because we will be competing against significantly larger companies with established track records, we will have to demonstrate to physicians that, based on experience, clinical data, side-effect profiles and other factors, our products are preferable to existing cancer drugs. If we are unable to compete effectively in the cancer drug market and differentiate our products from currently marketed cancer drugs, we may never generate meaningful revenue.

Numerous pharmaceutical and biotechnology companies have developed anthracycline drugs used to treat acute leukemias similar to our compound, L-Annamycin. These compounds include Adriamycin® and Ellence® which are marketed by Pfizer and Cerubidine® which is marketed by Boehringer Ingelheim. These drugs have been approved by the FDA and are currently being marketed as opposed to L-Annamycin which is in clinical development. Atiprimod, our drug candidate for relapsed multiple myeloma, works through a different mechanism of action than Velcade which is currently marketed by Millenium Pharmaceuticals and other drugs in development, such as Celgene Corporation's Revlimid.

WE CURRENTLY HAVE NO SALES AND MARKETING ORGANIZATION. IF WE ARE UNABLE TO ESTABLISH A DIRECT SALES FORCE IN THE UNITED STATES TO PROMOTE OUR PRODUCTS, THE COMMERCIAL OPPORTUNITY FOR OUR PRODUCTS MAY BE DIMINISHED.

We currently have no sales and marketing organization. If any of our product candidates are approved by the FDA, we intend to market that product directly to hospitals in the United States of America through our own sales force. We will incur significant additional expenses and commit significant additional management resources to establish this sales force. We may not be able to establish these capabilities despite these additional expenditures. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire and train sales and marketing personnel. If we elect to rely on third parties to sell our product candidates in the United States, we may receive less revenue than if we sold our products directly. In addition, we may have little or no control over the sales efforts of those third parties. In the event we are unable to develop our own sales force or collaborate with a third party to sell our product candidates, we may not be able to commercialize our product candidates which would negatively impact our ability to generate revenue.

WE MAY NEED OTHERS TO MARKET AND COMMERCIALIZE OUR PRODUCT CANDIDATES IN INTERNATIONAL MARKETS.

In the future, if appropriate regulatory approvals are obtained, we intend to commercialize our product candidates in international markets. However, we have not decided how to commercialize our product candidates in those markets. We may decide to build our own sales force or sell our products through third parties. Currently, we do not have any plans to enter international markets. If we decide to sell our product candidates in international markets through a third party, we may not be able to enter into any marketing arrangements on favorable terms or at all. In addition, these arrangements could result in lower levels of income to us than if we marketed our product candidates entirely on our own. If we are unable to enter into a marketing arrangement for our product candidates in international markets, we may not be able to develop an effective international sales force to successfully commercialize those products in international markets. If we fail to enter into marketing arrangements for our products and are unable to develop an effective international sales force, our ability to generate revenue would be limited.

IF OUR RELATIONSHIP WITH OUR CONTRACT MANUFACTURER FOR L-ANNAMYCIN TERMINATES, OR THEIR FACILITIES ARE DAMAGED OR DESTROYED, WE MAY BE UNABLE TO DEVELOP OR COMMERCIALIZE L-ANNAMYCIN.

Currently, Antibioticos S.p.A. is our sole supplier of Annamycin (drug substance that is the active component of the final formulated L-Annamycin drug product). If our relationship with this contract manufacturer, or any other contract manufacturer we might use, terminates or if any of their facilities are damaged for any reason, including fire, flood, earthquake or other similar event, we may be unable to obtain supply of Annamycin. If any of these events were to occur, we may need to find alternative manufacturers or manufacturing facilities. The number of contract manufacturers with the expertise, required regulatory approvals and facilities to manufacture Annamycin on a commercial scale is extremely limited, and it would take a significant amount of time to arrange for alternative manufacturers. If we need to change to other commercial manufacturers, the FDA and comparable foreign regulators must approve these manufacturers' facilities and processes prior to our use, which would require new testing and compliance inspections. In addition, we may not have the intellectual property rights, or may have to share intellectual property rights, to any improvements in the current manufacturing processes or any new manufacturing processes for Annamycin. Any of these factors could cause us to delay or suspend clinical trials, regulatory submissions, required approvals or commercialization of L-Annamycin, entail higher costs, and could result in our being unable to commercialize L-Annamycin successfully. Furthermore, if our contract manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, and we were unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality, and on a timely basis, we would likely be unable to meet demand for L-Annamycin and we would lose potential revenue.

IF THE FDA DOES NOT APPROVE OUR CONTRACT MANUFACTURERS' FACILITIES, WE MAY BE UNABLE TO DEVELOP OR COMMERCIALIZE OUR PRODUCT CANDIDATES.

We rely on third-party contract manufacturers to manufacture our product candidates, and currently have no plans to develop our own manufacturing facility. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA. If the FDA does not approve these facilities for the manufacture of our product, we may need to fund additional modifications to our manufacturing process, conduct additional validation studies, or find alternative manufacturing facilities, any of which would result in significant cost to us as well as a delay of up to several years in obtaining approval for and manufacturing of our product candidates. In addition, our contract manufacturers will be subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies for compliance with good manufacturing practices regulations, or cGMPs, and similar foreign standards. These regulations cover all aspects of the manufacturing, testing, quality control and record keeping relating to our product candidates. We do not have control over our contract manufacturers' compliance with these regulations and standards. Failure by our contract manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant market approval of drugs, delays, suspension or withdrawals of approvals, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. In addition, we have no control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Failure by our contract manufacturers to comply with or maintain any of these standards could adversely affect the development of our product candidates and our business.

IF PRODUCT LIABILITY LAWSUITS ARE SUCCESSFULLY BROUGHT AGAINST US, WE MAY INCUR SUBSTANTIAL LIABILITIES AND MAY BE REQUIRED TO LIMIT COMMERCIALIZATION OF OUR PRODUCT CANDIDATES.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates, and will face an even greater risk if we sell our product candidates commercially. Currently, we are not aware of any anticipated product liability claims with respect to our product candidates. In the future, an individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for our product candidates;

injury to our reputation;

withdrawal of clinical trial participants;

costs of related litigation;

substantial monetary awards to patients;

product recalls;

loss of revenue; and

the inability to commercialize our product candidates.

We have clinical trial liability insurance with a \$5,000,000 annual aggregate limit for up to 40 patients participating at the same time in our Atiprimod and L-Annamycin clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our product candidates. Our current insurance coverage may prove insufficient to cover any liability claims brought against us. In addition, because of the increasing costs of insurance coverage, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise.

EVEN IF WE RECEIVE REGULATORY APPROVAL FOR OUR PRODUCT CANDIDATES, WE WILL BE SUBJECT TO ONGOING SIGNIFICANT REGULATORY OBLIGATIONS AND OVERSIGHT.

If we receive regulatory approval to sell our product candidates, the FDA and foreign regulatory authorities may, nevertheless, impose significant restrictions on the indicated uses or marketing of such products, or impose ongoing requirements for post-approval studies. Following any regulatory approval of our product candidates, we will be subject to continuing regulatory obligations, such as safety reporting requirements, and additional post-marketing obligations, including regulatory oversight of the promotion and marketing of our products. If we become aware of previously unknown problems with any of our product candidates here or overseas or our contract manufacturers' facilities, a regulatory agency may impose restrictions on our products, our contract manufacturers or on us, including requiring us to reformulate our products, conduct additional clinical trials, make changes in the labeling of our products, implement changes to or obtain re-approvals of our contract manufacturers' facilities or withdraw the product from the market. In addition, we may experience a significant drop in the sales of the affected products, our reputation in the marketplace may suffer and we may become the target of lawsuits, including class action suits. Moreover, if we fail to comply with applicable regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Any of these events could harm or prevent sales of the affected products or could substantially increase the costs and expenses of commercializing and marketing these products.

WE RELY ON THIRD PARTIES TO CONDUCT OUR CLINICAL TRIALS. IF THESE THIRD PARTIES DO NOT SUCCESSFULLY CARRY OUT THEIR CONTRACTUAL DUTIES OR MEET EXPECTED DEADLINES, WE MAY NOT BE ABLE TO SEEK OR OBTAIN REGULATORY APPROVAL FOR OR COMMERCIALIZE OUR PRODUCT CANDIDATES.

We have agreements with third-party contract research organizations, ("CRO" or "CROs"), to provide monitors and to manage data for our clinical programs. We and our CROs are required to comply with current Good Clinical Practices, ("GCP" or "GCPs"), regulations and guidelines enforced by the FDA for all of our products in clinical development. The FDA enforces GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. In the future, if we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials for products in clinical development comply with GCPs. In addition, our clinical trials must be conducted with product produced under cGMP regulations, and will require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

IF WE FAIL TO ATTRACT AND KEEP SENIOR MANAGEMENT AND KEY SCIENTIFIC PERSONNEL, WE MAY BE UNABLE TO SUCCESSFULLY DEVELOP OUR PRODUCT CANDIDATES, CONDUCT OUR CLINICAL TRIALS AND COMMERC