PALATIN TECHNOLOGIES INC
Form 10-K
September 28, 2009

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended June 30, 2009

or

[ ] 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 001-15543

_____

PALATIN TECHNOLOGIES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**95-4078884**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
4C Cedar Brook Drive **Cranbury, New Jersey**	**08512**
(Address of principal executive offices)	(Zip Code)

(609) 495-2200
(Registrant'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, par value $.01 per share	NYSE Amex

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes o No x

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 o No x

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 x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes o No o

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 the 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.

x

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 the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company 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

State the aggregate market value of the voting and non-voting common equity held by non-affiliates, computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant s most recently completed second fiscal quarter (December 31, 2008): $8,643,861.

Indicate the number of shares outstanding of each of the registrant s classes of common stock, as of the latest practicable date (September 25, 2009): 96,155,249.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant s Quarterly Report on Form 10-Q for the quarter ended March 31, 2009 are incorporated into Part I of this Form 10-K.

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PART I

Item 1. Business.

Forward-looking statements

Statements in this Annual Report on Form 10-K (this Annual Report), as well as oral statements that may be made by us or by our officers, directors, or employees acting on our behalf, that are not historical facts constitute forward-looking statements, which are made pursuant to the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 (the Exchange Act). The forward-looking statements in this Annual Report do not constitute guarantees of future performance. Investors are cautioned that statements which are not strictly historical statements contained in this Annual Report, including, without limitation, current or future financial performance, management s plans and objectives for future operations, clinical trials and results, product plans and performance, management s assessment of market factors, as well as statements regarding our strategy and plans and our strategic partners, constitute forward-looking statements. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to be materially different from our historical results or from any results expressed or implied by such forward-looking statements. Our future operating results are subject to risks and uncertainties and are dependent upon many factors, including, without limitation, the risks identified under the caption Risk Factors and elsewhere in this Annual Report, as well as in our other Securities and Exchange Commission (SEC) filings.

In this Annual Report, references to we, our, us or Palatin means Palatin Technologies, Inc.

Overview

We are a biopharmaceutical company dedicated to the development of peptide, peptide mimetic and small molecule agonist compounds with a focus on melanocortin and natriuretic peptide receptor systems. We have a diverse pipeline of active development programs targeting melanocortin and natriuretic receptors, including development of proposed products for treatment of heart failure, sexual dysfunction, obesity, diabetes and metabolic syndrome.

We currently have the following active drug development programs:

- Bremelanotide, a peptide melanocortin receptor agonist, for treatment of sexual dysfunction, targeting female sexual dysfunction (FSD) and erectile dysfunction (ED) in patients non-responsive to current therapies.
- PL-6983, a peptide melanocortin receptor agonist, for treatment of sexual dysfunction.
- PL-3994, a peptide mimetic natriuretic peptide receptor A (NPRA) agonist, for treatment of heart failure (HF).
- Melanocortin receptor-based compounds for treatment of obesity, diabetes and related metabolic syndrome pursuant to an ongoing research collaboration and global license with AstraZeneca AB (AstraZeneca).

Key elements of our business strategy include: using our technology and expertise to develop and commercialize therapeutic products; entering into alliances and partnerships with pharmaceutical companies to facilitate the development, manufacture, marketing, sale and distribution of product candidates we are developing; partially funding our development and discovery programs with the cash flow from our AstraZeneca collaboration agreement and any future agreements with other companies; and, depending on the availability of sufficient funding, expanding our pipeline by using our expertise in drug discovery technologies for melanocortin and natriuretic peptide receptor systems and acquiring synergistic products and technologies.

We incorporated in Delaware in 1986 and commenced operations in the biopharmaceutical area in 1996. Our corporate offices and research and development facility are located at 4C Cedar Brook Drive, Cranbury, New Jersey 08512 and our telephone number is (609) 495-2200. We maintain an Internet site at http://www.palatin.com, where among other things, we make available free of charge on and through this website our Forms 3, 4 and 5, annual reports 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) and Section 16 of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Our website and the information contained in it or connected to it shall not be deemed to be incorporated into this Annual Report.

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Melanocortin Receptor-Specific Programs

The melanocortin system is involved in a large and diverse number of physiologic functions, and therapeutic agents modulating this system may have the potential to treat a variety of conditions and diseases, including sexual dysfunction, obesity and related disorders, ischemia reperfusion injury (injury resulting from inadequate blood flow or reintroduction of blood flow), hemorrhagic shock and inflammation-related diseases.

Bremelanotide for Sexual Dysfunction. We are developing subcutaneously administered bremelanotide for the treatment of ED and FSD. Bremelanotide, a melanocortin agonist (which promotes a biologic function response) drug candidate, is a synthetic peptide analog of the naturally occurring hormone alpha-MSH (melanocyte-stimulating hormone).

Medical Need ED and FSD. ED is the consistent inability to attain and maintain an erection sufficient for sexual intercourse. The condition is correlated with increasing age, cardiovascular disease, hypertension, diabetes, hyperlipidemia and smoking. In addition, certain prescription drugs and psychogenetic issues may contribute to ED. According to the Massachusetts Male Aging Study, more than 50% of men aged 40-70 report episodes of ED and more than 30 million men in the United States may be afflicted with some form of ED, with less than 20% seeking treatment. The incidence of ED increases with age. Studies show that chronic ED affects about 5% of men in their 40s and 15% to 25% of men by the age of 65. The current market size for ED is more than $2.5 billion per year.

Phosphodiesterase-5 (PDE-5) inhibitors such as sildenafil (Viagra®), vardenafil (Levitra®) and tadalafil (Cialis®) are used to treat ED, but an estimated 35% of ED patients are non-responsive to PDE-5 inhibitor therapy. There are limited therapeutic options for ED patients non-responsive to PDE-5 inhibitor therapy, including alprostadil for direct penis injection or urethral suppositories, surgical penile implants and various devices.

FSD is a multifactorial condition that has anatomical, physiological, medical, psychological and social components. Studies estimate FSD is prevalent in approximately 50% of women over the age of 30 and that more than 35 million women in the United States may be afflicted with some form of FSD. FSD includes disorders associated with desire, arousal, orgasm and pain.

There are no drugs in the United States approved for FSD indications.

Mechanisms of Action with Bremelanotide. Bremelanotide is believed to act through activation of melanocortin receptors in the central nervous system, which is a different mechanism of action from currently marketed PDE-5 inhibitor ED therapies that act directly on the vascular system. Studies have demonstrated efficacy with bremelanotide in patients non-responsive to PDE-5 inhibitor therapies. Studies have also demonstrated an additive effect in patients co-administered both bremelanotide and a PDE-5 inhibitor.

Clinical Trials with Intranasal Formulations. We extensively studied bremelanotide for sexual dysfunction in nasal formulations, administered as a single spray in one nostril. Increases in blood pressure were observed in some patients receiving nasally administered bremelanotide, and this observed increase was a significant factor leading us to discontinue work on nasally administered bremelanotide as a first-line therapy for sexual dysfunction. We believe that increases in blood pressure, as well as the rate of nausea and emesis (vomiting), were due, at least partially, to variability in drug uptake with nasal administration. Studies showed significant variation in plasma levels of bremelanotide in patients receiving nasally administered bremelanotide.

While we are no longer developing intranasal formulations of bremelanotide for commercialization, trials with intranasal formulations of bremelanotide did demonstrate potential utility of bremelanotide. Phase 2B double blind, placebo-controlled, parallel doses clinical trials evaluating nasal bremelanotide for ED, conducted in 726 non-diabetic and 294 diabetic patients, showed that over 30% of ED patients were restored to a normal level of function. Phase 2A clinical trials of post-menopausal FSD patients showed a statistically significant increase in the level of sexual desire and genital arousal in subjects receiving bremelanotide compared to subjects receiving placebo and, in pre-menopausal FSD patents, a trend to increases in the level of sexual desire and genital arousal in subjects receiving bremelanotide compared to subjects receiving placebo. In trials conducted to date, almost 2,000 patients received at least one dose of bremelanotide, with about 1,500 receiving multiple doses.

Subcutaneous Administration of Bremelanotide. In a recently completed Phase 1 clinical trial designed to evaluate the blood pressure effects of subcutaneously administered bremelanotide, no statistically significant difference in mean changes in blood pressure was seen in subjects receiving bremelanotide compared to placebo. No subject discontinued participation in the study as a result of protocol stopping rules

based on blood pressure changes. In addition, there was no difference in the incidence of emesis in subjects receiving bremelanotide compared to placebo. This Phase 1 trial was a two-week, randomized, double-blind, placebo-controlled study in subjects who received 45 repeat doses of bremelanotide or placebo subcutaneously. Each administered dose of

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bremelanotide achieved plasma levels shown to be efficacious for improving erectile function in multiple previous Phase 1 and Phase 2 erectile dysfunction studies.

With subcutaneous administration of bremelanotide variability in plasma exposure was significantly decreased. This study supports the hypothesis that increases in blood pressure seen with nasally administered bremelanotide were due, at least partially, to variability in drug uptake, with increases in blood pressure in patients with greater uptake. With subcutaneous administration of bremelanotide, variability in plasma exposure is controlled.

We have met with the U.S. Food and Drug Administration (FDA) to discuss data from our recently completed Phase 1 bremelanotide study supporting the switch to subcutaneous administration and our development program for subcutaneously administered bremelanotide in ED patients non-responsive to PDE-5 inhibitors. Our clinical program is commencing this year, and is planned, depending on program results, concurrence of the FDA and the availability of sufficient funding, to lead to initiation of at-home Phase 2 clinical studies in the first half of calendar 2010.

We are exploring various delivery devices for subcutaneous administration of bremelanotide. Injection sites for subcutaneous injection include the abdomen, thigh and upper arms. We believe that fine needle devices, pen injectors and needle-free injector systems can be used for subcutaneous administration of bremelanotide, and we are evaluating various delivery devices for potential commercialization. If Phase 2 clinical trials are successful, we anticipate that Phase 3 clinical trials will be conducted with a delivery device intended for commercialization.

PL-6983 for Treatment of Sexual Dysfunction. PL-6983 is our lead compound in a new series of melanocortin receptor-specific peptides we have developed. We have demonstrated efficacy of PL-6983 in inducing erections in animal models and in inducing sexual behavior in an animal model of FSD.

In developing PL-6983, we used a novel screening platform that examined the effectiveness of peptides in animal models of sexual response and also determined cardiovascular effects, primarily looking at changes in blood pressure. In these animal models, PL-6983 resulted in significantly smaller increases in blood pressure at doses effective for a sexual response than blood pressure increases in the same models seen with bremelanotide.

We are planning preclinical toxicology and other studies required by the FDA prior to initiating human clinical trials. Initial human clinical trials will be designed to measure safety parameters, including changes in blood pressure following administration.

Obesity. In 2007, we entered into an exclusive global licensing and research collaboration agreement with AstraZeneca to discover, develop and commercialize compounds that target melanocortin receptors for the treatment of obesity, diabetes and related metabolic syndrome. In June and December 2008, the collaboration agreement was amended to include additional compounds and associated intellectual property we developed. On September 24, 2009, the collaboration agreement was amended to provide additional payments to us totaling $5 million and to modify terms of the agreement.

Obesity is a multifactorial condition with significant biochemical components relating to satiety (feeling full), energy utilization and homeostasis. A number of different metabolic and hormonal pathways are being evaluated by companies around the world in efforts to develop better treatments for obesity. Scientific research has established that melanocortin receptors have a role in eating behavior and energy homeostasis, and that some melanocortin receptor agonists decrease food intake and induce weight loss.

Obesity is a significant healthcare issue, often correlated with a variety of cardiovascular and other diseases, including diabetes. More than 1.1 billion adults and over 150 million children worldwide are overweight, with over 300 million adults categorized as obese. According to the American Obesity Association, obesity is the second leading cause of preventable death after smoking and nearly one-third of adults in the United States are obese. Increased mortality, high blood pressure, diabetes and other substantial health risks are associated with being overweight and obese. Over 2.6 million deaths are attributed to diabetes each year worldwide and almost $120 billion is spent on related costs of obesity, according to the U.S. Surgeon General.

We have developed classes of small molecule and peptide compounds targeting melanocortin receptors which are effective in the treatment of obesity in animal models. Certain of these compounds have been demonstrated to be effective in normal diet-induced obese and genetically obese animal models for decreasing food intake and body weight, without an increase in sexual response in normal animals at the same or higher dose levels. During 2009, pursuant to an agreement with AstraZeneca we conducted a proof-of-principle clinical study on the effects of a melanocortin receptor-specific compound on food intake, obesity and other metabolic parameters.

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Pursuant to the terms of the agreement with AstraZeneca, we received up-front payments totaling $10.0 million. Effective with the September 2009 amendment, we are eligible for milestone payments totaling up to $145.2 million, with up to $85.2 million contingent upon development and regulatory milestones and the balance on achievement of sales targets, plus royalties on sales of approved products. AstraZeneca has responsibility for product commercialization, product discovery and development costs. We are providing certain scientific expertise in the research collaboration at a negotiated rate through January 2010, and agreed in the September 2009 amendment to conduct additional clinical studies.

Other Melanocortin Programs. We have early stage research and discovery programs exploring additional indications and targets. These programs include development of highly-selective melanocortin-1 and melanocortin-3 receptor agonists for treatment of inflammation-related diseases and disorders, melanocortin-4 receptor antagonists for treatment of cachexia and melanocortin-4 receptor agonists for prevention of organ damage, particularly kidney damage. We do not anticipate that any of these programs will advance to clinical trials during the next twelve months.

Natriuretic Peptide Receptor-Specific Programs

The natriuretic peptide receptor system has numerous cardiovascular functions, and therapeutic agents modulating this system may be useful in treatment of heart failure, hypertension and other cardiovascular diseases.

PL-3994 for Heart Failure Indications. PL-3994 is an NPRA agonist compound in development for treatment of HF. Heart failure is an illness in which the heart is unable to pump blood efficiently, and includes acutely decompensated HF with dyspnea (shortness of breath) at rest or with minimal activity. Endogenous (naturally produced) natriuretic peptides have a number of beneficial effects, including vasodilation (relaxation of blood vessels), natriuresis (excretion of sodium), and diuresis (excretion of fluids).

Patients who have been admitted to the hospital with an episode of worsening HF have an increased risk of either death or hospital readmission in the three months following discharge. Up to 15% of patients die in this period and as many as 30% need to be readmitted to the hospital. We believe that decreasing mortality and hospital readmission in patients discharged following hospitalization for worsening HF is a large unmet medical need for which PL-3994 may be effective. PL-3994 would be utilized as an adjunct to existing HF medications, and may, if successfully developed, be self-administered by patients as a subcutaneous injection following hospital discharge.

Medical Need in Heart Failure. Over 5.7 million Americans suffer from HF, with 670,000 new cases of HF diagnosed each year, with disease incidence expected to increase with the aging of the American population. Despite the treatment of HF with multiple drugs, almost all HF patients will experience at least one episode of acute HF that requires treatment with intravenous medications in the hospital. Heart failure has tremendous human and financial costs. Estimated direct costs in the U.S. for HF are $37.2 billion in 2009, with HF constituting the leading cause of hospitalization in people over 65 years of age, with over 1.1 million hospital discharges for HF in 2006. Heart failure is also a high mortality disease, with approximately one-half of HF patients dying within five years of initial diagnosis.

Mechanisms of Action with PL-3994. PL-3994 activates NPRA, a receptor known to play a role in cardiovascular homeostasis. We believe that PL-3994, through activation of NPRA, will reduce cardiac hypertrophy, which is an independent risk factor for cardiovascular morbidity and mortality. PL-3994 increases plasma cyclic guanosine monophosphate (cGMP) levels, a pharmacological response consistent with the effects of endogenous natriuretic peptides on cardiovascular function. PL-3994 also decreases activity of the renin-angiotensin-aldosterone system (RAAS), a hormone system that regulates blood pressure and fluid balance. The RAAS system is frequently over-activated in HF patients, leading to worsening of cardiovascular function.

PL-3994 is one of a number of natriuretic peptide receptor agonist compounds we have developed. PL-3994 is a synthetic molecule incorporating a novel and proprietary amino acid mimetic structure. It has an extended half-life, with reduced affinity for endogenous natriuretic peptide clearance receptors and significantly increased resistance to neutral endopeptidase, an endogenous enzyme that degrades natriuretic peptides.

Clinical Studies with PL-3994. Preclinical studies in animals established a dose-dependent effect on blood pressure and diuresis, and in animal models of HF showed improved kidney function and prevention of cardiac hypertrophy (increase in heart size due to disease). Safety toxicology studies were conducted in animals prior to filing an Investigational New Drug (IND) application with the FDA.

Human clinical studies of PL-3994 commenced with a Phase 1 trial which concluded in the first quarter of calendar year 2008. This was a randomized, double-blind, placebo-controlled, study in 26 healthy volunteers who received either PL-3994 or a placebo subcutaneously. The evaluations included safety, tolerability, pharmacokinetics and several pharmacodynamic endpoints, including levels of cGMP, a natural messenger

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nucleotide. Dosing concluded with the successful achievement of the primary endpoint of the study, a prespecified reduction in systemic blood pressure. No volunteer experienced a serious or severe adverse event. Elevations in plasma cGMP levels, increased diuresis and increased natriuresis were all observed for several hours after single subcutaneous doses.

In the second quarter of calendar year 2008, we conducted a Phase 2A trial in volunteers with controlled hypertension who were receiving one or more conventional antihypertensive medications. In this trial, which was a randomized, double-blind, placebo-controlled, single ascending dose study in 21 volunteers, the objective was to demonstrate that PL-3994 can be given safely to patients taking antihypertensive medications commonly used in HF and hypertension patients. Dosing concluded with the successful achievement of the primary endpoint of the study, a prespecified reduction in systemic blood pressure. No volunteer experienced a serious or severe adverse event. Elevations in plasma cGMP levels were observed for several hours after single subcutaneous doses.

We have planned a repeat dose Phase 2B clinical trial in patients hospitalized with HF, which will evaluate safety profiles in patients given repeat doses of PL-3994 as well as pharmacokinetic and pharmacodynamic endpoints. This trial is projected to commence, depending on sufficient funding, during the first half of calendar year 2010.

PL-3994 is being developed as a subcutaneously administered drug, and is well absorbed through this route of administration. In human studies, the pharmacokinetic (period to metabolize or excrete the drug) and pharmacodynamic (period of action or effect of the drug) half-lives were on the order of hours, significantly longer than the comparable half-lives of endogenous natriuretic peptides. We believe that PL-3994, if successful, will be amenable to self-administration by patients, similar to insulin and other self-administered drugs.

Other Natriuretic Peptide Receptor-Specific Programs. We have early stage discovery and development programs in the natriuretic peptide receptor field, including compounds with varied pharmacology, including compounds with increased diuretic effect and decreased effect on blood pressure, and compounds effective at more than one natriuretic peptide receptor.

Other Programs

We previously marketed NeutroSpec®, a radiolabeled monoclonal antibody product for imaging and diagnosing infection, which is the subject of a strategic collaboration agreement with the Mallinckrodt division of Covidien Ltd. In 2005, we suspended marketing, clinical trials and securing regulatory approvals of NeutroSpec, and do not anticipate conducting any substantive work or incurring substantial expenditures on NeutroSpec over the next twelve months.

Technologies We Use

We use a rational drug design approach to discover and develop proprietary peptide, peptide mimetic and small molecule agonist compounds, focusing on melanocortin and natriuretic peptide receptor systems. Computer-aided drug design models of receptors are optimized based on experimental results obtained with peptides and small molecules we develop, supported by conformational analyses of peptides in solution utilizing nuclear magnetic resonance spectroscopy. By integrating both technologies, we believe we are developing an advanced understanding of the factors which drive agonism.

We have developed a series of proprietary technologies used in our drug development programs. One technology employs novel amino acid mimetics in place of selected amino acids. These mimetics provide the receptor-binding functions of conventional amino acids, while providing structural, functional and physiochemical advantages. The amino acid mimetic technology is employed in PL-3994, our compound in

development for treatment of HF.

We maintain expertise in both peptide and small molecule chemistries, and have developed a series of drug selection technologies for selecting compounds with desired pharmacological profiles, particularly in the melanocortin receptor field. The drug selection technologies are used to develop and select melanocortin receptor-specific small molecules and peptides with novel properties, including compounds that are effective in the treatment of obesity in animal models but which induce a limited or no sexual response.

Some compound series have been derived using our proprietary and patented platform technology, called MIDAS (Metal Ion-induced Distinctive Array of Structures). This technology employs metal ions to fix the three-dimensional configuration of peptides, forming conformationally rigid molecules that remain folded specifically in their active state. These MIDAS molecules are generally simple to synthesize, are chemically and proteolytically stable, and have the potential to be orally bioavailable. In addition, MIDAS molecules are information-rich and provide data on structure-activity relationships that may be used to design small molecule, non-peptide drugs.

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Estimate of Amount Spent on Research and Development Activities

Research and development expenses were $13.4 million for the fiscal year ended June 30, 2009 (fiscal 2009) and $21.2 million for the fiscal year ended June 30, 2008 (fiscal 2008). In fiscal 2009, $4.7 million of the foregoing was borne by AstraZeneca pursuant to the collaboration agreement, and in fiscal 2008, $2.5 million of the

foregoing was borne by AstraZeneca and other pharmaceutical companies pursuant to collaboration or license agreements.

Competition

Our products under development will compete on the basis of quality, performance, cost effectiveness and application suitability with numerous established products and technologies. We have many competitors, including pharmaceutical, biopharmaceutical and biotechnology companies. Furthermore, there are several well-established products in our target markets that we will have to compete against. Products using new technologies which may be competitive with our proposed products may also be introduced by others. Most of the companies selling or developing competitive products have financial, technological, manufacturing and distribution resources significantly greater than ours and may represent significant competition for us.

The pharmaceutical and biotechnology industry is characterized by extensive research efforts and rapid technological change. Many biopharmaceutical companies have developed or are working to develop products similar to ours or that address the same markets. Such companies may succeed in developing technologies and products that are more effective or less costly than any of those that we may develop. Such companies may be more successful than us in developing, manufacturing and marketing products.

We cannot guarantee that we will be able to compete successfully in the future or that developments by others will not render our proposed products under development or our future product candidates obsolete or non-competitive or that our collaborators or customers will not choose to use competing technologies or products.

Bremelanotide and PL-6983 for Treatment of Sexual Dysfunction. There is competition and financial incentive to develop, market and sell drugs for the treatment of ED and FSD. Leading drugs approved for ED indications are PDE-5 inhibitors which target the vascular system, such as sildenafil (sold under the trade name Viagra®), vardenafil (sold under the trade name Levitra®) and tadalafil (sold under the trade name Cialis®). In addition, we are aware of other PDE-5 inhibitors under development. Other drugs approved for ED indications include alprostadil for injection (sold under the trade name Caverject Impulse®), which is injected directly into the penis, and alprostadil in urethral suppository format (sold under the trade name MUSE®). In addition, a variety of devices, including vacuum devices and surgical penile implants, have been approved for ED indications. We are aware of a number of companies developing new drugs for ED indications, some of which are in clinical trials in the United States and elsewhere. We are not aware of any company actively developing a melanocortin receptor-agonist drug for ED.

There are no products specifically approved for an FSD indication in the United States. A number of hormonal therapies have been commercialized for other indications, including progestin, androgen and localized estrogen therapies, but none have been approved by the FDA for FSD indications. A number of drugs are in various stages of research or development for FSD. We are not aware of any company actively developing a melanocortin receptor-agonist drug for FSD.

PL-3994 for Heart Failure Indications. Nesiritide (sold under the trade name Natrecor®), a recombinant human B-type natriuretic peptide drug, is marketed in the United States by Scios Inc., a Johnson & Johnson company. Nesiritide is approved for treatment of acutely decompensated congestive HF patients who have dyspnea at rest or with minimal activity. Carperitide, a recombinant human atrial natriuretic peptide drug, is marketed in Japan and is reported to be available for licensing in other countries. Both nesiritide and carperitide are administered by intravenous infusion. Because of the very short half-life of nesiritide, we believe it is unlikely to be suitable for subcutaneous administration or for long-term treatment of HF. We are aware of at least two companies developing intravenously administered natriuretic peptide drugs reported to be in Phase 2 clinical trials for acute HF. In addition, there are a number of approved drugs and drugs in development for treatment of HF through mechanisms or pathways other than agonism of NPRA.

Obesity. There are several FDA-approved drugs for the treatment of obesity, and a large number of products in clinical development by other companies, including products which target melanocortin receptors. Clinical trials for obesity are lengthy, time-consuming and expensive, and we may not be able to proceed if AstraZeneca discontinues work under or terminates our January 2007 license agreement. See the discussion under the heading We do not control the development of compounds licensed to third parties and, as a result, we may not

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realize a significant portion of the potential value of any such license arrangements in Item 1A, Risk Factors in this Annual Report.

Patents and Proprietary Information

Patent protection. Our success will depend in substantial part on our ability to obtain, defend and enforce patents, maintain trade secrets and operate without infringing upon the proprietary rights of others, both in the United States and abroad. We own a number of issued United States patents and have pending United States patent applications, many with issued or pending counterpart patents in selected foreign countries. We seek patent protection for our technologies and products in the United States and those foreign countries where we believe patent protection is commercially important.

We own issued United States and foreign patents claiming the bremelanotide substance. The issued United States patents have a term until 2020, which term may be subject to extension for a maximum period of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process, pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments). Whether we will be able to obtain patent term extensions under the Hatch-Waxman Amendments and the length of the extension to which we may be entitled cannot be determined until the FDA approves for marketing, if ever, a product in which bremelanotide is the active ingredient. In addition, the claims of issued patents covering bremelanotide may not provide meaningful protection. Further, third parties may challenge the validity or scope of any issued patent.

We have patent applications pending in the United States and foreign countries claiming the PL-3994 substance and other natriuretic peptide receptor agonist compounds we have developed. One United States patent application claiming PL-3994 has been allowed, but other patent applications have not yet been examined, and in any event we do not know the full scope of patent coverage we will obtain, or whether any patents will issue other than the allowed application claiming PL-3994. The allowed patent application will have a term, assuming the patent issues in due course, until 2027, which term may be subject to extension for a maximum period of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process, pursuant to the Hatch-Waxman Amendments. Whether we will be able to obtain patent term extensions under the Hatch-Waxman Amendments and the length of the extension to which we may be entitled cannot be determined until the FDA approves for marketing, if ever, a product in which PL-3994 is the active ingredient.

We have filed patent applications on melanocortin receptor-specific peptides including PL-6983. Until these applications are examined, we do not know the scope of patent claims that will be allowed, or whether any patents will issue.

We have a number of United States and foreign patent applications claiming compounds included in our agreement with AstraZeneca relating to our obesity program. However, many of these patent applications have not yet been examined, and we do not know the scope of patent claims that will be allowed, or whether any patents will issue. Additionally, until one or more compounds are selected for commercialization, which may never occur, we cannot evaluate the duration of patents or their effect on the program.

In the event that a third party has also filed a patent application relating to an invention we claimed in a patent application, we may be required to participate in an interference proceeding adjudicated by the United States Patent and Trademark Office to determine priority of invention. The possibility of an interference proceeding could result in substantial uncertainties and cost, even if the eventual outcome is favorable to us. An adverse outcome could result in the loss of patent protection for the subject of the interference, subjecting us to significant

liabilities to third parties, the need to obtain licenses from third parties at undetermined cost, or requiring us to cease using the technology.

Future patent infringement. We do not know for certain that our commercial activities will not infringe upon patents or patent applications of third parties, some of which may not even have been issued. Although we are not aware of any valid U.S. patents which are infringed by bremelanotide, PL-3994 or PL-6983 or by our methods of making the foregoing, we cannot exclude the possibility that such patents might exist or arise in the future. We may be unable to avoid infringement of any such patents and may have to seek a license, defend an infringement action, or challenge the validity of such patents in court. Patent litigation is costly and time consuming. If such patents are valid and we do not obtain a license under any such patents, or we are found liable for infringement, we may be liable for significant monetary damages, may encounter significant delays in bringing products to market, or may be precluded from participating in the manufacture, use or sale of products or methods of treatment covered by such patents.

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Proprietary information. We rely on proprietary information, such as trade secrets and know-how, which is not patented. We have taken steps to protect our unpatented trade secrets and know-how, in part through the use of confidentiality and intellectual property agreements with our employees, consultants and certain contractors. If our employees, scientific consultants, collaborators or licensees develop inventions or processes independently that may be applicable to our product candidates, disputes may arise about the ownership of proprietary rights to those inventions and processes. Such inventions and processes will not necessarily become our property, but may remain the property of those persons or their employers. Protracted and costly litigation could be necessary to enforce and determine the scope of our proprietary rights.

If trade secrets are breached, our recourse will be solely against the person who caused the secrecy breach. This might not be an adequate remedy to us, because third parties other than the person who causes the breach will be free to use the information without accountability to us. This is an inherent limitation of the law of trade secret protection.

Governmental Regulation

The FDA, comparable agencies in other countries and state regulatory authorities have established regulations and guidelines which apply to, among other things, the clinical testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising, promotion, marketing and distribution of our proposed products. Noncompliance with applicable requirements can result in fines, recalls or seizures of products, total or partial suspension of production, refusal of the regulatory authorities to approve marketing applications, withdrawal of approvals and criminal prosecution.

Before a drug product is approved by the FDA for commercial marketing, three phases of human clinical trials are usually conducted to test the safety and effectiveness of the product. Phase 1 clinical trials most typically involve testing the drug on a small number of healthy volunteers to assess the safety profile of the drug at different dosage levels. Phase 2 clinical trials, which may also enroll a relatively small number of patient volunteers, are designed to further evaluate the drug s safety profile and to provide preliminary data as to the drug s effectiveness in humans. Phase 3 clinical trials consist of larger, well-controlled studies that may involve several hundred or thousand patient volunteers representing the drug s targeted population. During any of these phases, the clinical trial can be placed on clinical hold, or temporarily or permanently stopped for a variety of reasons, principally for safety concerns.

After approving a product for marketing, the FDA may require post-marketing testing, including extensive Phase 4 studies, and surveillance to monitor the safety and effectiveness of the product in general use. The FDA may withdraw product approvals if compliance with regulatory standards is not maintained or if problems occur following initial marketing. In addition, the FDA may impose restrictions on the use of a drug that may limit its marketing potential. The failure to comply with applicable regulatory requirements in the U.S. and in other countries in which we conduct development activities could result in a variety of fines and sanctions, such as warning letters, product recalls, product seizures, suspension of operations, fines and civil penalties or criminal prosecution.

In addition to obtaining approval of a New Drug Application (an NDA) from the FDA for any of our proposed products, any facility that manufactures such a product must comply with current good manufacturing practices (GMPs). This means, among other things, that the drug manufacturing establishment must be registered with, and subject to inspection by, the FDA. Foreign manufacturing establishments must also comply with GMPs and are subject to periodic inspection by the FDA or by corresponding regulatory agencies in such other countries under reciprocal agreements with the FDA. In complying with standards established by the FDA, manufacturing establishments must continue to expend time, money and effort in the areas of production and quality control to ensure full technical compliance. We will use contract manufacturing establishments, in the United States or in foreign countries, to manufacture our proposed products, and will depend on those establishments to comply with GMPs and other regulatory requirements.

Third-Party Reimbursements

Successful sales of our proposed products in the United States and other countries will depend on the availability of adequate reimbursement from third-party payors such as governmental entities, managed care organizations, health maintenance organizations (HMOs) and private insurance plans. Reimbursement by a third-party payor may depend on a number of factors, including the payor s determination that the product has been approved by the FDA for the indication for which the claim is being made, that it is neither experimental nor investigational, and that the use of the product is safe and efficacious, medically necessary, appropriate for the specific patient and cost effective. Since reimbursement by one payor does not guarantee reimbursement by another, we or our licensees may be required to seek approval from each payor individually. Seeking such approvals is a time-consuming and costly process. Third-party payors routinely limit the products that they will cover and the

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amount of money that they will pay and, in many instances, are exerting significant pressure on medical suppliers to lower their prices. There is significant uncertainty concerning third-party reimbursement for the use of any pharmaceutical product incorporating new technology and we are not sure whether third-party reimbursement will be available for our proposed products once approved, or that the reimbursement, if obtained, will be adequate. There is also significant uncertainty concerning third-party reimbursement for products treating FSD and ED. Less than full reimbursement by governmental and other third-party payors for our proposed products would adversely affect the market acceptance of these proposed products. Further, healthcare reimbursement systems vary from country to country, and we are not sure whether third-party reimbursement will be made available for our proposed products under any other reimbursement system.

Manufacturing and Marketing

To be successful, our proposed products will need to be manufactured in commercial quantities under GMPs prescribed by the FDA and at acceptable costs. We do not have the facilities to manufacture any of our proposed products under GMPs. We intend to rely on collaborators, licensees or contract manufacturers for the commercial manufacture of our proposed products.

Our bremelanotide product candidate is a synthetic peptide. While the production process involves well-established technology, there are few manufacturers capable of scaling up to commercial quantities under GMPs at acceptable costs. We have identified and contracted with a third-party manufacturer for the production of bremelanotide, and have validated manufacturing of the bremelanotide drug substance under GMPs. However, we have not negotiated a long-term supply agreement with the third-party manufacturer, and may not be able to enter into a supply agreement on acceptable terms, if at all.

Our PL-3994 product candidate is a peptide mimetic molecule, incorporating a proprietary amino acid mimetic structure and amino acids. We have identified a manufacturer which made the product in quantities sufficient for Phase 1 and some anticipated Phase 2 clinical trials, and are in the process of evaluating commercial-scale manufacturers. Scaling up to commercial quantities may involve production, purification, formulation and other problems not present in the scale of manufacturing done to date.

Our PL-6983 product candidate is also a synthetic peptide. We have manufactured PL-6983 in-house, but have not contracted with a third-party manufacturer to produce the product for either clinical trials or commercial purposes. While the production process involves well-established technology, there are few manufacturers capable of scaling up to commercial quantities under GMPs at acceptable costs. Additionally, scaling up to commercial quantities may involve production, purification, formulation and other problems not present in the scale of manufacturing done to date.

The failure of any manufacturer or supplier to comply with FDA GMPs or to supply the drug substance and services as agreed, would force us to seek alternative sources of supply and could interfere with our ability to deliver product on a timely and cost effective basis or at all. Establishing relationships with new manufacturers or suppliers, any of whom must be FDA-approved, is a time-consuming and costly process.

Product Liability and Insurance

Our business may be affected by potential product liability risks which are inherent in the testing, manufacturing, marketing and use of our proposed products. We have liability insurance providing up to $10.0 million coverage in the aggregate as to certain clinical trial risks.

Employees

As of September 25, 2009, we employed 43 persons full time, of whom 30 are engaged in research and development activities and 13 are engaged in administration and management. Of our employees, 15 hold Ph.D. or M.D. degrees. While we have been successful in attracting skilled and experienced scientific personnel, competition for personnel in our industry is intense. None of our employees are covered by a collective bargaining agreement. All of our employees have executed confidentiality and intellectual property agreements. We consider relations with our employees to be good.

From time to time, we hire scientific consultants to work on specific research and development programs. We also rely on independent organizations, advisors and consultants to provide services, including aspects of manufacturing, clinical management, regulatory strategy and market research. Our independent advisors and consultants sign agreements that provide for confidentiality of our proprietary information and rights to any intellectual property developed while working for us.

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Item 1A. Risk Factors.

We expect to continue to incur substantial losses over the next few years and we may never become profitable.

We have never been profitable and we may never become profitable. As of June 30, 2009, we had an accumulated deficit of $207.4 million. We expect to incur additional losses as we continue our development of bremelanotide, PL-3994 and PL-6983. Unless and until we receive approval from the FDA or other equivalent regulatory authorities outside the United States, we cannot sell our products and will not have product revenues from them. Therefore, for the foreseeable future, we will have to fund all of our operations and capital expenditures from reimbursements and other contract revenue under collaborative development agreements, existing cash balances and outside sources of financing, which may not be available on acceptable terms, if at all.

We expect that we will need to continue to raise funds in the future, and funds may not be available on acceptable terms, or at all.

As of June 30, 2009, we had cash and cash equivalents of $4.4 million and available-for-sale investments of $3.4 million, with current liabilities of $1.7 million excluding the current portion of deferred revenues of $2.7 million. In August 2009, we received net proceeds of $2.8 million resulting from a registered direct offering of units consisting of our common stock and warrants. In September 2009, we signed an amendment to our collaboration agreement with AstraZeneca providing for $5 million in payments to us, with an initial payment of $2.5 million and the balance in the first quarter of calendar 2010. While we believe that the foregoing is adequate to fund operations through at least September 30, 2010, we will need additional funds to continue development of bremelanotide, PL-3994 and PL-6983, as well as our early stage research and discovery programs, and to fund operations after that date.

We may raise additional funds through public or private equity financings, collaborative arrangements on our product candidates or other sources. However, additional funding may not be available on acceptable terms or at all. If adequate funds are not available when needed, we will need to further curtail operations significantly, including the delay, modification or cancelation of operations and plans, including preclinical studies and clinical trials, related to bremelanotide, PL-3994 and PL-6983. To obtain additional funding, we may need to enter into arrangements that require us to develop only certain of our product candidates or relinquish rights to certain technologies, product candidates and/or potential markets.

Based upon the recent price of our common stock on the NYSE Amex LLC (the NYSE Amex), even if we are able to raise additional capital it is likely that our existing stockholders will experience substantial dilution.

In order to raise any meaningful amount of capital, as we intend, based upon our recent stock price we will almost certainly need to sell a significant amount of equity securities, either in the form of new shares of common stock or some other form of convertible security. Any significant sale of equity securities in any form at these prices will result in significant dilution to our existing stockholders. The prospect of this dilution is likely to continue to have a negative effect on the market price and trading volume of our common stock until such time as an actual financing occurs.

Our common stock may be delisted from the NYSE Amex, making it difficult to trade shares of our common stock.

On December 23, 2008, we received notice from the exchange now known as NYSE Amex notifying us that NYSE Amex had determined that we did not meet continued listing standards based on a review of our Form 10-Q for the fiscal quarter ended September 30, 2008. In a letter to us, NYSE Amex stated that Palatin was not in compliance with Section 1003(a)(ii) of NYSE Amex s Company Guide (the Company Guide) because our stockholders equity was less than the required $4,000,000 and we had losses from continuing operations and net losses in three of our four most recent fiscal years and not in compliance with Section 1003(a)(iii) of the Company Guide because our stockholders equity was less than the required $6,000,000 and we had losses from continuing operations and net losses in our five most recent fiscal years. The letter from NYSE Amex also stated that because our stock had been trading below $0.25 per share over the previous seven months, NYSE Amex deemed it appropriate for us to effect a reverse stock split in accordance with Section 1003(f)(v) of the Company Guide.

In order to maintain our NYSE Amex listing, we submitted a plan on January 23, 2009 advising NYSE Amex what we intend to do to bring us into compliance with the continued listing standards identified above by June 23, 2010. On February 27, 2009, NYSE Amex notified us that it had accepted our plan for regaining compliance, and that our listing on NYSE Amex was being continued pursuant to an extension. We may be able to continue our listing during the plan period through June 23, 2010, subject to periodic review by NYSE Amex to determine if we are making progress consistent with the plan. If we do not regain compliance with Sections 1003(a)(ii) and (iii) by

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June 23, 2010, or if we do not make progress consistent with the plan during the plan period, NYSE Amex may initiate delisting procedures.

If we are delisted from NYSE Amex then our common stock will trade, if at all, only on the over-the-counter market, such as the OTC Bulletin Board securities market, and then only if one or more registered broker-dealer market makers comply with quotation requirements. In addition, delisting of our common stock could further depress our stock price, substantially limit liquidity of our common stock and materially adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from NYSE Amex could also have other negative results, including the potential loss of confidence by suppliers and employees, the loss of institutional investor interest and fewer business development opportunities.

We may implement a reverse stock split, which will reduce our trading volume and may result in a decrease in our market capitalization.

As discussed in the risk factor above, NYSE Amex deems it appropriate for us to implement a reverse stock split because our stock had been trading below $0.25 per share over a seven month period. At the annual meeting of stockholders held on May 13, 2009, the stockholders authorized a reverse stock split which, if implemented, will combine between two and fifteen shares of outstanding common stock into one share of new common stock. The reverse stock split may be implemented at any time until May 13, 2010 upon a determination by our board of directors that the reverse stock split is in the best interests of the company and its stockholders. If the board decides to proceed with the reverse split, the board will determine the exact reverse split ratio and effective date. If we do not complete a reverse stock split within a reasonable amount of time, NYSE Amex may consider suspending dealings in our common stock or initiate delisting procedures. In determining whether to proceed with the reverse split and setting the exact ratio of the split, the board will consider a number of factors, including additional funding requirements, the amount of our authorized but unissued common stock, market conditions, existing and expected trading prices of our common stock and NYSE Amex listing requirements. We anticipate that the reverse split, if the board determines to proceed with the reverse split, will be implemented in conjunction with an equity financing or other transaction. We believe it is likely that the per share market price of our common stock will increase after a reverse split. However, we cannot guarantee that our common stock price will increase, and even if it does, we cannot guarantee that the price increase:

will be proportionate to the reverse split ratio;

will last in the marketplace for any length of time;

will be sufficient to meet the listing requirements of NYSE Amex; or

will be sufficient to facilitate raising capital.

We have a limited operating history upon which to base an investment decision.

Our operations to date have been primarily focused on acquiring, developing and securing our proprietary technology, conducting preclinical and clinical studies and formulating and manufacturing on a small-scale basis our principal product candidates. These operations provide a limited basis for stockholders to assess our ability to commercialize our product candidates.

We have not yet demonstrated our ability to perform the functions necessary for the successful commercialization of any of our current product candidates. The successful commercialization of our product candidates will require us to perform a variety of functions, including:

continuing to conduct preclinical development and clinical trials;

participating in regulatory approval processes;

formulating and manufacturing products, or having third parties formulate and manufacture products;

post-approval pharmacovigilance;

conducting sales and marketing activities, either alone or with a partner; and

obtaining additional capital.

If we are unable to obtain regulatory approval of any of our product candidates, to successfully commercialize any products for which we receive regulatory approval or to obtain additional capital, we may not be able to recover our investment in our development efforts.

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Development and commercialization of our product candidates involves a lengthy, complex and costly process, and we may never successfully develop or commercialize any product.

Our product candidates are at various stages of research and development, will require regulatory approval, and may never be successfully developed or commercialized. Our product candidates will require significant further research, development and testing before we can seek regulatory approval to market and sell them.

We must demonstrate that our product candidates are safe and effective for use in patients in order to receive regulatory approval for commercial sale. Preclinical studies in animals, using various doses and formulations, must be performed before we can begin human clinical trials. Even if we obtain favorable results in the preclinical studies, the results in humans may be different. Numerous small-scale human clinical trials may be necessary to obtain initial data on a product candidate s safety and efficacy in humans before advancing to large-scale human clinical trials. We face the risk that the results of our trials in later phases of clinical trials may be inconsistent with those obtained in earlier phases. Adverse or inconclusive results could delay the progress of our development programs and may prevent us from filing for regulatory approval of our product candidates. Additional factors that can cause delay or termination of our human clinical trials include:

timely completion of clinical site protocol approval and obtaining informed consent from subjects;

the rate of patient enrollment in clinical studies;

adverse medical events or side effects in treated patients; and

lack of effectiveness of the product being tested.

You should evaluate us in light of these uncertainties, delays, difficulties and expenses commonly experienced by early stage biopharmaceutical companies, as well as unanticipated problems and additional costs relating to:

product approval or clearance;

regulatory compliance;

good manufacturing practices;

intellectual property rights;

product introduction; and

marketing and competition.

The regulatory approval process is lengthy, expensive and uncertain, and may prevent us from obtaining the approvals we require.

Government authorities in the United States and other countries extensively regulate the advertising, labeling, storage, record-keeping, safety, efficacy, research, development, testing, manufacture, promotion, marketing and distribution of drug products. Drugs are subject to rigorous regulation by the FDA in the United States and similar regulatory bodies in other countries. The steps ordinarily required by the FDA before a new drug may be marketed in the United States include:

completion of non-clinical tests including preclinical laboratory and formulation studies and animal testing and toxicology;

submission to the FDA of an IND, which must become effective before clinical trials may begin;

performance of adequate and well-controlled Phase 1, 2 and 3 human clinical trials to establish the safety and efficacy of the drug for each proposed indication;

submission to the FDA of an NDA; and

FDA review and approval of the NDA before any commercial marketing or sale.

Satisfaction of FDA pre-market approval requirements for new drugs typically takes a number of years and the actual time required for approval may vary substantially based upon the type, complexity and novelty of the product or disease. The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA. The NDA also must contain extensive manufacturing information. Once the submission has been accepted for filing, the FDA generally has ten months to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification.

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Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical trials is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of the advisory committee. The FDA may deny or delay approval of applications that do not meet applicable regulatory criteria or if the FDA determines that the clinical data do not adequately establish the safety and efficacy of the drug. Therefore, our proposed products could take a significantly longer time than we expect or may never gain approval. If regulatory approval is delayed or never obtained, our business and our liquidity would be adversely affected.

Upon approval, a product candidate may be marketed only in those dosage forms and for those indications approved by the FDA. Once approved, the FDA may withdraw the product approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require post-marketing studies, referred to as Phase 4 studies, to monitor the approved products in a larger number of patients than were required for product approval and may limit further marketing of the product based on the results of these post-market studies. The FDA has broad post-market regulatory and enforcement powers, including the ability to seek

injunctions, levy fines and civil penalties, criminal prosecution, withdraw approvals and seize products or request recalls.

If regulatory approval of any of our product candidates is granted, it will be limited to certain disease states or conditions. Adverse experiences with the product must be reported to the FDA and could result in the imposition of market restriction through labeling changes or in product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

Outside the United States, our ability to market our product candidates will also depend on receiving marketing authorizations from the appropriate regulatory authorities. The foreign regulatory approval process generally includes all of the risks associated with FDA approval described above. The requirements governing the conduct of clinical trials and marketing authorization vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Community, or EC, registration procedures are available to companies wishing to market a product to more than one EC member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficiency has been presented, a marketing authorization will be granted.

If any approved product does not achieve market acceptance, our business will suffer.

Regulatory approval for the marketing and sale of any of our product candidates does not assure the product s commercial success. Any approved product will compete with other products manufactured and marketed by major pharmaceutical and other biotechnology companies. The degree of market acceptance of any such product will depend on a number of factors, including:

perceptions by members of the healthcare community, including physicians, about its safety and effectiveness;

cost-effectiveness relative to competing products and technologies;

availability of reimbursement for our products from third party payors such as health insurers, health maintenance organizations and government programs such as Medicare and Medicaid; and

advantages over alternative treatment methods.

If any approved product does not achieve adequate market acceptance, our business, financial condition and results of operations will be adversely affected.

We rely on third parties to conduct clinical trials for our product candidates and their failure to timely perform their obligations could significantly harm our product development.

We rely on outside scientific collaborators such as researchers at clinical research organizations and universities in certain areas that are particularly relevant to our research and product development plans, such as the conduct of clinical trials and non-clinical tests. There is competition for these relationships, and we may not be able to maintain our relationships with them on acceptable terms. These outside collaborators generally may terminate their engagements with us at any time. As a result, we can control their activities only within certain limits, and they will devote only a certain amount of their time to conduct research on our product candidates and develop them. If they do not successfully carry out their duties under their agreements with us, fail to inform us if these trials fail to

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comply with clinical trial protocols or fail to meet expected deadlines, our ability to develop our product candidates and obtain regulatory approval on a timely basis, if at all, may be adversely affected.

Production and supply of our product candidates depend on contract manufacturers over whom we have no control.

We do not have the facilities to manufacture bremelanotide, PL-3994 or PL-6983 or our other potential products. Our contract manufacturers must perform these manufacturing activities in a manner that complies with FDA regulations. Our ability to control third-party compliance with FDA requirements will be limited to contractual remedies and rights of inspection. The manufacturers of approved products and their manufacturing facilities will be subject to continual review and periodic inspections by the FDA and other authorities where applicable,

and must comply with ongoing regulatory requirements, including the FDA s GMPs regulations. Failure of third-party manufacturers to comply with GMPs or other FDA requirements may result in enforcement action by the FDA. Failure to conduct their activities in compliance with FDA regulations could delay our development programs or negatively impact our ability to receive FDA approval of our potential products or continue marketing if they are approved. Establishing relationships with new suppliers, who must be FDA-approved, is a time-consuming and costly process.

We are subject to extensive regulation in connection with the laboratory practices and the hazardous materials we use.

We are subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as noted above, the FDA and other regulatory authorities have broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products and withdraw approvals, any one or more of which could have a material adverse effect on us. We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Contamination or injury from hazardous materials used in the development of our products could result in a liability exceeding our financial resources.

Our research and development involves the use of hazardous materials and chemicals, including radioactive compounds. We