PEPLIN INC
Form 424B3
January 20, 2009
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**Filed Pursuant to Rule 424(b)(3)**
**Registration No. 333-156484**

**P R O S P E C T U S**

# Peplin, Inc.

## 819,378 shares of Common Stock

This prospectus covers the offer and resale by the selling stockholders identified in this prospectus of up to 819,378 shares of common stock, $0.001 par value, of Peplin, Inc., issued by us to certain stockholders of Neosil, Inc., or Neosil, in connection with the acquisition by us of all the outstanding capital stock of Neosil. We refer to the shares of common stock covered by this prospectus as the Resale Shares. We will not receive any of the proceeds from the sale or other disposition of the Resale Shares by the selling stockholders.

The selling stockholders or their pledgees, assignees or successors-in-interest may offer and sell or otherwise dispose of the Resale Shares described in this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling stockholders will bear all commissions and discounts, if any, attributable to the sales of Resale Shares. We will bear all other costs, expenses and fees in connection with the registration of the Resale Shares. See Plan of Distribution beginning on page 104 for more information about how the selling stockholders may sell or dispose of their shares of the Resale Shares.

There is no public market for the shares of our common stock in the United States. Currently, the beneficial ownership of our common stock is listed on the ASX in the form of CDIs under the ASX trading code PLI. The CDIs are convertible at the option of the holders into shares of our common stock on a 1-for-20 basis.

**Investing in our securities involves risks that are described in the Risk Factors section beginning on page 6 of this prospectus.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 20, 2009

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You should rely only on the information contained in this prospectus. We have not, and the selling stockholders have not, authorized anyone to provide you with information different from or in addition to that contained in this prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. The selling stockholders are offering to sell, and seeking offers to buy, the Resale Shares only in jurisdictions where such offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our securities. Our business, prospects, financial condition and results of operations may have changed since that date.

For investors outside the United States: Neither we nor any of the selling stockholders have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

Peplin Pharmaceuticals for Life (R) is our registered trademark in the United States. PepTalk(R), Peplin Pharmaceuticals for Life(R), Peplin(R) and Peplin Biotech(R) are our registered trademarks in Australia. All other trademarks, tradenames and service marks appearing in this prospectus are the property of their respective owners.

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## PROSPECTUS SUMMARY

*This summary highlights information about this offering and our business. It does not contain all of the information that may be important to you. You should read this entire prospectus and should consider, among other things, the matters set forth under the headings Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and related notes thereto of Peplin, Inc., appearing elsewhere in the prospectus.*

### Our Company

We are a development stage specialty pharmaceutical company focused on advancing and commercializing innovative medical dermatology products. We are currently developing PEP005 (ingenol mebutate), or PEP005, which is the first in a new class of compounds and is derived from *Euphorbia peplus*, or *E. peplus*, a rapidly growing, readily-available plant, commonly referred to as petty spurge or radium weed. The sap of *E. peplus* has a long history of traditional use for a variety of conditions, including the topical self-treatment of various skin disorders, such as skin cancer and pre-cancerous skin lesions. Our lead product candidate, for which we recently commenced a Phase III clinical trial, is a patient-applied topical gel containing PEP005, a compound the use of which we have patented for the treatment of actinic keratosis, or AK. AK is generally considered the most common pre-cancerous skin condition and typically appears on sun-exposed areas of the skin as small, rough, scaly patches. AK lesions may progress to a form of skin cancer called squamous cell carcinoma, or SCC. We believe that our lead product candidate, PEP005 Gel for AK, once developed and, if approved for commercialization by the appropriate regulatory authorities, could offer patients an effective and well-tolerated treatment alternative for AK with a short, two-to-three day application regimen that could be performed by the patient at home.

We are also developing a product candidate containing PEP005 for the treatment of superficial basal cell carcinoma, or superficial BCC. This product candidate is currently in Phase IIa clinical trials and is referred to as PEP005 Gel for BCC. BCC is the most commonly occurring cancerous skin tumor and can present itself in two forms, nodular BCC, which appears as a shiny bump or nodule that may be confused with a mole, and superficial BCC, which has a slightly raised, ulcerated or crusted surface. Our development of PEP005 Gel for BCC is at an earlier stage than that of PEP005 Gel for AK. However, we believe that this product candidate, once developed and, if approved for commercialization by the appropriate regulatory authorities, could offer patients an effective and well-tolerated treatment alternative for superficial BCC with a short, one or two day application regimen.

### Pre-Cancerous Skin Lesions and Skin Cancer

Repeated or prolonged exposure to ultraviolet light, the invisible but intense rays of the sun, can result in skin damage. Some of the effects, such as suntan or sunburn, are quickly visible. However, other skin changes, including liver spots and deep wrinkles, appear slowly and worsen over time. With repeated and long-term sun exposure, skin damage, particularly in fair skinned people, may result in skin disorders including pre-cancerous skin lesions and various skin cancers.

AK is generally considered the most common pre-cancerous skin condition. AK usually appears as small, rough, scaly areas on the face, lips, ears, back of hands, forearms, scalp or neck. AK lesions may progress to a form of skin cancer called squamous cell carcinoma, or SCC.

Melanoma, SCC and BCC, are the three primary forms of skin cancer, all of which typically develop on areas of the body that are exposed to the sun. Given its propensity to rapidly spread to other organs of the body, melanoma is the most serious and difficult to treat of all skin cancers. According to the American Academy of Dermatology, melanoma accounts for approximately 4% of all new cases of skin cancer each year. SCC usually develops in the epidermis, the upper layer of the skin, and accounts for approximately 16% of all new cases of skin cancer annually. BCC develops in the basal, or lower, layer of the epidermis, and accounts for approximately 80% of all new cases of skin cancer annually. BCC can present itself in two forms, nodular BCC, which appears as a shiny bump or nodule that may be confused with a mole, and superficial BCC, which has a slightly raised, ulcerated or crusted surface. SCC and BCC, together, are often referred to as non-melanoma skin cancers.

AK and BCC are, respectively, the most commonly occurring pre-cancerous skin condition and cancerous tumor, and we expect their incidence to increase at a significant rate, given societal trends that emphasize tanning and clothing styles that expose skin, increased participation in outdoor activities and increased longevity. We are

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initially developing a topical gel based on our lead compound, PEP005, to treat AK and superficial BCC. However, we also intend to evaluate the utility of PEP005 in treating other skin disorders, including nodular BCC, SCC and cutaneous warts.

**Our Product Candidates**

*PEP005 Gel for AK*

We completed our PEP005-006 Phase IIb clinical trial of PEP005 Gel for AK as a field-directed therapy for non-facial AK lesions, including lesions on the scalp in July 2007. Results from the trial of 222 patients suggest that the drug presents a favorable safety profile and is well tolerated at all tested doses. The trial involved a single application of either 0.025% or 0.05% of PEP005 gel each day, for two or three consecutive days. The most common side effects were local skin responses, such as redness, flaking or scaling and crusting. Local skin responses typically resolved in two to four weeks after completion of treatment. The trial evaluated three efficacy measures using various lesion clearance metrics. On the primary efficacy measure, the partial AK clearance rate, 75% of the patients in the highest dose group cleared three quarters or more of their lesions 57 days post-treatment and 56% of patients in the lowest dose group cleared three quarters or more of their lesions 57 days post-treatment. The two secondary efficacy measures were the complete AK clearance and the baseline AK clearance rate. In the highest dose group the complete AK clearance rate and baseline AK clearance rate were 54% and 58% of patients, respectively, and in the lowest dose group were 40% and 42% of patients, respectively. All of these clearance results were statistically significant when compared with the vehicle gel.

We also completed our PEP005-007 Phase IIa clinical trial of PEP005 Gel for AK as a field-directed therapy for AK in treatment locations on the face in December 2007. This trial of 86 patients examined concentrations from 0.0025% to 0.025% PEP005 Gel for AK for two and three consecutive day dosing regimens. We believe that the results from this trial suggest that each dose of PEP005 Gel for AK studied at and below the maximum tolerated dose, or MTD, presents a favorable safety profile and is well tolerated.

As compared with other treatment alternatives, we believe that PEP005 Gel for AK could offer a combination of attractive benefits to patients seeking treatment of AK, including:

- a short two-to-three day treatment regimen;
- localized, transient and well-tolerated side effects;
- a mode of action distinct from other AK treatment modalities;
- a convenient, patient-applied, take-home prescription medication; and
- the ability to treat visible lesions and the surrounding sun-damaged skin where lesions may develop in the future.

In January 2009, we completed our PEP005-015 Phase IIb clinical trial of PEP005 Gel for AK for the treatment of AK lesions on head locations. This trial was an eight-arm, double blind, vehicle-controlled trial of 265 patients that examined concentrations of 0.005%, 0.010%, and 0.015% PEP005 Gel for AK for both two and three consecutive day treatment regimens. The most common side effects were primarily transient, short term, local skin responses at the treatment site which peaked at day 4 and returned to baseline by day 15. At all concentrations, for both the two day and three day treatments, the PEP005 Gel demonstrated a favorable safety profile and was well tolerated. The complete clearance rates ranged from 15.6% to 42.3% across the six active treatment groups. In the highest dose group the complete clearance rate was 42.3% and the median reduction in lesion count was 84.5%. We believe that the data from this trial will allow us to select both a dose and regimen for our Phase III development of PEP005 Gel for AK for on head locations.

*PEP005 Gel for BCC*

The preliminary results from our recent PEP005-003 Phase IIa clinical trial of PEP005 Gel for BCC, suggest that this drug candidate presents a favorable safety profile and is well tolerated. Further, 71% of superficial BCC tumors were cleared with just two applications of 0.05% PEP005 Gel for BCC and this result was statistically significant when compared with the vehicle gel. We intend to develop PEP005 Gel for BCC as a treatment for superficial BCC tumors. We are presently conducting a further Phase II dose escalation clinical trial, which we call PEP005-009, in which we are increasing the dosage of PEP005 Gel for BCC to establish the MTDs when administered as a single application and when administered as two applications one week apart. We plan to evaluate the histological tumor clearance rate at the MTDs. We must successfully complete these and other trials before we can seek regulatory approval to commercialize this product candidate. We do not expect to commence our Phase III clinical program for PEP005 Gel for BCC until 2010.

The vast majority of BCC tumors are treated by surgical methods. However, we believe that the associated pain and morbidity, together with the potential for long term surgical scars that accompany surgery represent an important short coming of this treatment approach. Further, we believe that physicians and their patients would embrace an effective and well-tolerated topical alternative to surgery. We believe PEP005 Gel for BCC has the potential to be a prominent treatment option for smaller and well demarcated superficial BCC tumors.

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While we believe PEP005 Gel for AK and PEP005 Gel for BCC offer advantages to other currently existing treatment options for AK or BCC, the potential side effects of these product candidates include redness, flaking or scaling, crusting, swelling, blistering, and ulceration. The side effects from these product candidates may last as long as four weeks or more. Moreover, patients may believe that treatment with products containing PEP005 will be uncomfortable or inconvenient. Physicians and patients may perceive that the side effects of our products outweigh the benefits of their use and, and as result, may be unwilling to change their current treatment regimens. Furthermore, even if approved by the FDA, physicians may not prescribe our products until we do have long term data regarding their safety and efficacy.

**Risk Factors**

Our business is subject to a number of risks, which you should be aware of before you decide to buy our common stock or warrants. In particular, you should consider the following risks, which are discussed more fully in Risk Factors beginning on page 6:

- We have incurred losses since inception and anticipate that we will continue to incur losses for the foreseeable future. Our net loss for the year ended June 30, 2008 and the three months ended September 30, 2008 was $25,956,248 and $10,202,927, respectively. As of September 30, 2008, we had an accumulated deficit of $82,265,770.

- We are dependent on the success of our lead product candidate PEP005 Gel for AK, which is in an early stage of development, and we cannot give any assurance that it will be successfully commercialized.

- Results from our recent Phase IIb clinical trial related to PEP005 for AK for head applications may not be sufficient to enable us to commence our Phase III clinical trial.

- If we are not able to successfully complete a Phase III clinical trial program, we will not be able to commercialize PEP005 Gel for AK. Furthermore, even if we complete these clinical trials, the FDA may require us to perform further studies before we can commercialize PEP005 Gel for AK.

- Even if our products receive regulatory approval, we may still face development and regulatory difficulties that may delay or impair future sales of our products and we would be subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our products.

- Resale of our common stock may be difficult because there is not an active trading market for our shares in the United States, and it is possible that no market will develop.

**Corporate Information**

We were incorporated in Delaware on July 31, 2007 as a wholly-owned subsidiary of Peplin Limited. Peplin Limited, originally Peplin Biotech Ltd., was initially formed as an Australian company in 1999. Our principal executive offices are located at 6475 Christie Avenue, Emeryville, California 94608. Our telephone number is (510) 653-9700, and our website address is *www.peplin.com*. Information contained on our website is not a prospectus and does not constitute part of this prospectus.

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**The Offering**

| | |
|---|---|
| Common stock being offered by the selling stockholders: | 819,378 shares of common stock. |
| Use of Proceeds: | We will not receive any proceeds from the sale of the Resale Shares by the selling stockholders in this offering. |

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## SPECIAL NOTE REGARDING FOREIGN CURRENCY AND EXCHANGE RATES

Our functional currency for accounting purposes is the Australian dollar and our reporting currency is the U.S. dollar. All dollar figures contained in this prospectus are set forth in U.S. dollars, except as otherwise indicated. All Australian dollars translated into U.S. dollars have been translated at the following rates per A$, except as otherwise indicated:

| Year Ended June 30, | | For Revenues, Expenses and Compensation Numbers(1) | For Assets and Liabilities(2) |
|---|---|---|---|
| | 2008 | $ 0.9046 | $ 0.9626 |
| | 2007 | $ 0.7925 | $ 0.8491 |
| | 2006 | $ 0.7472 | $ 0.7423 |
| | 2005 | $ 0.7568 | $ 0.7618 |
| | 2004 | $ 0.7155 | $ 0.6952 |
| **Three Months Ended September 30,** | | | |
| | 2008 | $ 0.8894 | $ 0.7996 |
| | 2007 | $ 0.8750 | $ 0.8776 |

(1) These exchange rates represent average exchange rates during the period.
(2) These represent the exchange rates as of June 30 or September 30, as applicable.

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## RISK FACTORS

*You should carefully consider the following risks, as well as all of the other information contained in this prospectus, any of which could materially affect our business, business prospects, cash flow, results of operations or financial condition. In assessing these risks, you should also refer to the other information contained in this prospectus, including our consolidated financial statements and related notes therein.*

### Risks Related to Our Business and Industry

**We have incurred net losses since inception and anticipate that we will continue to incur losses for the foreseeable future.**

We are a development stage pharmaceutical company with no products approved for commercial sale, and we may never be able to develop a marketable product. To date, we have funded our operations principally through the issuance of securities in Australia, the entrance by Peplin Limited, our wholly-owned subsidiary, into a $15 million loan agreement and other domestic and international capital raising activities. We are not profitable and have incurred net losses in each year since inception in 1999. We have only generated a limited amount of grant income and license fee revenue from our collaborative relationships, and we have never generated any revenue from product sales. We do not anticipate that we will generate revenue from the sale of products in the foreseeable future. We have not yet submitted any products for approval by regulatory authorities and we do not currently have rights to any products that have been approved for marketing. We continue to incur research and development and general and administrative expenses related to our operations. Our net loss for the year ended June 30, 2008 and the three months ended September 30, 2008 was $25,956,248 and $10,202,927, respectively. As of September 30, 2008, we had an accumulated deficit of $82,265,770. Net cash used in operating activities was $10,054,261 during the three months ended September 30, 2008. We expect to continue to incur net losses for the foreseeable future. We expect these losses to increase as we continue our research activities and conduct development of, and seek regulatory approvals for, our product candidates, and as we prepare for and begin to commercialize any approved products. We also expect to incur increased general and administrative expenses in support of our increased operations. Over the longer term, the costs referred to above will fluctuate and will primarily depend on the number and type of clinical trials being undertaken by us at any one time. If our product candidates fail in clinical trials or do not gain regulatory approval, or if our product candidates do not achieve market acceptance and are not successfully commercialized, we may never become profitable.

**We are dependent on the success of our lead product candidate PEP005 Gel for AK, which is in an early stage of development, and we cannot give any assurance that it will be successfully commercialized.**

Our business is dependent on the success of our lead product candidate, PEP005 (ingenol mebutate) Gel for AK, or PEP005 Gel for AK, a topical gel for the treatment of actinic keratosis, or AK. We are not permitted to market PEP005 Gel for AK in the United States until we have submitted and received approval of a new drug application, or NDA, from the U.S. Food and Drug Administration, or FDA, or in any other country, including Australia and New Zealand, until we receive the requisite approval from such countries. Before we can seek regulatory approval, we must successfully complete our clinical trials underway and future trials that we have not yet begun. We do not believe we will be able to submit a single NDA for PEP005 Gel for AK until mid 2010, at the earliest.

Given the early stage of development of PEP005 Gel for AK, which contains an untested new chemical entity with a novel mode of action and is the first of a new class of investigational agents, we believe that it may be more challenging to develop and commercialize than products which incorporate either molecules of already existing classes with a well understood mode of action or which are not new chemical entities. If these challenges prove insurmountable or if any of these risks materialize, they may cause a material adverse effect on our business, prospects, financial condition and results of operations.

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**Results from our recent Phase IIb clinical trial related to PEP005 Gel for AK for head applications may not be sufficient to advance our regulatory approval process for head applications to the next phase of clinical development.**

Prior to filing an NDA for PEP005 Gel for AK, we will need to complete a series of clinical trials in head and non-head treatment locations. We believe the market for head applications of PEP005 Gel for AK is substantially larger than the market for non-head applications. In January 2009, we completed a Phase IIb dose ranging clinical trial for head applications, which initiated in June 2008. We believe this trial will help us determine the appropriate concentration of PEP005 Gel for AK for head field-directed therapy and will support the design of our subsequent Phase III clinical trial. Consequently, the results of our Phase IIb trial are critical to our advancement to a Phase III clinical trial program for head applications. We expect to conduct our formal end-of-Phase II meeting with the FDA upon finalizing the results of the trial. Accordingly, we cannot assure you that the results from our Phase IIb clinical trial will be sufficient for the FDA to support our moving forward to the next phase of clinical development for head applications. Additionally, the FDA may continue to impose greater scrutiny on the results from our clinical trials for head applications, which include the face, as there may be a greater safety concern for the treatment of the face, and even if we believe the results from our Phase IIb clinical trial are favorable, the FDA may disagree.

If the FDA does not support our moving forward to the next phase of clinical development for head applications, we may alter our strategy with the FDA to initially seek approval for PEP005 Gel for AK only for non-head applications. If our only approved product is PEP005 Gel for AK for use in non-head applications, our potential market and our ability to commercialize that product would be substantially reduced, which would negatively impact our business.

**If we are not able to successfully complete a Phase III clinical trial program, we will not be able to commercialize PEP005 Gel for AK. Furthermore, even if we complete these clinical trials, the FDA may require us to perform further studies before we can commercialize PEP005 Gel for AK.**

The safety and efficacy of PEP005 Gel for AK may not be demonstrated in larger future clinical trials. The FDA generally requires successful completion of at least two adequate and well-controlled Phase III clinical trials prior to the submission of an NDA. While we believe that our two proposed Phase III trials, one for head and one for non-head application, will serve as our two required adequate and well-controlled studies, the FDA upon reviewing the results of the trials may disagree and require us to conduct one or more additional Phase III clinical trials to support our NDA approval for either of these applications. In this event, we may not have adequate financial or other resources to pursue this product candidate for either or both indications through the clinical trial process or through commercialization.

We secured a clinical Special Protocol Assessment from the FDA with respect to the design and conduct of our Phase III clinical trial for non-head applications; however, we will not complete the design of our Phase III clinical trial for head applications until after our end-of-Phase II meeting with the FDA. Our Phase III clinical trials may not achieve positive results, and, even if we believe the results are positive, the FDA may disagree or the results may not adequately support or reproduce the results of any corresponding earlier clinical trial. If we fail to complete our Phase III clinical trials for PEP005 Gel for AK, or if these clinical trials fail to demonstrate with substantial evidence that PEP005 Gel for AK is both safe and effective, we will not be able to commercialize this product candidate in the United States or elsewhere and our business will be significantly harmed. Moreover, given that we have not conducted our formal end-of-Phase II meeting with the FDA, and we may not do so before we completing our Phase IIb clinical trials, we cannot assure you that our Phase IIb and Phase III clinical trials will not be materially modified or that, once completed, they will be sufficient to support a single NDA approval. For instance, based on correspondence with the FDA and guidelines recognized by the FDA, we expect that a carcinogenicity study for PEP005 Gel for AK will not be required to support our NDA filing. The FDA, however, may require us to complete a carcinogenicity study for PEP005 Gel for AK prior to filing an NDA in the event that our clinical use of PEP005 Gel for AK changes, for example, changes in our expected treatment regimen. If the FDA requires additional clinical trials, including additional supportive safety studies, to support an NDA, our ability to commercialize PEP005 Gel for AK may be further delayed or substantially reduced.

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**Our PEP005 product candidate for the treatment of superficial BCC is at a much earlier stage than our AK treatment, and we cannot assure you that this product candidate will advance to Phase III clinical trials in a timely manner, if ever.**

We are currently developing a product for the treatment of superficial basal cell carcinoma, or superficial BCC, which we call PEP005 (ingenol mebutate) Gel for BCC, or PEP005 Gel for BCC. We are currently evaluating this product candidate when used as a tumor-directed therapy in a Phase II clinical trial designed to assess safety and dosage tolerance. We must complete this trial, and potentially others, before we can commence our Phase III clinical trials for this application. We expect that we will have to conduct two successful Phase III clinical trials for BCC before we can submit an NDA for this indication.

Results of clinical trials of PEP005 Gel for AK do not necessarily predict the results of clinical trials involving other indications. Clinical trials for PEP005 Gel for BCC may fail to show the desired safety and efficacy, despite favorable results from earlier clinical trials involving AK. Moreover, because superficial BCC is a cancerous condition, the FDA and regulatory agencies in other countries are likely to require our future BCC trials to be longer and more complex than trials for AK, which is a pre-cancerous condition. We expect these trials would be more time consuming and costly. Any failure or significant delay in completing clinical trials for PEP005 Gel for BCC would delay our ability to submit an NDA for its approval and ultimately market this product.

**Our clinical trials may fail to demonstrate acceptable levels of safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.**

Our product candidates are prone to the risks of failure inherent in drug development. Before obtaining regulatory approvals for our product candidates for a target indication, we must demonstrate with substantial evidence gathered in well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA and, with respect to approval in other countries, similar regulatory authorities in those countries, that the product candidate is safe and effective for use for that target indication. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials.

The results from the preclinical and clinical trials that we have completed for our product candidates may not be replicated in future trials, or we may be unable to demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for any product candidate. For example, all of our clinical trials have evaluated treatment areas that are equal to or less than 25 $cm^2$. In future clinical trials, we expect to evaluate and document the safety profile of PEP005 Gel for AK when applied to larger treatment areas, either individually or in the aggregate. We cannot assure you that we will be able to safely dose larger treatment areas.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for any indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;
- we may be unable to demonstrate that a product candidate presents an advantage over existing therapies, or over its vehicle in any indications for which the FDA requires the results of a product to be measured against its vehicle, which is the portion of the product that does not have an active pharmaceutical ingredient;

the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

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- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If our product candidates are not shown to be safe and effective in clinical trials, our clinical development programs could be delayed or terminated. The FDA may also approve a product candidate for fewer or more limited indications than we request, or may grant approval contingent on the performance of post-approval clinical trials, which may be costly. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. Any failure to obtain regulatory approval of our product candidates would limit our ability to ever generate revenues.

**We may not be successful in obtaining Australian and other foreign country regulatory approvals for PEP005 Gel for AK.**

The commercialization of our product candidates will be subject to regulation by governmental entities in Australia and other countries in which we intend to market our products. In particular, our products will be subject to regulation by the Therapeutics Goods Administration, or TGA, under the Australian Therapeutic Goods Act, and by comparable agencies and laws in foreign countries. Approval for inclusion in the Australian Register of Therapeutic Goods is required before a pharmaceutical drug product may be marketed in Australia. This process generally involves:

- completion of preclinical laboratory and animal testing;

- submission to the TGA of a clinical trial notification, or a clinical trial exemption application for human trials;

- in the case of a clinical trial notification, submission of an investigator s brochure, clinical protocols, related patient information and supporting documentation to the Human Research Ethics Committee, or HREC, of each institution at which the trial is to be conducted;

- in the case of a clinical trial exemption, information relating to the overseas status of the medicine, proposed usage guidelines, a pharmaceutical data sheet and a summary of preclinical and clinical data to the HREC of each institution at which the trial is to be conducted;

- adequate and well-controlled clinical trials to demonstrate the safety and efficacy of the product;

- compilation of evidence which demonstrates that the manufacture of the product complies with the principles of current Good Manufacturing Practices, or cGMP; and

- submission of the manufacturing and clinical data to, and approval by, the Drug Safety and Evaluation Branch of the TGA.

The testing and approval processes for a drug require substantial time, effort and financial resources. Furthermore, post-market surveillance must be carried out, and any adverse reactions to the drug must be reported to the TGA. We cannot make any assurances that any approval will be granted on a timely basis, if at all. Product development and approval within this regulatory framework is uncertain, could take a number of years and require the expenditure of substantial resources. Any failure to obtain regulatory approval or any delay in obtaining such approvals could have a material adverse effect on our business, financial condition and results of operations.

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**Delays in the commencement or completion of clinical trials are common and could result in increased costs to us and delay or limit our ability to generate revenue.**

Delays in the commencement or completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- manufacturing sufficient quantities of a product candidate for use in clinical trials;
- obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of skin cancer or similar indications; and
- retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; and
- a lack of adequate funding to continue the clinical trial.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes, which could impact the cost, timing or successful completion of a clinical trial. If we experience delays in the commencement or completion of our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to the denial of regulatory approval of a product candidate.

**We depend on clinical investigators and clinical sites to manage our clinical trials and perform related data collection and analysis, which exposes us to potential costs and delays outside our control.**

We do not currently conduct clinical trials on our own, and instead rely on CROs to provide us with clinical trial design and administration services, and on independent clinical investigators to provide services in connection with our preclinical pharmacology and toxicology research and development and our clinical trials. Furthermore, in the future we may need to rely on other independent CROs to provide us with clinical trial design and administration services. Our agreements with CROs can generally be terminated by either party upon 30 to 60 days notice. Our preclinical pharmacology and toxicology research and development and our clinical trials are conducted by several third parties at a number of different sites in different jurisdictions, including the United States, Australia and New Zealand, and these third parties play a significant role in the conduct of these trials and the subsequent collection and analysis of data. We own no laboratories or other research space and, therefore, must rely on third parties for these services. To date, we have been able to manage the use of these third parties in order to effectively carry out our preclinical pharmacology and toxicology research and development and our clinical trials, despite the fact that these third-parties are not our employees, and we have limited ability to control the amount or timing of resources that they devote to our programs. If these third parties do not successfully carry out their contractual duties or regulatory

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obligations or meet expected deadlines, or if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our preclinical or clinical protocols or regulatory requirements or for other reasons; our preclinical or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. In addition, the execution of research and clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another.

**Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial attractiveness of any approved product.**

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities. Furthermore, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

Additionally, in light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of the U.S. Congress, the U.S. Government Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and changes in regulatory requirements and guidance. If we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenues will be delayed.

**Even if our products receive regulatory approval, we will be subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our products.**

Even if we receive regulatory approval for any of our product candidates, potentially costly follow-up or post-marketing clinical trials may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Our product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, including the FDA s general prohibition against promoting products for unapproved or off-label uses, recordkeeping and submission of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we, or a regulatory agency, discover previously unknown problems with a product or the manufacturing facilities of our contract manufacturers, a regulatory agency may impose restrictions on that product, on us or on our third party contract manufacturers, including requiring us to withdraw the product from the market.

If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

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- issue warning letters;
- impose civil or criminal penalties;
- suspend our regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on our operations, including costly new manufacturing requirements, closing our contract manufacturers facilities or terminating licenses to manufacture cGMP grade material;
- impose import or export bans; or
- seize or detain products or require us to initiate a product recall.

Any of the foregoing could seriously harm the commercialization of our products and our results of operations may be seriously harmed. Likewise, any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize our products.

In addition, the law or regulatory policies governing our products may change. New statutory requirements or additional regulations may be enacted that could prevent or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action. If we are not able to maintain regulatory compliance, we might not be permitted to market our products, which would have a material adverse effect on our business, prospects, financial condition and results of operations.

**The suspension or termination of our government research grants may result in lost revenue. We may also be required to repay previously received grant revenue in certain circumstances, which would have an adverse effect on our cash position, business, prospects, financial condition and results of operations.**

We have received $4.3 million in grant funding from the Commonwealth of Australia since inception under the R&D START Program Grant Agreement, or START Program, and the Pharmaceuticals Partnerships Program Funding Agreement, or P3 Agreement. We expect we will continue to receive funding until June 2009 under the P3 Agreement. There is a risk that we will lose entitlement to the grant payments for failing to incur eligible expenditures or failing to undertake activities associated with the applicable grant or for otherwise failing to satisfy the relevant conditions in the applicable grant agreement. Furthermore, there is a risk we will not be entitled to the grants under the P3 Agreement, including, if the Commonwealth of Australia has insufficient funding for the relevant grant program, if we fail to submit reports when required, if we have not otherwise complied with our obligations under the P3 Agreement, or if the Commonwealth of Australia is entitled to or does terminate the relevant agreements. The Commonwealth of Australia may terminate the P3 Agreement under certain circumstances, including if we are in breach of the P3 Agreement, if we fail to submit reports, if there is a change of control of us, or if we become insolvent.

Under the START Program, in certain circumstances where we fail to use our best endeavors to commercialize the funded project within a reasonable time of completion of the project, or upon termination of a grant due to our breach of agreement or our insolvency, the Commonwealth of Australia may require us to repay some or all of the grants received under the program. The grants under the START Program funded certain aspects of the development of our PEP005 Gel for AK and related clinical trials. We do not expect to be required to repay the grants received under the START Program so long as we continue our efforts to commercialize the project funded by the START Program. However, if required to repay such grants, we may be required to reallocate funds needed to continue the commercialization of our products and such repayment may have an adverse effect on our cash position, business, prospects, financial condition and results of operations.

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**We will continue to need significant amounts of additional financing, which may not be available to us on favorable terms, or at all. If we fail to obtain additional financing, we may be unable to fund our operations and commercialize our product candidates and may never achieve profitability.**

Since inception, we have financed our operations primarily through placements of equity securities. We believe that the net proceeds from the private placement completed on October 23, 2008 and interest earned thereon, together with our current cash and cash equivalents, will be sufficient to satisfy our anticipated cash needs for working capital and capital expenditures for at least 12 months. We expect that we will need additional funds to complete the development, manufacturing, sales and marketing capabilities necessary to commercialize PEP005 Gel for AK and our other product candidates.

Given the early stage of product development of our product candidates, we cannot accurately predict the additional funds that will be required to conduct additional research and clinical trials, obtain additional regulatory approvals or to commercially launch any approved products. Our future funding requirements will depend on many factors, including:

- the scope, results, rate of progress, timing and costs of preclinical studies and clinical trials and other development activities;
- the costs and timing of seeking and obtaining regulatory approvals;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs of developing our sales and marketing capabilities and establishing distribution capabilities;
- the costs of securing coverage, payment and reimbursement of our product candidates, if any of our product candidates receive regulatory approval;
- the effects of competing clinical, technological and market developments; and
- the terms, timing and cash requirements of any future acquisitions, collaborative arrangements, licensing of product candidates or investing in businesses, product candidates and technologies.

To meet these capital raising requirements, we may raise funds through a variety of means, including:

- public or private equity offerings;
- debt financing;
- collaborations with pharmaceutical companies; and
- license agreements.

If we are not able to secure additional funding in the manners described above when needed, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the development of one

or more of our product candidates.

**Raising additional funds by issuing securities, debt financings or through licensing arrangements may cause our stockholders to experience significant dilution in their ownership interest, restrict our operations or require us to relinquish proprietary rights.**

To the extent that we raise additional capital by issuing equity securities, our existing stockholders ownership will be diluted. Peplin Limited, our wholly-owned subsidiary, entered into a $15 million loan agreement with General Electric Capital Corporation, as agent for the lenders party thereto, on December 28, 2007. The loan agreement is guaranteed by Peplin, Inc. and each of the subsidiaries of Peplin Limited. The loan agreement is secured by a pledge of all of our assets other than intellectual property, including the shares of the outstanding capital stock, or other equity interests, of each of our subsidiaries, and contains a variety of operational covenants, including limitations on our ability to incur liens or additional debt, make dispositions, pay dividends, redeem our stock, make certain investments and engage in certain merger, consolidation or asset sale transactions and transactions with affiliates, among other restrictions. Any future debt financing we enter into may involve similar or more onerous covenants that restrict our operations. Peplin Limited s borrowings under the loan agreement or any

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future debt financing we do will need to be repaid, which creates additional financial risk for our company, particularly if our business, or prevailing financial market conditions, are not conducive to paying-off or refinancing our outstanding debt obligations. Furthermore, our failure to comply with the covenants in the loan agreement could result in an event of default that, if not cured or waived, could result in the acceleration of all or a substantial portion of our debt, which could have a material adverse effect on our cash position, business, prospects, financial condition and results of operations.

In addition, to the extent that we raise additional funds through collaborations and licensing agreements, we may have to relinquish valuable rights and controls over our technologies, research programs or products or grant licenses on terms that may not be favorable to us.

**Even if our product candidates obtain regulatory approval, they may not be accepted in the marketplace by physicians, patients and the medical community.**

There is a risk that our product candidates, if they receive regulatory approval, may not gain market acceptance among physicians, patients and the medical community. There is a risk that certain doctors and patients will not transition to using our products from currently entrenched therapeutic alternatives. In some cases, such reluctance to transition may not be based on the relative effectiveness of our products as compared to currently available alternatives. The degree of market acceptance of our products may depend on a number of factors, which include:

- timing of marketing introduction and number and clinical profile of competitive products;
- our ability to provide acceptable evidence of safety and efficacy and our ability to secure the support of key clinicians and physicians for our products;
- relative convenience and ease of administration;
- cost effectiveness and pricing compared to existing and new treatments;
- availability of coverage reimbursement and adequate payment from health maintenance organizations and other third-party payers;
- personal preferences for more entrenched therapeutic alternatives;
- the commercial design of our products, including our ability to tailor our products to the specific needs of physicians and patients;
- prevalence and severity of adverse side effects; and
- other advantages over other treatment methods.

**If we are unable to obtain adequate coverage or reimbursement from third-party payers for PEP005 Gel for AK or PEP005 Gel for BCC, or any other product candidates that we may seek to commercialize, our revenues and prospects for profitability will suffer.**

Our lead product is targeted at the treatment of a disease which is most prevalent in older populations, and many patients will not be capable of paying for our products themselves and will rely on third-party payers, such as Medicare, Medicaid and private health insurers, including managed care organizations and other third-party payers, to pay for their medical needs. As such, the commercial success of our product candidates, if approved, will be substantially dependent on whether coverage and reimbursement is available from third-party payers. Importantly, third-party payers in the United States, the European Union, Australia and other jurisdictions are increasingly attempting to contain

healthcare costs by limiting both coverage and the level of reimbursement of new drugs and, as a result, they may not cover or provide adequate payment for our products.

Our products may not be considered cost-effective and reimbursement may not be available to consumers or may not be sufficient to allow our products to be marketed on a competitive basis. Large private payers, managed care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payers,

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including Medicare, are challenging the prices charged for medical products and services, and many third-party payers limit or delay reimbursement for newly approved health care products. In particular, third-party payers may limit the covered indications. Cost-control initiatives could cause us to decrease the price we might establish for our products, which could result in lower than anticipated product revenues. If the prices for our product candidates decrease or if governmental and other third-party payers do not provide adequate coverage or reimbursement, our prospects for revenue and for profitability will suffer.

Furthermore, many healthcare providers, such as hospitals, receive a fixed reimbursement amount per procedure or other treatment therapy, and these amounts are not necessarily based on the actual costs incurred. As a result, these healthcare providers may choose only the least expensive therapies. We cannot guarantee that our product candidates will be the least expensive alternative and providers may decide not to use them or buy them for treatment. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize our products successfully, or at all, which would harm our business and prospects.

Physicians typically receive reimbursement not only for the office visit relating to the treatment, but also for the cryotherapy treatment itself. We expect that physicians will only receive reimbursement for the office visit where PEP005 Gel for AK might be prescribed. We cannot assure you what type or amount of reimbursement will be available for our PEP005 Gel for AK. If physicians do not receive attractive reimbursement for PEP005 Gel for AK, they may choose to prescribe other treatment alternatives, such as cryotherapy.

**We do not expect to advance the application of PEP005 for other indications in the foreseeable future.**

We believe that there are other potential uses for PEP005 in topical formulations, such as to treat squamous cell carcinoma, or SCC, and nodular BCC, and as a therapy for certain forms of leukemia and for superficial forms of bladder cancer. While our early preclinical studies and clinical trials have indicated a potential for PEP005 to treat these skin and other cancers, our research and development efforts are at a very early stage for these indications. We do not expect to launch significant clinical trials of these indications in the foreseeable future.

**If we are unable to establish sales, marketing and distribution capabilities or enter into and maintain arrangements with third parties to sell, market and distribute our product candidates, our business may be harmed.**

We do not have a sales organization and have no experience as a company in the marketing, sales and distribution of our product candidates in the United States or elsewhere. To achieve commercial success for any approved product we must either develop a sales and marketing force or enter into arrangements with others to market and sell our products. Following product approval, we currently plan to establish a direct sales force to market our products in the United States, Australia and New Zealand. Our sales force will be competing with experienced and well-funded marketing and sales operations of competitors. Developing a sales force is expensive and time consuming and could delay or limit the success of any product launch. The size and cost of the required sales force will depend on a number of future developments including results of clinical trials for PEP005 Gel for AK, the final prescribing information or label content that will dictate the scope of product promotional activities, the competitive environment for products and technologies to treat AK, the size and concentration of the various physician specialties that treat AK, the prescribing habits of those physician specialties and the number of patients seeking treatment for AK. Due to these uncertainties, we cannot currently predict the cost to us of developing such a sales force. In addition, we may not be able to develop this capacity on a timely basis, or at all. If we are unable to establish sales and marketing capabilities, we will need to contract with third parties to market and sell our approved products in these locations. To the extent that we enter into arrangements with third parties to perform sales, marketing and distribution services in the United States or other territories, our product revenue could be lower than if we directly marketed and sold our products. Furthermore, to the extent that we enter into co-promotion or other marketing and sales arrangements with other companies, any revenue received will depend on the skills and efforts of others, and we do not know whether these efforts will be successful. If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenue and may not become profitable.

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**Our success depends in part on our ability to protect our intellectual property. If we are not able to protect our intellectual property, trade secrets and know-how, our competitors may use it to develop competing products.**

We have no patent protection for the compound PEP005 itself. Our basic patents are for the use of PEP005 and related compounds in the treatment of certain diseases. As a result, competitors who obtain the requisite regulatory approval may be able to offer products with the same active ingredient as PEP005 so long as they do not infringe any of our use and formulation patents. In total, we own exclusive rights to three patents and seven patent applications in the United States, and 34 patents and 9 patent applications (including one pending Patent Cooperation Treaty application) outside the United States, relating to uses and formulations of PEP005. Our issued U.S. and non-U.S. patents expire between August 2018 and August 2026, subject to any patent term extension which might be available under the Hatch-Waxman legislation or similar laws in Europe and other foreign jurisdictions. Of these issued patents and patent applications, four and seven, respectively, relate to the treatment of skin cancers, including SCC and BCC, and pre-cancerous skin lesions, including AK. We also have patents and patent applications related to the treatment of other conditions, including solid cancers, tumors, colon cancer, bladder cancer, prostate cancer, cervical cancer, breast cancer and warts. All of our patents and patent applications relate to technology that we have developed in-house or have exclusive rights to.

The additional risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- the pending patent applications we have filed or to which we have exclusive rights may not result in issued patents or may take longer than we expect to result in issued patents;
- the claims of any patent that are issued may not provide meaningful protection or may subsequently be held to be invalid or unenforceable;
- the process by which we make PEP005, which we hold as a trade secret, may become publicly known
- we may not be able to develop additional proprietary technologies that are patentable;
- other companies may be able to develop alternative, economically feasible, sources of PEP005, which may be a source of competition for us;
- other companies may challenge patents licensed or issued to us or our industry partners;
- other companies may design around technologies we have licensed or developed; and
- we have limited patent protection outside the United States, which may make it easier for third parties to compete in foreign jurisdictions. Our basic use patents and applications have counterparts in only nine foreign countries and under the European Patent Convention.

We may incur substantial costs in asserting any patent or intellectual property right and defending legal action against such rights. Such disputes could substantially delay our product development or our marketing activities.

In addition to patents and patent applications, we depend upon trade secrets and know-how to protect our proprietary technology. We require all employees, consultants, and collaborators to enter into nondisclosure agreements that prohibit the disclosure of confidential information to any other parties. We require that our employees and consultants disclose and assign to us their ideas, developments, discoveries and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure.

**We can provide no assurance that third parties will not claim that we have infringed their proprietary rights or that our products or methods will not infringe upon the patents of third parties.**

From time to time, we may receive notices of claims of infringement, misappropriation or misuse of other parties proprietary rights. Some of these claims may lead to litigation. There can be no assurance that we will prevail in these actions, or that other actions alleging misappropriation or misuse by us of third-party trade secrets, infringement by us of third-party patents and trademarks or the validity of our patents, will not be asserted or prosecuted against us. Intellectual property litigation, regardless of outcome, is expensive and time-consuming, could divert management s attention from our business and have a material negative effect on our business, operating results or financial condition. If there is a successful claim of infringement against us, we may be required

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to pay substantial damages (including treble damages if we were to be found to have willfully infringed a third party s patent) to the party claiming infringement, develop non-infringing technology, stop selling or using technology that contains the allegedly infringing intellectual property or enter into royalty or license agreements that may not be available on acceptable or commercially practical terms, if at all.

**Our intellectual property rights may not provide meaningful commercial protection for our products, which could enable third parties to use our technology or methods, or very similar technology or methods, and could reduce our ability to compete.**

Our success depends significantly on our ability to protect our proprietary rights to the technologies used in our products. Our patents might be challenged by third parties as being invalid or unenforceable, or third parties may independently develop similar or competing technology that avoids our patents. Further, we cannot guarantee that we will continue to develop our own patentable technologies. We may need to assert claims or engage in litigation to protect our proprietary rights, which could cause us to incur substantial costs, could place significant strain on our financial resources, and could divert the attention of management from our business. We may incur substantial costs in pursuing this litigation and the outcome of this litigation is uncertain. We rely on patent protection, as well as a combination of copyright, trade secret and trademark laws and nondisclosure, confidentiality and other contractual restrictions to protect our proprietary technology. However, these legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Although we have taken steps to protect our intellectual property and proprietary technology, we cannot assure you that third parties will not be able to design around our patents. In addition, although we have entered into confidentiality agreements and intellectual property assignment agreements with our employees, consultants and advisors, such agreements may not be enforceable or may not provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure or other breaches of the agreements.

Furthermore, the laws of foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States. If our intellectual property does not provide significant protection against competition, our competitors could compete more directly with us, which could result in a decrease in our market share. All of these factors may harm our competitive position.

**Our manufacturing operations are, in part, dependent on a single source supplier and the loss of this supplier could harm our business.**

We rely on a single third-party supplier for the formulation and filling of our product candidates. Currently, formulation, filling and packaging of our AK product candidates is undertaken by DPT Laboratories, Ltd., or DPT, a contract manufacturing organization in San Antonio, Texas. Pursuant to our development and clinical supply agreement with DPT, DPT is responsible for supplying us with PEP005 Gel for AK in quantities sufficient for our Phase III clinical trial. Clinical batches are formulated, filled and packaged under cGMP conditions at DPT s facilities in San Antonio, Texas. The clinical supplies are then shipped to locations designated by us or our clinical research organization for use in trials. Our development and clinical supply agreement with DPT has a four-year term, ending October 2011. We may terminate the agreement for any reason upon thirty days written notice to DPT. DPT may terminate the agreement upon thirty days written notice to us upon our uncured breach or our insolvency. Our reliance on this supplier also subjects us to other risks that could harm our business, including:

- increased component costs if DPT raises its prices;
- we are not a major customer of DPT, and DPT may therefore give other customers needs higher priority than ours;
- we may not be able to obtain adequate supply of PEP005 Gel for AK in a timely manner or on commercially reasonable terms, or at all;
- if our supply relationship should be terminated, we may have difficulty locating and qualifying an alternative supplier, which we expect could take a year or longer; and
- DPT may encounter financial hardships, which could inhibit its ability to fulfill our orders and meet our requirements.

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If we receive regulatory approval, it may become more difficult to quickly establish additional or replacement suppliers, particularly because of the FDA approval process. Any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand of our customers and cause them to cancel orders or switch to competitive products.

**PEP005 is naturally sourced. We may not be able to ensure quantity and quality of supply.**

Plant materials used in the production of botanical drug products often are not completely characterized and defined or are prone to contamination, deterioration and variation in composition and properties. In many cases, the active constituent in a botanical drug is not identified, nor is its biological activity well characterized. Therefore, unlike synthetic or highly purified drug products, it may be difficult to ensure the quality of a botanical drug by controlling only the corresponding drug substance and drug product. If we fail to implement adequate quality and in-process controls during manufacturing and final process validation, we may be unable to adequately ensure the quality of our product candidate and may be unable to obtain approval to market our product candidates. This would have a material adverse effect on our business and our profitability.

The active pharmaceutical ingredient in PEP005 is naturally sourced from southeast Queensland, Australia. Accordingly, supply may be subject to adverse weather conditions and other natural events affecting that region, including droughts and severe storms.

**We have limited manufacturing capabilities and manufacturing personnel, and if our manufacturing capabilities are insufficient to produce an adequate supply of products, our growth could be limited and our business could be harmed.**

We operate our leased manufacturing facility for the drying, milling, extraction and purification of pharmaceutical grade PEP005. We outsource other manufacturing activities, such as formulation and filling, to a third-party manufacturer. We intend to continue this practice for any future clinical trials and large-scale commercialization of any product candidates that receive regulatory approval and become commercial drugs.

Our ability to develop and commercialize PEP005 Gel for AK, PEP005 Gel for BCC and any other product candidates will depend in part on our ability to arrange for third parties to manufacture our products at a competitive cost, in accordance with strictly enforced regulatory requirements and in sufficient quantities for clinical testing and eventual commercialization. We have not yet manufactured commercial batches of PEP005 Gel for AK or PEP005 Gel for BCC or any of our other product candidates. Third-party manufacturers that we select to manufacture our product candidates for clinical testing or on a commercial scale may encounter difficulties with the small and large-scale formulation and manufacturing processes required for commercialization of our product candidates. Such difficulties could result in delays in clinical trials, regulatory submissions or commercialization of our product candidates. Our inability to enter into and maintain agreements with third-party manufacturers on acceptable terms could cause shortages of clinical trial supplies of our product candidates, thereby delaying or preventing regulatory approval or commercialization of the affected product candidate, and adversely affecting our ability to generate revenue. Once a product candidate is approved and being marketed, we may need to increase our manufacturing capacity by a significant level to meet anticipated market demand. Further, development of large-scale manufacturing processes will require additional validation trials, which the FDA must review and approve. We may not successfully complete any required increase in manufacturing capacity in a timely manner or at all. Even if our products receive regulatory approval, if we are unable to manufacture a sufficient supply, maintain control over expenses or otherwise adapt to anticipated growth, or if we underestimate growth, we may not have the capability to satisfy market demand and our business will suffer.

**If we or our current or future third-party manufacturers fail to comply with FDA, state, local or foreign regulatory requirements, we may be unable to produce our products and our business could suffer.**

We and any current or future third-party manufacturers of our products must comply with strictly enforced cGMP requirements enforced by the FDA through its facilities inspection program. These requirements apply to the manufacture of product candidates for clinical trials, as well as commercially marketed products, and include quality control, quality assurance and the maintenance of records and documentation. We or any current or future third-

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party manufacturers of our products may be unable to comply with cGMP requirements and with other FDA, state, local or foreign regulatory requirements. We have little control over third-party manufacturers compliance with these regulations and standards. A failure to comply with these requirements by our current or future third-party manufacturers could result in the issuance of warning letters from authorities, as well as sanctions being imposed on us, including fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure, recall or withdrawal of product approval. In addition, we have limited control over these manufacturers ability to maintain adequate quality control, quality assurance and qualified personnel. If the safety of any quantities supplied by third parties is compromised due to their failure to adhere to applicable laws or for other reasons, we may not be able to obtain or maintain regulatory approval for, or successfully commercialize, one or more of our product candidates, and we may be held liable for any injuries sustained as a result, which would harm our business and prospects significantly. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our products. Furthermore, if our current or future manufacturers fail to deliver the required commercial quantities on a timely basis and at commercially reasonable prices, we may be unable to meet demand for our products and would lose potential revenues.

**We operate in a highly competitive industry. Organizations which compete with us may be better resourced and more competitive.**

We operate in a highly competitive industry with intense competition coming from more established and better-resourced organizations, as well as from academic institutions, government agencies and private and public research institutions. We are seeking to develop and market products that will compete with other products and drugs that currently exist or are being developed or may be developed in the future.

Currently, there are many technologies, techniques and products for the treatment of AK, including cryotherapy with liquid nitrogen, photodynamic therapy, or PDT, which involves the in-office application of a topical solution to the AK lesion followed by the application of light therapy to activate the drug in the topical solution, and various topical agents such as Efudex, Solaraze, Carac, Fluoroplex and Aldara. The companies that are developing or marketing the topical products include Graceway Pharmaceuticals, LLC, Meda AB, iNova Pharmaceuticals (Australia) Pty Limited, Valeant Pharmaceuticals International, Dermik Laboratories, Shire plc and Bradley Pharmaceuticals, Inc. Commercial development of PDT agents is currently being pursued by a number of companies, including DUSA Pharmaceuticals, Inc., QLT Inc., Axcan Pharma Inc., Miravant, Inc., Pharmacyclics, Inc., QLT PhotoTherapeutics, Inc., medac GmbH, photonamic GmbH & Co. KG and PhotoCure ASA.

Many of the companies that we compete against enjoy several competitive advantages, including:

- significantly greater name recognition;
- established relations with healthcare professionals, customers and third-party payers;
- greater experience in conducting research and development, manufacturing, clinical trials, obtaining regulatory approval for products and marketing approved products; and
- greater financial and human resources for product development, sales and marketing and patent litigation.

Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient, are less expensive, or that reach the market sooner than our product candidates.

**If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.**

As a manufacturer of pharmaceuticals, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and the privacy and security of individually identifiable health information are or will be applicable to our business. We could be subject to healthcare fraud and abuse and patient

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privacy regulation by both the U.S. federal government and the states in which we conduct our business, without limitation. The regulations that may affect our ability to operate include, without limitation:

- the federal healthcare program Anti-Kickback Law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, and which may apply to entities like us which may provide coding and billing advice to customers;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and

- state law equivalents of each of the above U.S. federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and in some cases are not preempted by HIPAA, thus complicating compliance efforts.

There also have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels that will affect our operations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us or will, when adopted, apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management s attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

**We may not be able to successfully integrate Neosil into our business.**

We will have to integrate the assets of Neosil with our existing operations. While we do not expect to continue the development of Neosil s products until calendar year 2009, if at all, the integration of Neosil s assets into our business will require significant efforts from both companies. We may find it difficult to integrate the assets of Neosil. Furthermore, Neosil suppliers or licensors of intellectual property may terminate their arrangements with Neosil, or demand amended terms to these arrangements. In addition, our management may have its attention diverted while trying to integrate the operations and assets of the two companies. Such diversion of management s attention or difficulties in the transition process could have an adverse impact our business. If we are not able to integrate successfully the assets of Neosil, our future results of operations may suffer and the benefits of the merger may not be achieved.

**Changes in foreign currency exchange rates could result in fluctuations in our reported sales and earnings.**

We are exposed to foreign exchange risk, particularly with the U.S. dollar, Australian dollar and the Great British pound, as a result of certain research and development activities that are undertaken internationally. We had foreign currency translation losses in recent periods and may have further losses in the future. Although we plan to assess annually our functional currency in accordance with GAAP, our current functional currency is the Australian dollar. Because our functional currency is the Australian dollar, our reported results are subject to fluctuation resulting from changes in the Australian to U.S. exchange rate.

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**We will need to increase the size of our operations, and we may experience difficulties in managing our growth.**

We will need to continue to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize our product candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- manage our clinical trials effectively, including our ongoing Phase III clinical trial for PEP005 Gel for AK and our ongoing Phase II clinical trials for PEP005 Gel for BCC, which are being conducted at numerous clinical trial sites;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- attract and retain sufficient numbers of talented employees.

Any growth may place significant strain on our management and financial and operational resources. If we fail to manage these challenges effectively, our business could be harmed.

**Recent proposed legislation may permit re-importation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results and our overall financial condition.**

We may face competition for our products from lower priced products from foreign countries that have placed price controls on pharmaceutical products. The Medicare Modernization Act of 2003, or MMA, contains provisions that may change U.S. importation laws and expand consumers ability to import lower priced versions of our and competing products from Canada, where there are government price controls. These changes to U.S. importation laws will not take effect unless and until the Secretary of Health and Human Services certifies that the changes will lead to substantial savings for consumers and will not create a public health safety issue. The Secretary of Health and Human Services has not yet announced any plans to make the required certification. Even if the changes do not take effect, and other changes are not enacted, imports from Canada and elsewhere may continue to increase due to market and political forces, and the limited enforcement resources of the FDA, the U.S. Customs Service, and other government agencies. For example, Pub. L. No. 109-295, which was signed into law on October 4, 2006 and provides appropriations for the Department of Homeland Security for fiscal year 2007, expressly prohibits the U.S. Customs Service from using funds to prevent individuals from importing from Canada less than a 90-day supply of a prescription drug for personal use, when the drug otherwise complies with the Federal Food, Drug and Cosmetic Act. Further, several states and local governments have implemented importation schemes for their citizens, and, in the absence of federal action to curtail such activities, we expect other states and local governments to launch importation efforts. The importation of foreign products that compete with our own product candidates could negatively impact our business and prospects.

**Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to sell our product candidates profitably.**

In both the United States and certain foreign jurisdictions, there have been, and we anticipate there will continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, the MMA added an outpatient prescription drug benefit to Medicare, a publicly funded health insurance program in the United States generally for the elderly and disabled, which became effective on January 1, 2006. Drug benefits under this new benefit are administered through private plans that negotiate price concessions from pharmaceutical manufacturers. We cannot be certain that our drug candidates will successfully be placed on the list of drugs covered by particular health plan formularies, nor can we predict the negotiated price for our drug candidates, which will be determined by market factors.

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The MMA also changed the formula for determining payment for certain drugs provided in physician offices and other outpatient settings. Further, with respect to the Medicaid program, the Deficit Reduction Act of 2005 made changes to certain formulas used to calculate pharmacy reimbursement which could lead to reduced payments to pharmacies. Many states have also created preferred drug lists and include drugs on those lists only when the manufacturers agree to pay a supplemental rebate. If our current or future drug candidates are not included on these preferred drug lists, physicians may not be inclined to prescribe them to their Medicaid patients, thereby diminishing the potential market for our products.

**We may enter into collaborative relationships and conflicts may arise between us and our collaborators that could delay or prevent the development or commercialization of our product candidates.**

We may enter into collaborative agreements to develop and commercialize our products. These agreements may require our partners to undertake or fund certain research and development activities, make payments to us on achievement of certain milestones and pay royalties or make profit-sharing payments when and if a product is marketed.

Conflicts may arise between our collaborators and us, such as conflicts concerning the interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. If any conflicts arise with existing or future collaborators, they may act in their self-interest, which may be adverse to our best interests. In addition, collaborative agreements may be terminable by our industry partners. Suspension or termination of collaborative agreements may have a material and adverse impact on our business, prospects, financial condition and results of operations.

**Our future growth may depend on our ability to identify and acquire or in-license additional products. If we do not successfully identify and acquire or in-license related product candidates or integrate them into our operations, we may have limited growth opportunities.**

We believe that an important part of our business strategy will be to develop a pipeline of product candidates by acquiring or in-licensing products, businesses or technologies that we believe are a strategic fit for our business.

We have limited resources to identify, evaluate and execute the acquisition or in-licensing of third-party products, businesses and technologies and to integrate them into our current infrastructure. In particular, we may compete with larger pharmaceutical companies and other competitors in our efforts to establish new collaborations and in-licensing opportunities. These competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. Our competitors may have stronger relationships with certain third parties with whom we are interested in collaborating or may have more established histories of developing and commercializing products. As a result, our competitors may have a competitive advantage in entering into partnering arrangements with those third parties. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

**A loss of key executives or failure to attract qualified personnel could limit our growth and adversely effect our business.**

Our future success depends in part on the continued service of our executive officers, including, in particular, Mr. Wiggans and Dr. Welburn. Although we have entered into employment agreements with each of our executive officers, including, Mr. Wiggans and Dr. Welburn, we employ these individuals on an at-will basis and their employment can be terminated by us or them at any time, for any reason, with notice. The notice requirements for termination range from one month to three months. In addition, with the exception of Dr. Welburn, we do not have key person insurance on any of our executives. The loss of any one or more of our executive officers could place a significant strain on our remaining management team and would require the remaining executive officers to divert immediate and substantial attention to seeking a replacement. Furthermore, our future growth will depend in part upon our ability to identify, hire and retain additional key personnel, including qualified management, research and other highly skilled technical personnel. Competition for such skilled personnel is intense, and the loss of services of

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a number of key individuals, or our inability to hire new personnel with the requisite skill sets, could harm and/or delay our research and development programs, including the commercialization of some or all of our product candidates.

**We use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.**

We use hazardous materials, such as ethanol, which could be dangerous to human health and safety or the environment. Our operations also produce hazardous waste products. Federal, state and local, including Australian, laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our drug development efforts.

In addition, we cannot entirely eliminate the risk of accidental injury from improper use of our products or otherwise or from contamination from these materials or wastes. If one of our employees was accidentally injured from the use, storage, handling or disposal of these materials or wastes, the medical costs related to his or her treatment would be covered by our workers compensation insurance policy. In the event of contamination or injury, we could be held liable for any resulting damages, and any liability could significantly exceed our insurance coverage, which is limited to $4,052,000 for pollution cleanup, and we are uninsured for third-party contamination injury. Accordingly, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

**We face costs associated with importing our products into markets outside of Australia and our business may become subject to economic, political, regulatory and other risks associated with international operations.**

The cultivation of the plants extracted for use in our product candidates is substantially undertaken in southeast Queensland, Australia. As much as our product is likely to be manufactured in Australia, we may face difficulties in importing our products into various jurisdictions as a result of, among other things, import inspections, incomplete or inaccurate import documentation or defective packaging. There may be significant costs associated with importing and exporting our product.

In addition, our business is subject to risks associated with conducting business internationally, in part due to our suppliers being located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country s or region s political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non U.S. governments; and
- negative consequences from changes in tax laws.

**If product liability lawsuits are successfully brought against us, we will incur substantial liabilities and damage to our reputation.**

Our clinical trials might potentially expose us to product liability claims in the event our products in development have unexpected effects on subjects. In addition, if any of our products are approved for sale, we may face exposure to claims by an even greater number of persons than were involved in the clinical trials once we begin marketing, distribution and sales of our products commercially.

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Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our products;
- injury to our reputation;
- suspension of our clinical trials;
- withdrawal of clinical trial participants;
- costs of related litigation;
- substantial monetary awards to patients and others;
- loss of revenues; and
- the inability to commercialize our products.

We maintain a group of insurance policies covering our global clinical trial programs of up to approximately $10 million per occurrence annually. Although we believe that our existing policies are adequate, we cannot assure you that our insurance would fully protect us from the financial impact of defending against any product liability claim. Any product liability claim brought against us, with or without merit, could increase our insurance rates or prevent us from securing insurance coverage in the future.

**Our compliance efforts may not be sufficient to meet the rules of the ASX, subjecting us to liability, fines and lawsuits.**

The shares of our common stock are publicly traded on the Australian Securities Exchange, or the ASX, in the form of CHESS Depositary Interests, or CDIs. As a result, we must comply with the ASX Listing Rules. We have policies and procedures that we believe are designed to provide reasonable assurance of our compliance with the ASX Listing Rules. If, however, we do not follow those procedures and policies, or they are not sufficient to prevent non-compliance, we could be subject to liability, fines and lawsuits.

**If we fail to maintain effective internal control over financial reporting in the future, the accuracy and timing of our financial reporting may be adversely affected.**

In connection with our September 30, 2008 quarterly filing, we, together with our independent registered public accounting firm, identified a material weakness in our internal controls over financial reporting. A material weakness is a control deficiency, or a combination of control deficiencies, that results in a more than remote likelihood that a material misstatement of the annual or interim financial statements will not be prevented or deterred. Our management and independent registered public accounting firm did not perform an evaluation of our internal control over financial reporting during such periods in accordance with the provisions of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act. Had we and our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional control deficiencies may have been identified by management or our independent registered public accounting firm, and those control deficiencies could have also represented one or more material weaknesses.

The material weakness related to our period end close process and specifically the accrual process and resulted in the recording of a material adjustment in the three month period ending September 30, 2008.

We are currently taking remedial measures to improve the effectiveness of our internal controls including engaging our independent registered public accounting firm to review and test our current internal controls and provide recommendations for improvements to these internal controls processes, providing additional training to existing personnel and improving internal review processes regarding accruals and the period end close process.

We plan to continue to assess our internal controls and procedures and intend to take further action as necessary or appropriate to address any other matters we identify, including to effect compliance with Section 404 of the Sarbanes-Oxley Act of 2002 when we are required to make an assessment of our internal controls under Section 404 which is anticipated to be for fiscal 2010.

The existence of a material weakness is an indication that there is a more than remote likelihood that a material misstatement of our financial statements will not be prevented or detected in a future period while that material weakness continues to exist. The process of designing and implementing effective internal controls and procedures is a continuous effort that requires us to anticipate and react to changes in our business and the economic and regulatory environments and to expend significant resources to maintain a system of internal controls that is adequate to satisfy our reporting obligations as a public company. We cannot assure you that the measures taken to date or to be taken in the future will remediate the material weakness noted by our independent public accounting firm or that we will implement and maintain adequate controls over our financial processes in the future. In addition, we cannot assure you that additional material weaknesses or significant deficiencies in our internal controls will not be discovered in the future.

The standards required for a Section 404 analysis under the Sarbanes-Oxley Act of 2002 are significantly more stringent than those for a similar analysis for non-public companies. These more stringent standards require that our audit committee be advised and regularly updated on management s review of internal controls. Our management may not be able to effectively and timely implement controls and procedures that adequately respond to the increased regulatory compliance and reporting requirements that will be applicable to us as a public company. If we are not able to timely remedy the material weakness identified in connection with our interim quarterly review, or if we are not able to implement the requirements of Section 404 in a timely manner or with adequate compliance, management may not be able to assess that its internal controls over financial reporting are effective, which may subject us to adverse regulatory consequences and could result in a negative reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we fail to develop and maintain effective controls and procedures, we may be unable to provide the required financial information in a timely and reliable manner or otherwise comply with the standards applicable to us as a public company. Any failure by us to timely provide the required financial information could materially and adversely impact our financial condition and the market value of our securities.

**Risks Related To Our Common Stock**

**Our holding company structure makes us dependent on our subsidiaries for our cash flow and subordinates the rights of our stockholders to the rights of creditors of our subsidiaries in the event of an insolvency or liquidation of any of our subsidiaries.**

We are a holding company and, accordingly, all of our operations are conducted through our subsidiaries. Our subsidiaries are separate and distinct legal entities. As a result, our cash flow in the future may depend upon the earnings of our subsidiaries. The ability of our subsidiaries to provide us with funds may be limited by other obligations. In addition, we depend on the distribution of earnings, loans or other payments by our subsidiaries to us. Our subsidiaries have no obligation to provide us with funds for our payment obligations. If there is an insolvency, liquidation or other reorganization of any of our subsidiaries, our stockholders will have no right to proceed against their assets. Creditors of those subsidiaries will be entitled to payment in full from the sale or other disposal of the assets of those subsidiaries before we, as a shareholder, would be entitled to receive any distribution from that sale or disposal.

**We will incur significant increased costs as a result of having to comply with the Sarbanes-Oxley Act of 2002 and maintaining listing on the ASX, and as a result of the increasing complexity of our business as we grow and execute our strategies.**

The Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the Securities and Exchange Commission, have imposed various requirements on public companies, including requiring the establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. We have no experience with the various requirements of public companies in the United States, and will need to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations will increase

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our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. Furthermore, we expect to incur additional costs related to implementation of suitable finance and accounting systems, procedures and controls as we grow.

The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective internal controls over financial reporting and disclosure controls and procedures. In particular, for the year ended June 30, 2010, we will need to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of, and to allow our auditors to provide an attestation as to the effectiveness of, our internal controls over financial reporting for that fiscal year, as required by Section 404 of the Sarbanes-Oxley Act of 2002. As a result of our compliance with Section 404, we will incur substantial accounting expense, expend significant management efforts and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge to ensure such compliance.

Our CDIs are listed on the ASX. As a result, we will be subject to ongoing listing and other requirements under the ASX. Compliance with these ongoing listing requirements can be expensive and time consuming and may cause us to incur ongoing additional expenses.

**Our certificate of incorporation and by-laws contain provisions that could discourage a third party from acquiring us.**

Our certificate of incorporation and by-laws contain provisions that may make the acquisition of our company more difficult without the approval of our board of directors, including, but not limited to, the following:

- our board of directors is classified into three classes, each of which serves for a staggered three-year term;
- only our board of directors and our chairman of the board may call special meetings of our stockholders;
- we have authorized undesignated preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- our stockholders have only limited rights to amend our by-laws; and
- we require advance notice for stockholder proposals.

These provisions could discourage proxy contests, make it more difficult for our stockholders to elect directors and take other corporate actions and may discourage, delay or prevent a change in control or changes in our management that a stockholder might consider favorable.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any broad range of business combinations with any stockholder who owns, or at any time in the last three years owned, 15% or more of the company s outstanding voting stock, referred to as an interested stockholder, for a period of three years following the date on which the stockholder became an interested stockholder. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

**We have never paid a dividend and we do not intend to pay dividends in the foreseeable future which means that stockholders may not receive any return on their investment from dividends.**

We have never declared or paid any cash dividends on shares of our common stock and we do not anticipate paying any cash dividends in the foreseeable future. Dividends may only be paid out of our profits, and will depend upon our results of operations, financial condition, current and anticipated cash needs, contractual restrictions, restrictions imposed by applicable law and such other factors that our board of directors deems relevant. Furthermore, our loan agreement prohibits us from paying cash dividends. Any future determination to pay cash dividends will be at the discretion of our board of directors and would require the consent of the lenders in accordance with the terms of our loan agreement. As

a result, capital appreciation, if any, of our common stock will be our stockholders only source of gain.

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**Resale of our common stock may be difficult because there is not an active trading market for our shares in the United States, and it is possible that no market in the United States will develop. This may reduce or limit the potential value of our shares.**

Although our CDIs are traded on the ASX, there is not currently an active trading market for our shares of common stock in the United States, and there is no assurance that such a public market will develop in the future. Even in the event that a public market does develop, there is no assurance that it will be maintained or that it will be sufficiently active or liquid to allow stockholders to easily dispose of their shares. The lack of a public market or the existence of a public market with little or no activity or liquidity is likely to reduce or limit the potential value of our common stock.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus includes forward-looking statements. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements should not be read as a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and management s good faith belief as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward looking statements. Important factors that could cause such differences include, but are not limited to:

- our business and scientific strategies;
- the progress of our product development programs, including our clinical trials;
- our expectations with respect to regulatory submissions and approvals;
- our expectations with respect to corporate collaborations, including revenues expected from such collaborations;
- our estimates regarding our research and development expenses;
- the protection of our intellectual property;
- our estimates regarding our capital requirements, the sufficiency of our cash resources and our need for additional financing;
- general economic and business conditions, both nationally and in our markets;
- our ability to manage our growth and development;
- our ability to attract and retain key management and scientific personnel; and
- existing and future regulations that affect our business.

In addition, in this prospectus, the words believe, may, will, estimate, continue, anticipate, intend, expect, plan, predict, pote expressions, as they relate to our business and our management, are intended to identify forward-looking statements. In light of these risks and uncertainties, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially from those anticipated or implied in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the cautionary statements in this prospectus, particularly in the section entitled Risk Factors. However, new factors emerge from time to time and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

Forward-looking statements speak only as of the date the statements are made. You should not place undue reliance on any forward-looking statements. We assume no obligation to update forward-looking statements to reflect actual results, changes in assumptions or changes in other factors affecting forward-looking information, except to the extent required by applicable securities laws. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

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## USE OF PROCEEDS

We will not receive any of the proceeds from the sale of Resale Shares in this offering. The selling stockholders will receive all of the proceeds from this offering.

## DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock and we do not anticipate paying any cash dividends in the foreseeable future. We currently intend to retain all of our future earnings to finance the growth and development of our business. The payment of dividends by us on our common stock is prohibited by our loan agreement, for the term of the loan. Any future determination to pay cash dividends will be at the discretion of our board of directors, subject to consent from the lenders in accordance with the terms of our loan agreement, and will depend upon our results of operations, financial condition, current and anticipated cash needs, contractual restrictions, restrictions imposed by applicable law, operating results, capital requirements and such other factors as our board of directors deems relevant.

## PRICE RANGE OF COMMON STOCK

Our common stock is listed on the Australian Stock Exchange in the form of CHESS Depositary Interests, or CDIs, under the ASX trading code PLI. The CDIs are convertible at the option of the holders into shares of our common stock on a 1-for-20 basis. The following table sets forth, for the periods indicated, the range of high and low sale prices of our common stock.

| | High | Low |
|---|---|---|
| **Year Ended June 30, 2007** | | |
| Third Quarter | $ 13.84 | $ 11.64 |
| Fourth Quarter | $ 14.79 | $ 12.47 |
| **Year Ended June 30, 2008** | | |
| First Quarter | $ 16.95 | $ 12.71 |
| Second Quarter | $ 16.92 | $ 12.65 |
| Third Quarter | $ 15.59 | $ 9.06 |
| Fourth Quarter | $ 10.19 | $ 6.98 |
| **Year Ended June 30, 2009** | | |
| First Quarter | $ 9.78 | $ 5.51 |
| Second Quarter (through December 29, 2008) | $ 6.31 | $ 3.76 |

The last reported sales price of our CDIs on the ASX on December 29, 2008 was A$0.33 per share. There were approximately 106 holders of record of our common stock as of December 9, 2008.

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## SELECTED FINANCIAL DATA

We derived the consolidated statements of operations data presented below for each of the three years ended June 30, 2006, 2007 and 2008, and the consolidated balance sheet as of June 30, 2007 and 2008, from our audited consolidated financial statements included elsewhere in this prospectus. We derived the consolidated statements of operations data for the three months ended September 30, 2007 and 2008 and for the period from inception to September 30, 2008 and the consolidated balance sheet data as of September 30, 2008 from our unaudited consolidated financial statements included elsewhere in this prospectus. We derived the consolidated statement of operations data for each of the two years ended June 30, 2004 and 2005, and consolidated balance sheet data as of June 30, 2004, 2005 and 2006 from our audited consolidated financial statements not included in this prospectus. Interim financial results are not necessarily indicative of results that may be expected for the full fiscal year. The unaudited financial statements have been prepared on a basis consistent with the audited financial statements. You should read this financial data in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and accompanying notes, which are included elsewhere in this prospectus.

| | Year Ended June 30, | | | | | Three Months Ended September 30, | | Period from Inception to September 30, |
|---|---|---|---|---|---|---|---|---|
| | 2004 | 2005 | 2006 | 2007 | 2008 | 2007 (Unaudited) | 2008 (Unaudited) | 2008 (Unaudited) |
| | (Amounts in thousands, except for per share amounts) | | | | | | | |
| **Consolidated Statements of Operations Data:** | | | | | | | | |
| Revenues | $ 121 | $ 5,610 | $ | $ | $ | $ | $ | $ 5,771 |
| Cost of operations: | | | | | | | | |
| Research and development | 5,624 | 7,163 | 9,178 | 17,751 | 19,579 | 4,137 | 6,127 | 71,984 |
| Sales, general and administrative | 1,501 | 1,657 | 2,070 | 4,112 | 8,089 | 1,359 | 3,953 | 23,813 |
| Loss from operations | (7,004) | (3,210) | (11,335) | (22,350) | (27,668) | (5,496) | (10,080) | (90,026) |
| Other income (expenses) | 1,084 | 472 | 995 | 1,787 | 1,733 | 933 | (121) | |