REPLIDYNE INC
Form S-1/A
June 26, 2006

Table of Contents

As filed with the Securities and Exchange Commission on June 26, 2006
Registration No. 333-133021

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

Amendment No. 3
to
FORM S-1
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

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

Delaware	**2834**	**84-1568247**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

1450 Infinite Dr.
Louisville, CO 80027
(303) 996-5500
(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Kenneth J. Collins
President and Chief Executive Officer
Replidyne, Inc.
1450 Infinite Dr.
Louisville, CO 80027
(303) 996-5500
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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380 Interlocken Crescent	**Professional Corporation**
Suite 900	**650 Page Mill Road**
Broomfield, CO 80021	**Palo Alto, California 94304**
(720) 566-4000	**(650) 493-9300**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box. o

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective

registration statement for the same offering. o _____

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o _____

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering. o _____

If delivery of the prospectus is expected to be made pursuant to Rule 434, check the following box. o _____

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Aggregate Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee(3)(4)
Common Stock, $0.001 par value per share	5,750,000	$16.00	$92,000,000	$9,844

(1) Includes 750,000 shares of common stock that may be purchased by the underwriters to cover over-allotments, if any.
(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(a) under the Securities Act of 1933, as amended.
(3) Calculated pursuant to Rule 457(a) based on an estimate of the proposed maximum aggregate offering price.
(4) A registration fee of $10,700 has been paid previously in connection with this Registration Statement based on an estimate of the aggregate offering price

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell securities and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

P R O S P E C T U S (Subject to Completion)
Issued June 26, 2006

5,000,000 Shares
Common Stock

We are offering 5,000,000 shares of our common stock. This is our initial public offering and no public market currently exists for our shares. We anticipate that the initial public offering price will be between $14.00 and $16.00 per share.

Our common stock has been approved for quotation on the Nasdaq National Market under the symbol RDYN, subject to official notice of issuance.

Investing in our common stock involves risks. See Risk Factors beginning on page 7.

PRICE $ A SHARE

	Per Share	Total
Price to Public	$	$
Underwriting Discounts and Commissions	$	$
Proceeds to Replidyne	$	$

We have granted the underwriters the right to purchase up to an additional 750,000 shares of common stock from us at the public offering price, less the underwriting discounts and commissions to cover over-allotments.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about , 2006.

Merrill Lynch & Co. **Morgan Stanley**

Cowen and Company **Pacific Growth Equities, LLC**

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus. We have not, and the underwriters 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. We are offering to sell, and are seeking offers to buy, shares of common stock only in jurisdictions where 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 the common stock. Our business, financial conditions, results of operations and prospects may have changed since that date.

For investors outside the U.S.: Neither we nor any of the underwriters 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 U.S. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

Through and including , 2006 (25 days after the date of this prospectus), all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Table of Contents

PROSPECTUS SUMMARY

The following summary is qualified in its entirety by, and should be read together with, the more detailed information and financial statements and related notes thereto appearing elsewhere in this prospectus. Before you decide to invest in our common stock, you should read the entire prospectus carefully, including the risk factors and the financial statements and related notes included in this prospectus.

Our Company

We are a biopharmaceutical company focused on discovering, developing, in-licensing and commercializing innovative anti-infective products. Our lead product, Orapem, is a novel oral, community antibiotic, meaning that it is generally used to treat infections acquired in the community and not in a hospital setting. Forest Laboratories is our partner for the development and commercialization of Orapem in the U.S. Orapem is a member of the penem sub-class within the beta-lactam class of antibiotics. Beta-lactam antibiotics all share a core structural feature (a beta-lactam ring) and include antibiotics such as penicillins and cephalosporins. The penem sub-class of beta-lactam antibiotics has structural features that resemble a fusion of the penicillin and cephalosporin core structures and has an intrinsic ability to resist degradation by commonly encountered enzymes that inactivate some other beta-lactam antibiotics. Beta-lactams are generally characterized by their favorable safety and tolerability profiles, as well as their broad spectrum of activity, and as a result are typically used as first-line therapy in many respiratory and skin infections in adult and pediatric patients. In December 2005, we submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for Orapem. If approved by the FDA, Orapem would be the first orally available penem in the U.S. Our NDA is based on 11 Phase III studies, conducted by Bayer AG when it was a previous licensee of Orapem, and safety data for over 5,000 patients who have been treated with Orapem. We believe that Orapem s safety profile and activity against many common bacterial infections suggest the potential for Orapem to become a leading branded oral beta-lactam antibiotic.

According to IMS Health, the annual worldwide market for antibiotics was $25.0 billion in 2005, which includes U.S. sales of $8.5 billion for oral antibiotics, consisting of $7.0 billion in the adult market and $1.5 billion in the pediatric market. IMS Health estimates that, in 2005, beta-lactams had a 42.7% market share of the adult oral antibiotic market representing over 90 million prescriptions and a 74.5% market share of the pediatric oral antibiotic market representing over 40 million prescriptions.

We submitted an IND for the clinical development of our second product candidate, REP8839, in May 2006. We are developing REP8839 for topical use for skin and wound infections and prevention of *Staphylococcus aureus,* or *S. aureus*, infections, including methicillin resistant *S. aureus,* or MRSA, infections in hospital settings. We are also pursuing the development of other novel anti-infective products using compounds we have selected from a library of proprietary compounds, as well as compounds identified in assays we have developed to identify compounds that inhibit bacterial DNA replication.

Our Product Candidates

We believe that our innovative product candidates offer advantages over existing antibiotics by virtue of better overall profiles in terms of activity, safety, tolerability and induction of bacterial resistance. We also believe that the markets these products address present us with significant commercial opportunities.

Orapem

We believe that Orapem, with its broad spectrum of activity, increased potency and safety and tolerability profile, would be appropriate for use as a first-line antibiotic. We have submitted an NDA for Orapem for four indications: acute bacterial sinusitis; community-acquired pneumonia; acute exacerbation of chronic bronchitis; and uncomplicated skin and skin structure infections. Community-acquired pneumonia refers to pneumonia acquired outside of the hospital setting. Although the efficacy data for acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections may be

Table of Contents

adequate for FDA approval, we expect that the FDA will likely require additional clinical trials, including a placebo-controlled trial in the case of acute exacerbation of chronic bronchitis, before it will approve these indications. We are currently conducting a Phase III placebo-controlled clinical trial for acute exacerbation of chronic bronchitis for adult use.

We are also developing, together with Forest Laboratories, an oral liquid formulation of Orapem for the pediatric market and are currently conducting a Phase II clinical trial using a prototype oral liquid formulation among pediatric patients with acute otitis media. We intend to conduct Phase III clinical trials for the two largest pediatric indications: acute otitis media and tonsillitis/pharyngitis. Pediatric antibiotics compete primarily on safety, efficacy and taste. We believe Orapem s safety profile and broad spectrum of activity against bacteria that cause common infections in children make Orapem a promising product candidate for pediatric use. In addition, we believe that there will be fewer competitive branded pediatric oral antibiotics in the next several years. Under our agreement with Forest Laboratories, we have an option to exclusively promote Orapem to pediatricians. Assuming we successfully complete clinical development of an oral liquid formulation for Orapem, we currently intend to expand our sales force at our expense to promote Orapem to pediatricians, thereby increasing our economic interest in pediatric sales.

REP8839

REP8839 is an inhibitor of methionyl tRNA synthetase, which is an enzyme that plays an essential role in protein synthesis. Inhibition of methionyl tRNA synthetase results in reduced protein synthesis and attenuation of bacterial growth. We are developing REP8839 for topical use for skin and wound infections and prevention of *S. aureus* infections, including MRSA infections, in hospital settings. REP8839 has exhibited promising activity against *S. aureus,* including MRSA, in pre-clinical studies. We submitted an IND application in May 2006 for the clinical development of a REP8839/mupirocin combination product for topical use for skin and wound infections and prevention of *S. aureus* infections, including MRSA infections, in hospital settings. We believe that the distinctive mechanisms of action of the two drugs may greatly reduce the likelihood that *S. aureus* will develop resistance to this combination. We retain worldwide rights to REP8839.

Research and Discovery Programs

We are also pursuing the development of other novel anti-infective products based on our own research efforts. We have developed assays that identify compounds that inhibit bacterial DNA replication. The compounds may be useful to treat bacterial infections. We believe that bacterial DNA replication is an attractive target system for new antibacterial drugs because it is an essential cellular process and stalled DNA replication can trigger cell death. Our assays are designed to mimic the bacterial DNA replication systems of numerous bacteria. We have identified compounds that are able to inhibit bacterial DNA replication in these assays. We believe that the novel mechanism of action of our technology may reduce the risk that bacteria will develop resistance to drugs based on this technology. We are currently optimizing the initial inhibitors identified in the assays. We have also selected from a proprietary library several potential compounds for development to treat infections in hospital settings caused by *Clostridium difficile*, or *C. difficile*. We are currently in pre-clinical testing for these compounds. We retain worldwide rights to all of these programs.

Our Collaboration with Forest Laboratories

In February 2006, we entered into a collaboration and commercialization agreement with Forest Laboratories to co-develop and co-market Orapem in the U.S. We believe that Forest Laboratories experience in successfully launching branded primary care products and the lack of competing community antibiotics in its current product portfolio make it a strong partner for us in the development and commercialization of Orapem. We have received $60.0 million in upfront and milestone payments. We may receive up to an additional $90.0 million in development milestones and $100.0 million in commercial milestones for both adult and pediatric indications. In addition, we will receive a royalty on all sales of Orapem. Forest Laboratories will be responsible for sales and marketing of Orapem to primary care

Table of Contents

physicians. We intend to build our own marketing and sales force to promote Orapem to otolaryngologists (ear, nose and throat specialists) in major metropolitan areas. Forest Laboratories will reimburse us for most of these marketing and sales force expenses. We and Forest Laboratories may conduct additional clinical trials for other indications, which may include higher dose therapies. Forest Laboratories has committed to pay a substantial portion of the costs for further development of Orapem.

Our Strategy

Our goal is to discover, in-license, develop and commercialize novel anti-infective compounds that address unmet medical needs resulting from growing resistance to existing drug products. Key elements of our strategy are:

Maximize commercial potential for Orapem as a leading community antibiotic and a preferred branded oral beta-lactam in adult and pediatric markets.

Develop specialty sales and marketing capabilities to target specialist physicians in major metropolitan areas, including otolaryngologists, if Orapem is approved for adult use, and pediatricians, if Orapem is approved for pediatric use. We plan to leverage this sales force to market other products that we may develop, acquire or in-license.

Develop REP8839/mupirocin combination for topical use in treatment of skin and wound infections and prevention of *S. aureus* infections, including MRSA infections, in hospital settings.

Discover and develop novel anti-infective products by continuing to pursue our discovery research programs in DNA replication inhibition and our program to develop a treatment for *C. difficile*.

Leverage our development, regulatory and commercial resources by acquiring or in-licensing additional products or product candidates.

Risks Related to Our Business

Our ability to implement our current business strategy is subject to numerous risks, as more fully described in the section entitled Risk Factors immediately following this prospectus summary. These risks include, among others, delays in obtaining, or a failure to obtain, regulatory approval for our product candidates, failure of any approved product to achieve significant commercial acceptance in the medical community or receive reimbursement by third-party payors, our dependence upon third parties under our licensing and collaboration agreements, unfavorable clinical trial results, delays in product launch, and failure to maintain and protect our proprietary intellectual property assets. All of our product candidates are subject to regulatory approval by the FDA and comparable agencies in other countries. Orapem is our only product candidate in clinical development. To date, we have not obtained regulatory approval of any product candidate. All of our other compounds or potential product candidates are in preclinical development or the discovery stage. Although the FDA has recently accepted the filing of our first NDA for use of Orapem in four clinical indications, we cannot give any assurance that it, or any of our other product candidates, will receive regulatory approval or be successfully commercialized.

While we have generated limited amounts of revenue from license and milestone payments under our collaboration agreements and payments for funded research and development, we have not generated any revenue to date from product sales. We have incurred significant operating losses since our inception in 2000. We incurred net losses of approximately $14.0 million in 2003, $19.2 million in 2004, $33.7 million in 2005 and $7.7 million in the three months ended March 31, 2006. As of March 31, 2006, we had an accumulated deficit of $93.1 million, and we expect to incur losses for the foreseeable future. We are unable to predict the extent of future losses or when we will become profitable, if at all. Even if we succeed in developing and commercializing one or more of our product candidates, we may never generate sufficient revenue to achieve and sustain profitability.

Table of Contents

Corporate Information

We were incorporated under the laws of the state of Delaware on December 6, 2000. Our principal executive offices are located at 1450 Infinite Drive, Louisville, Colorado 80027, and our telephone number is (303) 996-5500. Our web site address is http://www.replidyne.com. The information contained in, or that can be accessed through, our website is not part of this prospectus and should not be considered part of this prospectus. Unless the context indicates otherwise, as used in this prospectus, the terms Replidyne, we, us and our refer to Replidyne, Inc.

The names Replidyne and Orapem are our trademarks. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Table of Contents

THE OFFERING

Common stock offered by us	5,000,000 shares
Common stock to be outstanding after this offering	26,327,003 shares
Use of proceeds	To fund clinical trials and other research and development activities; to fund activities in preparation for the potential commercial launch of Orapem; and for working capital, capital expenditures and other general corporate purposes.
Proposed Nasdaq National Market symbol	RDYN

The number of shares of common stock that will be outstanding immediately after this offering is based on 21,327,003 shares of common stock outstanding as of May 31, 2006, giving effect to the issuance of 1,182,332 shares of common stock to the holders of our Series A, B, C and D convertible preferred stock upon the closing of this offering in satisfaction of accumulated dividends and excludes:

- 1,779,318 shares of common stock issuable upon the exercise of outstanding options, with a weighted average exercise price of $3.11 per share;
- 111,375 shares of common stock reserved for future issuance under our benefit plans; and
- 53,012 shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of $5.47 per share.

Except as otherwise indicated, all information in this prospectus assumes:

- a one-for-4.904 reverse stock split of our common stock;
- the conversion of all our outstanding shares of preferred stock into 18,067,322 shares of common stock;
- the issuance of 1,182,332 shares of common stock to the holders of our Series A, B, C and D convertible preferred stock upon the closing of this offering in satisfaction of accumulated dividends, as required by the terms of the Series A, B, C and D convertible preferred stock, assuming for this purpose that the closing of this offering occurs on June 30, 2006 and the initial public offering price is $15.00 per share, all of which is described more fully under the section of this prospectus entitled Capitalization;
- the filing of our restated certificate of incorporation, which will occur immediately prior to the closing of this offering; and
- no exercise of the underwriters over-allotment option.

Table of Contents

SUMMARY FINANCIAL DATA

We have derived the following summary of our statements of operations data for the years ended December 31, 2003, 2004 and 2005 from our audited financial statements appearing elsewhere in this prospectus. We have derived the following summary of our statements of operations data for the three months ended March 31, 2005 and 2006 and the balance sheet data as of March 31, 2006 from our unaudited financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. The summary of our financial data set forth below should be read together with our financial statements and the related notes to those statements, as well as Management s Discussion and Analysis of Financial Condition and Results of Operations, appearing elsewhere in this prospectus.

The pro forma as adjusted balance sheet data reflects the balance sheet data at March 31, 2006 as adjusted for the sale of 5,000,000 shares of our common stock in this offering at an assumed initial offering price to the public of $15.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us and the automatic conversion of all preferred stock into common stock upon the completion of this offering.

	Year Ended December 31,			Three Months Ended March 31,	
	2003	2004	2005	2005	2006
				(unaudited)	(unaudited)
	(in thousands, except share and per share amounts)				
Statement of Operations Data:					
Revenue	$ 726	$ 834	$ 441	$ 267	$ 2,877
Costs and expenses:					
Research and development	12,331	16,282	29,180	5,013	8,970
Sales, general and administrative	2,155	2,994	5,329	686	1,953
Total costs and expenses	14,486	19,276	34,509	5,699	10,923
Loss from operations	(13,760)	(18,442)	(34,068)	(5,432)	(8,046)
Other (expense) income, net	(190)	(797)	399	42	344
Net loss	(13,950)	(19,239)	(33,669)	(5,390)	(7,702)
Preferred stock dividends and accretion	(1,294)	(3,560)	(7,191)	(1,291)	(2,653)
Net loss attributable to common stockholders	$ (15,244)	$ (22,799)	$ (40,860)	$ (6,681)	$ (10,355)
Basic and diluted net loss attributable to common stockholders per share(1):					
Historical	$ (20.82)	$ (30.55)	$ (39.20)	$ (8.13)	$ (7.21)
Pro forma			$ (2.24)		$ (0.38)
Weighted average shares outstanding(1):					
Historical	732,044	746,306	1,042,388	821,757	1,435,726
Pro forma			15,031,566		20,508,603

	As of March 31, 2006	
	Actual	Pro Forma As Adjusted
	(in thousands)	
Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 109,900	$ 178,050
Working capital	98,800	166,950
Total assets	116,112	184,262
Accumulated deficit	(93,060)	(93,060)
Preferred stock	139,568	
Total stockholders (deficit) equity	(92,539)	115,179

(1) Please see Note 1 to our financial statements for an explanation of the method used to calculate the historical and pro forma net loss attributable to common stockholders per share and the number of shares used in the computation of the per share amounts.

Table of Contents

RISK FACTORS

You should carefully consider the risks described below, which we believe are the material risks of our business and this offering, before making an investment decision. Our business could be harmed by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained in this prospectus, including our financial statements and related notes.

Risk Related to our Business

We are dependent on the success of our lead product candidate, Orapem, and we cannot give any assurance that it will receive regulatory approval, which is necessary before it can be commercialized.

If we are not able to commercialize Orapem, we will not generate product revenues for several years, if at all, and we may never generate sufficient revenue to achieve and sustain profitability. We need approval from the FDA prior to marketing our product candidates in the U.S. In December 2005, we submitted our first NDA to the FDA for use of Orapem in four clinical indications, and the FDA accepted this NDA for filing in February 2006. Even if we obtain FDA approval for Orapem, it may not cover all of the clinical indications for which we are seeking approval and we expect that the FDA will likely require additional clinical trials, including a placebo-controlled trial in the case of acute exacerbation of chronic bronchitis. Also, an approval might contain significant limitations with respect to conditions of use in the form of narrow indications, warnings, precautions or contra-indications. We cannot predict if or when we might seek regulatory review of Orapem for any other indications or of any of our other product candidates.

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

Our lead product candidate, Orapem, has been in-licensed from another pharmaceutical company, Daiichi Asubio Pharma Co., Ltd., or Daiichi Asubio. A previous licensee, Bayer AG, or Bayer, completed extensive pre-clinical studies and Phase II and Phase III clinical trials for a particular dosage of Orapem. We are relying on the data from these pre-clinical studies and clinical trials in our application to the FDA for approval to market Orapem. Any problems with these previous pre-clinical studies or clinical trials, including problems with the design or statistical analysis of such pre-clinical studies or clinical trials, could cause our application for regulatory approval to be delayed or rejected, in which case we might need to conduct additional trials. In addition, because these clinical trials were conducted using an active compound manufactured by Nippon Soda Co., Ltd., or Nippon Soda, at its facility in Takaoka, Japan, we expect the FDA will require us to demonstrate to its satisfaction the comparability of the active compound we are sourcing from Nippon Soda s new facility in Nihongi, Japan.

The FDA may change its approval policies or requirements, or apply interpretations to its policies or requirements, in a manner that could delay or prevent commercialization of Orapem for some or all indications that are the subject of our pending NDA.

Regulatory requirements for approval of antibiotics may change in a manner that requires us to conduct additional large-scale clinical trials, which may delay or prevent commercialization of Orapem for some or all indications. Historically, the FDA and foreign regulatory authorities have not required placebo-

controlled clinical trials for approval of antibiotics but instead have relied on non-inferiority studies. In a non-inferiority study, a drug candidate is compared with an approved antibiotic treatment and it must be shown that the product candidate is not less effective than the approved treatment. All efficacy studies upon which our NDA is based were designed as non-inferiority studies after consultation with the FDA. In September 2005, the FDA indicated to us that it will likely require data from a placebo-controlled trial of Orapem before it will consider approving it for acute exacerbation of chronic bronchitis. In May 2006, the FDA requested an explanation of how our non-inferiority studies contained in our NDA for Orapem support efficacy in each of the indications for which we are seeking approval. We cannot assure you that the FDA will not require placebo-controlled trials, or other trials involving comparator antibiotics, to demonstrate the superiority of Orapem to placebo before considering the approval of Orapem for one or more of the indications that are the subject of our pending NDA. Conducting placebo-controlled trials for antibiotics can be time consuming and expensive and can be difficult to complete. Institutional review boards may not grant approval for placebo-controlled trials because of ethical concerns about denying some participating patients access to any antibiotic therapy during the course of the trial. It may be difficult to enroll patients in placebo-controlled trials even if institutional review board approval is obtained because certain patients would receive no therapy. Although we are currently conducting a placebo-controlled trial for acute exacerbation of chronic bronchitis, we have not completed any placebo-controlled trials for Orapem for any indications. We may not be able to show a statistically significant advantage over placebo in any trials that we are able to complete. These factors could delay for several years or ultimately prevent commercialization of Orapem for any indications for which the FDA requires placebo-controlled trials.

The efficacy of Orapem in subjects with uncomplicated skin and skin structure infections was evaluated in two Phase III studies. The results of one study met the protocol-specified criterion for non-inferiority of Orapem to amoxicillin/clavulanate. A second study did not demonstrate non-inferiority of Orapem to cephalexin. The FDA has informed us that evidence based on only a single trial will not provide adequate evidence for efficacy for this indication. Therefore, unless the FDA accepts our pooled clinical data compiled in two studies, we will likely need to complete additional trials in order to obtain approval for this indication. Even if we complete these additional trials, we may not be able to obtain adequate evidence of efficacy to support approval in uncomplicated skin and skin structure infections.

We may experience significant delays in the launch of Orapem for commercialization, which in turn could delay or prevent us from generating significant revenues from the sale of Orapem products.

We could experience potentially significant delays in the commercial launch of Orapem due to many factors, such as:

- If any FDA approval of Orapem does not include approvals for at least two commercially viable respiratory indications, which must include both (i) acute sinusitis and (ii) either community-acquired pneumonia or acute exacerbation of chronic bronchitis, our partner, Forest Laboratories Holdings Limited, or Forest Laboratories, has the contractual right to delay launch of Orapem following such initial FDA approval.

- If any FDA approval of Orapem does not include approval of Orapem having at least an 18 month shelf-life, then Forest Laboratories has the contractual right to delay launch of Orapem following such initial FDA approval until sufficient supplies of Orapem having at least an 18 month shelf-life are available. The FDA will make a decision regarding shelf-life based on ongoing real time and accelerated stability studies combined with data from prior stability studies conducted by Bayer and we cannot assure you that, at the time of initial FDA approval, the FDA will consider this data sufficient for an 18 month shelf-life labeling.

- If the FDA s inspections of the manufacturing facilities for Orapem drug substance or Orapem tablets or the proposed packaging operations for Orapem products reveal problems with the manufacturer or the manufacturer s facilities, then the FDA may refuse to approve our pending NDA or issue a not

approvable letter or may require additional manufacturing validation studies

Table of Contents

or impose restrictions on operations, including new manufacturing requirements, any of which would be costly and time consuming and require further FDA review and approval.

The supply chain for Orapem for the U.S. market is a complex process with highly interactive components consisting of the manufacture of Orapem drug substance, the manufacture of Orapem tablets, the packaging and labeling of Orapem, and the distribution in the U.S. We rely on third parties for each of these activities, including management of the supply chain. Any failure in the complex execution that would influence the ability to establish or manage these manufacturing, packaging and distribution relationships in an effective or timely manner could prevent us from achieving or maintaining market acceptance of Orapem.

Any one or a combination of these events could significantly delay or prevent our ability to commercialize Orapem. If we are not successful in commercializing Orapem, or are significantly delayed in doing so, our business will be materially harmed.

The success of Orapem depends heavily on our collaboration with Forest Laboratories, which was established only in February 2006 and involves a complex sharing of decisions, responsibilities, costs and benefits. Any loss of Forest Laboratories as a partner, or any adverse developments in the collaboration, would materially harm our business.

In February 2006, we entered into a collaboration agreement with Forest Laboratories to develop and commercialize Orapem. We have granted Forest Laboratories an exclusive sublicense for the development and sale of Orapem for all indications in the U.S. We have also granted Forest Laboratories a right of first refusal to extend the territory to include Canada. Forest Laboratories is responsible for funding a substantial portion of the continued development of Orapem, including clinical trials and regulatory approval. If the FDA approves Orapem, Forest Laboratories will also have primary responsibility for the marketing and sales of the approved product and will share responsibility for compliance with regulatory requirements.

Although Forest Laboratories has an established sales force targeting primary care physicians, they do not have significant experience marketing antibiotics. We have limited control over the amount and timing of resources that Forest Laboratories will dedicate to the development, approval and marketing of Orapem. Although we share decision-making authority with respect to the marketing of Orapem through a joint marketing committee, Forest Laboratories generally has the right to make final decisions on this committee if the parties are unable to reach consensus.

We are subject to a number of additional risks associated with our dependence on our collaboration with Forest Laboratories, including:

We and Forest Laboratories could disagree as to development plans, including clinical trials or regulatory approval strategy, or as to which additional indications for Orapem should be pursued. Disputes regarding the collaboration agreement that delay or terminate the development, commercialization or receipt of regulatory approvals of Orapem would harm our business and could result in significant litigation or arbitration.

Forest Laboratories could fail to devote sufficient resources to the development, approval, commercialization, or marketing and distribution of Orapem. After the time periods stated in the collaboration agreement, Forest Laboratories could shift its research, development and commercialization resources to other product opportunities including those that might be competitive with Orapem.

Forest Laboratories has the contractual right to delay launch of Orapem following the initial FDA approval if that approval does not include both (i) acute sinusitis and (ii) either community-acquired pneumonia or acute exacerbation of chronic bronchitis.

Table of Contents

Forest Laboratories has the contractual right to delay launch of Orapem following the initial FDA approval until sufficient supplies of Orapem having at least an 18 month shelf-life are available, which we have not achieved to date.

Forest Laboratories could also fail to effectively manage its manufacturing relationship with its supplier of Orapem tablets, Tropon GmbH, or Tropon, or with our supplier of Orapem drug substance, Nippon Soda. Forest Laboratories is contractually bound to purchase all of its tablet requirements from Tropon, subject to certain exceptions. Tropon and Nippon Soda will be subject to ongoing periodic unannounced inspections by the FDA and corresponding state agencies for compliance with good manufacturing practices regulations, or cGMPs, and similar foreign standards. Neither we nor Forest Laboratories has control over compliance by Tropon and Nippon Soda with these regulations and standards.

Furthermore, Forest Laboratories may terminate our collaboration agreement upon our material breach of the collaboration agreement or our bankruptcy. Forest Laboratories may also terminate our agreement upon 90 days notice in the event that Forest Laboratories reasonably determines the development program indicates issues of safety or efficacy that are likely to prevent or significantly delay the filing or approval of an NDA for Orapem or to result in labeling or indications that would significantly adversely affect the marketing of any product developed under the agreement.

We do not currently have the resources necessary to develop and market Orapem on our own. If either we or Forest Laboratories do not perform our respective obligations under, or devote sufficient resources to, our collaboration, or if we and Forest Laboratories do not work effectively together, Orapem may not be successfully commercialized. If our collaboration were to be terminated, we would need to establish an alternative collaboration and may not be able to do so on acceptable terms or at all.

We are at an early stage of development as a company, with limited sources of revenue, and we may never become profitable.

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

obtaining U.S. and foreign regulatory approvals for our lead product candidate, Orapem;

successfully developing and securing regulatory approval for our other product candidate, REP8839; and

successfully commercializing any product candidates for which we receive FDA approval.

Our existing product candidates will require extensive additional clinical evaluation, regulatory approval, significant marketing efforts and substantial investment before they can provide us with any revenue. If we do not receive regulatory approval for and successfully commercialize Orapem, we will be unable to generate any revenue from product sales for many years, if at all. If we are unable to generate revenue, we will not become profitable, and we may be unable to continue our operations.

We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future.

We have experienced significant operating losses since our inception in 2000. At December 31, 2005, we had a deficit accumulated during the development stage of approximately $83.1 million. We have generated no revenue from product sales to date. We have funded our operations to date principally from the sale of our securities and from payments by Forest Laboratories under our collaboration agreement. We expect to continue to incur substantial additional operating losses for the next several years as we pursue our clinical trials and research and development efforts. Because of the numerous risks and uncertainties associated with developing and commercializing antibiotics, we are unable to predict the extent of any future losses. We may never have any significant future revenue or become profitable.

Table of Contents

The commercial success of our product candidates will depend upon attaining significant market acceptance of these products among physicians, patients, health care payors and the medical community.

None of our product candidates has been commercialized for any indication. Even if approved for sale by the appropriate regulatory authorities, physicians may not prescribe our product candidates, in which case we would not generate revenue or become profitable. Market acceptance of our lead product candidate, Orapem, and any future product candidates by physicians, healthcare payors and patients will depend on a number of factors, including:

- the clinical indications for which the product candidate is approved;
- acceptance by physicians and patients of each product candidate as a safe and effective treatment;
- perceived advantages over alternative treatments;
- the cost of treatment in relation to alternative treatments, including numerous generic antibiotics;
- the extent to which the product candidate is approved for inclusion on formularies of hospitals and managed care organizations;
- the extent to which bacteria develop resistance to the product candidate, thereby limiting its efficacy in treating or managing infections;
- whether the product candidate is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the availability of adequate reimbursement by third parties;
- relative convenience and ease of administration; and
- prevalence and severity of side effects.

If our product candidates are unable to compete effectively with generic and branded antibiotics, our commercial opportunity will be reduced or eliminated.

If approved, our lead product candidate, Orapem, will compete against both generic and branded community antibiotic therapies. The market for such products is very competitive and includes generic products, such as amoxicillin/clavulanate, and established branded products, such as Omnicef, Zithromax, Ketek and Levaquin, which are marketed by major pharmaceutical companies, all of which have significantly greater financial resources and expertise in research and development, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, manufacturing and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Over the next several years, our products will face more competition in the form of generic versions of branded products of competitors that will lose their patent exclusivity. For example, Orapem will begin to face competition from generic Omnicef in 2008. Generic antibiotic therapies typically are sold at lower prices than branded antibiotics and are preferred by managed care providers of health services. If we are unable to demonstrate to physicians that, based on experience, clinical data, side-effect profiles and other factors, our products are preferable to these generic antibiotic therapies, we may never generate meaningful revenue. Our commercial opportunity will also be reduced or eliminated if our competitors develop and commercialize generic or branded antibiotics that are safer, more effective, have fewer side effects or are less expensive than our product candidates.

Daiichi Asubio owns a portfolio of patents related to faropenem compounds, including the faropenem parent compound, Orapem and other faropenem prodrugs. We have licensed from Daiichi Asubio the patents to Orapem and other faropenem prodrugs. These patents may not prevent competitors from developing other faropenem drugs that are

not covered by the Daiichi Asubio patents. Beginning in

Table of Contents

2008, when the Daiichi Asubio patents expire, competitors may submit NDAs seeking approval of antibiotics containing the faropenem parent compound as the active ingredient. These applications would have to contain full reports of safety and efficacy data conducted by or for the applicants and could not in any way rely upon the safety and efficacy data utilized in the approval of Orapem. In addition, as early as four years after the approval of the Orapem NDA, competitors could also file NDAs seeking approval of faropenem drugs that would likely require the applicant to conduct clinical trials in order to bring the product to market in the U.S., though the FDA may allow the applicant to rely in part on the FDA s prior findings of safety and efficacy of Orapem.

We have limited manufacturing capabilities and will depend on third parties to manufacture Orapem and future products. If these manufacturers fail to meet our or Forest Laboratories requirements and strict regulatory standards, we may be unable to develop or commercialize our products.

We do not have the capability to manufacture commercial quantities of Orapem drug substance. We engaged a third party manufacturer, Nippon Soda, as our sole supplier of Orapem drug substance. We are contractually bound to purchase all of our requirements from this party and we expect Nippon Soda will be our and Forest Laboratories sole supplier of Orapem drug substance for the foreseeable future. Nippon Soda may terminate our supply agreement for a number of reasons, such as:

- an uncured material breach of the supply agreement by us;
- our liquidation or insolvency; or
- in some circumstances, following a change of control.

Nippon Soda has only a single facility located in Nihongi, Japan that can readily manufacture commercial quantities of Orapem. If that facility were to be damaged or destroyed, we would have no readily available source of supply. Nippon Soda has not yet manufactured Orapem at commercial scale on a consistent basis, nor has Nippon Soda completed the manufacturing process validations that are part of the regulatory requirements prior to obtaining marketing approval for Orapem.

Reliance on a third party manufacturer entails risks to which we would not be subject if we manufactured products ourselves, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party because of factors beyond our control; and
- the possibility of termination or nonrenewal of the agreement by the third party because of our breach of the manufacturing agreement or based on its own business priorities.

Any of these factors could cause delay or suspension of clinical trials, regulatory submissions, required approvals or commercialization of Orapem, cause us to incur higher costs and could prevent us from commercializing our product candidates successfully. Furthermore, if our contract manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices and we are unable to find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volumes and quality, and on a timely basis, we would likely be unable to meet demand for Orapem and we would lose potential revenue. It may take several years to establish an alternative source of supply for Orapem and to have any such new source approved by the FDA.

Forest Laboratories has agreed to assume responsibility for supply chain management for Orapem and we anticipate that Forest Laboratories will enter into a direct relationship with Nippon Soda as its sole supplier of Orapem drug substance under similar terms as those currently in place between us and Nippon Soda.

Table of Contents

If the FDA does not approve Nippon Soda s facility, we may be unable to develop or commercialize Orapem.

We rely on Nippon Soda to manufacture Orapem drug substance and currently have no plans to develop our own manufacturing facility. The facilities used by our contract manufacturer to manufacture our product candidates must be approved by the FDA. Nippon Soda s facility has never been inspected by the FDA. If Nippon Soda cannot successfully manufacture material that conforms to our specifications and strict regulatory requirements, Nippon Soda will not be able to secure FDA approval for its manufacturing facility. If the FDA does not approve this facility for the manufacture of Orapem, we and Forest Laboratories may need to find alternative manufacturing facilities, which would result in significant delay of up to several years in obtaining approval for and manufacturing Orapem. In addition, our contract manufacturer will be subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. These regulations cover all aspects of the manufacturing, testing, quality control and record keeping relating to our product candidates. We do not have control over Nippon Soda s compliance with these regulations and standards. Failure by Nippon Soda to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure to grant approval to market our product candidates, delays, suspension or withdrawals of approvals, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. In addition, we have no control over Nippon Soda s ability to maintain adequate quality control, quality assurance and qualified personnel. Failure by our contract manufacturer to comply with or maintain any of these standards could adversely affect our ability to develop, obtain regulatory approval for or market our product candidates.

The success of our current business strategy will depend in part on our ability to obtain FDA approval of Orapem for pediatric use and, if FDA approval is obtained, to successfully market an oral liquid formulation for the pediatric market.

The development of Orapem for pediatric use is an important part of our current business strategy. We are developing Orapem for pediatric use in conjunction with our strategic partner, Forest Laboratories. We have developed a prototype oral liquid formulation, have initiated a Phase II trial in acute otitis media (middle ear infection) and are considering conducting studies in tonsillitis/pharyngitis. Our ability to successfully develop and market this product candidate for pediatric use is subject to various risks, including the following:

Pre-clinical testing and clinical trials are protracted, expensive and uncertain processes. It might take us and our partner several years to complete the testing process, and failure can occur at any stage of the process. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. These risks are potentially more pronounced in clinical tests involving children.

We have not completed any clinical trials in children to date. A clinical trial conducted by Bayer for tonsillitis/pharyngitis in adults did not meet its primary end point.

Any regulatory approval we ultimately obtain may be limited or subject to post-approval commitments that render the product not commercially viable.

Any NDA or other marketing authorization applications that we may file might be denied by the FDA and analogous foreign regulators.

This product candidate, even if found to be safe and effective, might be difficult to develop into a commercially viable drug or to manufacture on a large scale or might be uneconomical to market commercially.

Third parties might market superior drugs or be more effective in marketing equivalent drugs.

Table of Contents

Even if this product candidate is successfully developed and effectively marketed, the size of the potential market might change such that our sales revenue is less than initially contemplated.

Because of our relationship with our partner, Forest Laboratories, we are dependent on Forest Laboratories to commercialize Orapem.

Any failure to obtain regulatory approval of Orapem for pediatric use or to effectively market an approved product would have a material and adverse impact on our ability to successfully execute our current business strategy and would significantly reduce the revenues that we might generate from Orapem.

Any of our product candidates that are in clinical trials or that we advance into clinical trials are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays, or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, export, marketing and distribution of any of our product candidates currently in clinical trials or that we advance into clinical trials are subject to extensive regulation by the FDA in the U.S. and by comparable governmental authorities in foreign markets. Currently, we are developing Orapem for pediatric use and for additional indications for adults and we are conducting pre-clinical testing of REP8839. In the U.S. and in many foreign jurisdictions, rigorous pre-clinical testing and clinical trials and an extensive regulatory review process must be successfully completed before a new drug can be sold. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. Clinical testing is expensive, can take many years to complete and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials, depending upon numerous factors. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change. We have not obtained regulatory approval for any product candidate.

Our product candidates may 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 a particular indication;

the results of clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval;

the FDA or other regulatory authorities may disagree with the design of our clinical trials;

we may be unable to demonstrate that a product candidate s benefits outweigh its risks;

we may be unable to demonstrate that the product candidate presents an advantage over existing therapies, or over placebo in any indications for which the FDA requires a placebo-controlled trial;

the FDA or comparable foreign regulatory authorities may disagree with out interpretation of data from pre-clinical studies or clinical trials;

the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a new drug application or to obtain regulatory approval in the U.S. or elsewhere;

Table of Contents

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

the approval policies or regulations of the FDA or comparable foreign regulatory authorities may change.

The FDA or comparable foreign regulatory authorities might decide that our data are insufficient for approval and require additional clinical trials or other studies. Furthermore, even if we do receive regulatory approval to market a commercial product, any such approval may be subject to limitations on the indicated uses for which we may market the product. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to begin selling them.

Also, recent events have raised questions about the safety of marketed drugs and may result in increased cautiousness by the FDA in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals and more stringent product labeling requirements. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us from commercializing our product candidates.

If product liability lawsuits are successfully brought against us or our partner Forest Laboratories, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability lawsuits related to the testing of our product candidates, and will face an even greater risk if product candidates are introduced commercially. An individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. We have agreed to indemnify Nippon Soda from product liability claims under our commercial arrangement with them. We have also agreed to indemnify Forest Laboratories from claims arising from our development, manufacture, use, handling, storage, promotion, marketing or sale of any product, except as related to certain Orapem products in the U.S. with respect to which Forest Laboratories has agreed to bear a substantial portion of any product liability claims. If we cannot successfully defend ourselves against the product liability claim, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for our product candidates;

injury to our reputation;

withdrawal of clinical trial participants;

significant litigation costs;

substantial monetary awards to or costly settlement with patients;

product recalls;

loss of revenue; and

the inability to commercialize our product candidates.

We are highly dependent upon consumer perceptions of us, the Orapem brand and the safety and quality of our products. We could be adversely affected if we or the Orapem brand is subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to consumers. Also, because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from consumers use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations.

15

Table of Contents

We have global clinical trial liability insurance that covers our clinical trials up to a $5.0 million annual aggregate limit. Our current or future insurance coverage may prove insufficient to cover any liability claims brought against us. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our product candidates. In addition, because of the increasing costs of insurance coverage, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise.

We currently have no sales organization. If we are unable to establish a direct sales force in the U.S. to promote our product candidates, the commercial opportunity for our product candidates may be diminished.

We currently have no sales organization. If our lead product candidate, Orapem, is approved by the FDA for adult use, Forest Laboratories will market that product candidate directly to primary care physicians in the U.S. but will rely on us to market to physician specialists, such as otolaryngologists. If Orapem is approved by the FDA for pediatric use and if we exercise our option, we would be responsible for marketing Orapem to pediatricians in the U.S. Although Forest Laboratories will provide some funding, we will incur significant additional expenses and commit significant additional management resources to establish a pediatric sales force. We may not be able to establish a specialty sales force in a cost effective manner or realize a positive return on this investment. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. If we elect to rely on third parties, such as Forest Laboratories, to sell our product candidates in the U.S., we may receive less revenue than if we sold our product candidates directly. In addition, we may have little or no control over the sales efforts of those third parties. In the event we are unable to develop our own sales force or collaborate with a third party to sell our product candidates, we may not be able to commercialize our product candidates which would negatively impact our ability to generate revenue.

Delays in clinical testing could result in increased costs to us and delay our ability to generate revenue.

We may experience delays in clinical testing of our product candidates, including with respect to any clinical trials that may be conducted by Forest Laboratories. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a trial, in reaching agreement on acceptable clinical trial terms with prospective sites, in obtaining institutional review board approval at each site, in recruiting patients to participate in a trial, or in obtaining sufficient supplies of clinical trial materials. Many factors affect patient enrollment, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, clinicians and patients perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating, and whether the clinical trial design involves comparison to placebo. Our antibiotics treat bacterial infections which tend to be seasonal in nature. As a result, during certain times of the year, it is difficult to find patients to enroll in our trials. Prescribing physicians would also face ethical issues associated with enrolling patients in clinical trials of our product candidates over existing antibiotics that have established safety and efficacy profiles or in placebo-controlled trials. These ethical issues may be even more pronounced in conducting clinical trials of antibiotics in children. Any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and delay our ability to generate revenue.

We may be required to suspend or discontinue clinical trials due to side effects or other safety risks that could preclude approval of our product candidates.

Our clinical trials may be suspended at any time for a number of reasons. We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants. In addition, regulatory agencies may order the temporary or permanent discontinuation of our

clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements or that they present an unacceptable safety risk to participants.

Many antibiotics can produce significant side effects. Side effects associated with many current antibiotics include kidney and liver toxicities, heart rhythm abnormalities, photosensitivity, rash, excessive flushing of the skin and central nervous system toxicities, such as seizures. In clinical trials, side effects of Orapem have included gastrointestinal disorders (such as diarrhea, nausea and vomiting), nervous system disorders (such as dizziness and headaches), as well as infections and infestations (such as pneumonia and vaginal mucosis). Later clinical trials in a larger patient population could reveal other side effects. These or other side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory authorities stopping further development of or denying approval of our product candidates for any or all targeted indications. Even if we believe our product candidates are safe, our data is subject to review by the FDA, which may disagree with our conclusions. Moreover, we could be subject to significant liability if any volunteer or patient suffers, or appears to suffer, adverse health effects as a result of participating in our clinical trials.

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of Orapem and other product candidates, or continue our research and development programs.

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

- complete the clinical development of Orapem and REP8839;
- license or acquire additional product candidates;
- launch and commercialize any product candidates for which we receive regulatory approval, including building our own sales force to address certain markets; and
- continue our research and development programs.

We estimate that our net proceeds from this offering will be approximately $68.8 million. We expect that the net proceeds from this offering, together with our existing capital resources, will be sufficient to fund our operations for at least the next 18 months. We may be required to raise additional capital to complete the development and commercialization of our current product candidates.

To date, our sources of cash have been limited primarily to the proceeds from the sale of our securities and payments by Forest Laboratories under our collaboration agreement. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants, such as limitations on our ability to incur additional indebtedness, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to raise additional capital when required or on acceptable terms, we may have to significantly delay, scale back or discontinue the development and/or commercialization of one or more of our product candidates. We also may be required to:

- seek collaborators for our product candidates at an earlier stage than otherwise would be desirable and on terms that are less favorable than might otherwise be available; and
- relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

Table of Contents

Our ability to pursue the development and commercialization of our product candidates depends upon the continuation of our licenses from third parties.

Our license agreement with Daiichi Asubio provides us with an exclusive license to develop and sell any products with the compound Orapem as an active ingredient for any indication in the U.S. and Canada, with a right to sublicense certain rights to Forest Laboratories under our collaboration with Forest Laboratories. Either we or Daiichi Asubio may terminate the license agreement immediately upon the bankruptcy or dissolution of the other party or upon a breach of any material provision of the agreement if the breach is not cured within 60 days following written notice. If our license agreement with Daiichi Asubio were terminated, we would lose our rights to develop and commercialize Orapem.

If we fail to gain and maintain approval for our product candidates in international markets, our market opportunities will be limited.

Sales of our product candidates outside of the U.S. will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing or marketing of the product candidate in those countries. Approval in the U.S., or in any other jurisdiction, does not ensure approval in other jurisdictions. Obtaining foreign approvals could result in significant delays, difficulties and costs for us and require additional trials and additional expenses. Regulatory requirements can vary widely from country to country and could delay the introduction of our products in those countries. Clinical trials conducted in one country may not be accepted by other countries and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. None of our products is approved for sale in international markets and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with these regulatory requirements or to obtain and maintain required approvals, our target market will be reduced and our ability to generate revenue will be diminished.

We may not be able to enter into acceptable agreements to market and commercialize our product candidates in international markets.

If appropriate regulatory approvals are obtained, we intend to commercialize our product candidates in international markets through collaboration arrangements with third parties. Our collaboration with Forest Laboratories does not cover any markets outside of the U.S. and Canada. If we decide to sell our product candidates in international markets, we may not be able to enter into any arrangements on favorable terms or at all. In addition, these arrangements could result in lower levels of income to us than if we marketed our product candidates entirely on our own. If we are unable to enter into a marketing arrangement for our product candidates in international markets, we may not be able to develop an effective international sales force to successfully commercialize those products in international markets. If we fail to enter into marketing arrangements for our products and are unable to develop an effective international sales force, our ability to generate revenue would be limited.

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. We are highly dependent upon our senior management and scientific staff, particularly Kenneth Collins, our President and Chief Executive Officer, Roger Echols, M.D., our Chief Medical Officer, Peter Letendre, Pharm. D., our Chief Commercial Officer, and Nebojsa Janjic, Ph.D., our Chief Scientific Officer. The loss of services of any of Mr. Collins, Dr. Echols, Dr. Letendre or Dr. Janjic or one or more of our other members of senior management could delay or prevent the successful completion of our planned clinical trials or the commercialization of our product candidates. In addition, we only recently formed our clinical

Table of Contents

and regulatory group, which is based in Connecticut, the services of which we highly depend upon in order to conduct our clinical programs and obtain regulatory approvals.

Competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms. We do not carry key person insurance covering any members of our senior management. Each of our officers and key employees may terminate his employment at any time without notice and without cause or good reason.

Even if we receive regulatory approval for our product candidates, we will be subject to ongoing significant regulatory obligations and oversight.

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

Our corporate compliance program cannot guarantee that we are in compliance with all potentially applicable regulations.

The development, manufacturing, pricing, marketing, sales, and reimbursement of our product candidates, together with our general operations, are subject to extensive regulation by federal, state and other authorities within the U.S. and numerous entities outside of the U.S. If we or Forest Laboratories fail to comply with any of these regulations, we or they could be subject to a range of regulatory actions, including suspension or termination of clinical trials, the failure to approve a product candidate, restrictions on our product candidates or manufacturing processes, withdrawal of products from the market, significant fines, or other sanctions or litigation, and exclusion of our products from the Medicare/Medicaid payment system. Further, becoming a publicly traded company will subject us to significant additional regulations. If we fail to comply with these new regulations, we could face enforcement or other civil or criminal actions by the Securities and Exchange Commission or delisting by The Nasdaq National Market.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We have agreements with third-party contract research organizations to provide monitors for and to manage data for our on-going clinical programs. We and our contract research organizations are required to comply with current Good Clinical Practices, or GCPs, regulations and guidelines enforced by the FDA for all of our products in clinical development. The FDA enforces GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our contract research organizations fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be

Table of Contents

deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. In addition, our clinical trials must be conducted with product produced under cGMP regulations, and will require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our contract research organizations have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our contract research organizations have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors, or if we are liquidated. If any of our relationships with these third-party contract research organizations terminate, we may not be able to enter into arrangements with alternative contract research organizations. If contract research organizations do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Reimbursement may not be available for our product candidates, which could diminish our sales or affect our ability to sell our products profitably.

Market acceptance and sales of our product candidates will depend on reimbursement policies and may be affected by future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for any of our product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. We have not commenced efforts to have our product candidates reimbursed by government or third party payors. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize our products.

In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, the Medicare Modernization Act of 2003 added an outpatient prescription drug benefit to Medicare, which became effective on January 1, 2006. Drug benefits under this provision are administered through private plans that negotiate price concessions from pharmaceutical manufacturers. We cannot be certain that Orapem will successfully be placed on the list of drugs covered by particular health plans, plan formularies, nor can we predict the negotiated price for Orapem, which will be determined by market factors. With respect to Medicaid, the Deficit Reduction Act of 2005 made several changes to the way pharmacies are reimbursed under Medicaid, most of which go into effect on January 1, 2007. These changes could lead to reduced drug prices. 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 Orapem is not included on these preferred drug lists, physicians may not be inclined to prescribe it to their Medicaid patients.

As a result of legislative proposals and the trend towards managed health care in the U.S., third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly-approved drugs, which in turn will put pressure on the pricing of drugs. The availability of numerous generic antibiotics at lower prices than branded antibiotics, such as Orapem, if it

Table of Contents

were approved for commercial introduction, can also be expected to substantially reduce the likelihood of reimbursement for Orapem. We expect to experience pricing pressures in connection with the sale of our products due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative proposals.

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

We are a small company with 61 employees as of March 31, 2006, approximately 30% of whom have joined us in the preceding 12 months. To continue our clinical trials and commercialize our product candidates, we will need to expand our employee base for managerial, operational, sales, financial and other resources, which we expect will result in our approximately doubling the number of employees we have by the end of 2006. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

manage our development efforts effectively;

manage our clinical trials effectively;

integrate additional management, administrative, manufacturing and sales and marketing personnel;

maintain sufficient administrative, accounting and management information systems and controls; and

hire and train additional qualified personnel.

We may not be able to accomplish these tasks, and our failure to accomplish any of them could harm our financial results.

If we fail to identify, acquire and develop other products or product candidates, we may be unable to grow our business.

A key element of our strategy is to commercialize a portfolio of new anti-infective products in addition to Orapem. To date, we have in-licensed rights to each of our product candidates. As a significant part of our growth strategy, we intend to develop and commercialize additional products and product candidates through our discovery research program or by licensing or acquiring additional products from third parties. The success of this strategy depends upon our ability to identify, select and acquire the right pharmaceutical product candidates and products on terms that are acceptable to us.

Any product candidate we identify, license or acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace.

Proposing, negotiating and implementing an economically viable product acquisition or license is a lengthy and complex process. Other companies, including those with substantially greater financial,

Table of Contents

marketing and sales resources, may compete with us for the acquisition or license of product candidates and approved products. We may not be able to acquire or license the rights to additional product candidates and approved products on terms that we find acceptable, or at all.

A significant portion of the research that we are conducting involves new and unproven technologies. Research programs to identify new disease targets and product candidates require substantial technical, financial and human resources whether or not we ultimately identify any candidates. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

If we are unable to develop suitable potential product candidates through internal research programs or by obtaining rights to novel therapeutics from third parties, our business will suffer.

If we do not find collaborators for our future product candidates, we may have to reduce or delay our rate of product development and commercialization and/or increase our expenditures.

Our strategy to develop and commercialize our products includes entering into various relationships with pharmaceutical or biotechnology companies to advance our programs. We may not be able to negotiate any collaborations on acceptable terms. If we are not able to establish collaborative arrangements, we may have to reduce or delay further development of some of our programs and/or increase our expenditures and undertake the development activities at our own expense.

If we are able to identify and reach agreement with collaborators for our product candidates, those relationships will also be subject to a number of risks, including:

- collaborators may not pursue further development and commercialization of compounds resulting from collaborations or may elect not to renew research and development programs;
- collaborators may delay clinical trials, underfund a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require the development of a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to one or more of our products may not commit sufficient resources to the marketing and distribution of our products, limiting our potential revenues from the commercialization of these products; and
- disputes may arise delaying or terminating the research, development or commercialization of our product candidates, or result in significant litigation or arbitration.

Seasonal fluctuations in demand for our current product candidates may cause our operating results to vary significantly from quarter to quarter.

We expect physician and patient demand for our antibiotic products to be higher between October and February due to greater amounts of respiratory illness in North America during that time period. As a result, our shipments, and therefore revenues, are expected to be higher in the fourth calendar quarter and first calendar quarter reflecting higher demand through that season. We generally expect our revenues during the third calendar quarter to be lower than the other quarters. In addition, fluctuations in the peak and trough of respiratory illness incidence may cause our operating results to vary from year to year. Due to these seasonal fluctuations in demand, our operating results in any particular quarter may not be indicative of the results for any other quarter or for the entire year.

Risks Related to our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our product candidates, and the methods used to manufacture them, as well as

Table of Contents

successfully defending these patents against third-party challenges. Our ability to protect our product candidates from unauthorized making, using, selling, offering to sell or importation by third parties is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

As of March 31, 2006, we have exclusively licensed from Daiichi Asubio two issued U.S. patents, one issued foreign patent and one pending U.S. patent application covering Orapem, a prodrug of faropenem. The two issued U.S. patents covering Orapem also cover other potential prodrugs of faropenem but do not cover all potential faropenem-based antibiotic compounds. We do not and have not had any control over the filing or prosecution of these patents or patent applications. We cannot be certain that such prosecution efforts have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. In addition, our enforcement of these Orapem patents or defense of any claims asserting the invalidity of these patents would be subject to the cooperation of Daiichi Asubio and Forest Laboratories. Although Daiichi Asubio and Forest Laboratories have agreed to cooperate with us in such efforts, if requested, we cannot be assured that Daiichi Asubio and Forest Laboratories would devote sufficient efforts to cooperate with us in these circumstances.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the U.S. The biotechnology patent situation outside the U.S. is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our licensed patents, our patents or in third-party patents.

Daiichi Asubio owns a portfolio of patents related to faropenem compounds, including the faropenem parent compound, Orapem and other faropenem prodrugs. We have licensed from Daiichi Asubio the patents to Orapem and other faropenem prodrugs. These patents may not prevent competitors from developing other faropenem drugs that are not covered by the Daiichi Asubio patents. Beginning in 2008, when the Daiichi Asubio patents expire, competitors may submit NDAs seeking approval of antibiotics containing the faropenem parent compound as the active ingredient. These applications would have to contain full reports of safety and efficacy data conducted by or for the applicants and could not in any way rely upon the safety and efficacy data utilized in the approval of Orapem. In addition, as early as four years after the approval of the Orapem NDA, generic and branded competitors could also file NDAs seeking approval of faropenem drugs that would likely require the applicant to conduct clinical trials in order to bring the product to market in the U.S., though the FDA may allow the applicant to rely in part on the FDA s prior findings of safety and efficacy of Orapem. To the extent that any competitor relies on any of the findings of safety or efficacy with respect to Orapem, the competitor will have to certify that its compound either does not infringe our patents or that our patents are invalid.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our licensed patents, or for which we are not licensed under our license agreements;
- we or our licensors might not have been the first to make the inventions covered by our pending patent application or the pending patent applications and issued patents of our licensors;
- we or our licensors might not have been the first to file patent applications for these inventions;

Table of Contents

others may independently develop similar or alternative technologies or duplicate any of our technologies;

it is possible that our pending patent applications will not result in issued patents;

our issued patents and the issued patents of our licensors may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges by third parties;

we may not develop additional proprietary technologies that are patentable; or

the patents of others may have an adverse effect on our business.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights and we may be unable to protect our rights to, or use, our technology.

If we choose to go to court to stop someone else from using the inventions claimed in our patents or our licensed patents, that individual or company has the right to ask the court to rule that these patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the other party on the ground that such other party s activities do not infringe our rights to these patents.

Furthermore, a third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party s patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our product candidates. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and technical personnel. There is a risk that a court would decide that we or our commercialization partners are infringing the third party s patents and would order us or our partners to stop the activities covered by the patents. In addition, there is a risk that a court will order us or our partners to pay the other party damages for having violated the other party s patents. We have indemnified our commercial partners against patent infringement claims. The biotechnology industry has produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use either do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid, and we may not be able to do this. Proving invalidity, in particular, is difficult since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents.

Because some patent applications in the U.S. may be maintained in secrecy until the patents are issued, because patent applications in the U.S. and many foreign jurisdictions are typically not published until eighteen months after filing, and because publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our licensors issued patents or our pending applications or our licensors pending applications, or that we or our licensors were the first to invent the technology. Our competitors may have filed, and

Table of Contents

may in the future file, patent applications covering technology similar to ours. Any such patent application may have priority over our or our licensors patent applications and could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the U.S. Patent and Trademark Office to determine priority of invention in the U.S. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our U.S. patent position with respect to such inventions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Risks Related to this Offering and Ownership of our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. We cannot assure you that an active trading market for our common stock will develop following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares will be determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the trading market.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

- announcement of FDA approval or non-approval of our product candidates, or specific label indications for their use, or delays in the FDA review process;
- actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing process or sales and marketing activities;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- the success of our development efforts and clinical trials;
- the success of our efforts to acquire or in-license additional products or product candidates;
- developments concerning our collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- actual or anticipated variations in our quarterly operating results;
- announcements of technological innovations by us, our collaborators or our competitors;
- new products or services introduced or announced by us or our commercialization partners, or our competitors and the timing of these introductions or announcements;
- actual or anticipated changes in earnings estimates or recommendations by securities analysts;
- conditions or trends in the biotechnology and biopharmaceutical industries;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors;

Table of Contents

changes in the market valuations of similar companies;

sales of common stock or other securities by us or our stockholders in the future;

additions or departures of key scientific or management personnel;

developments relating to proprietary rights held by us or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

trading volume of our common stock; and

sales of our common stock by us or our stockholders.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially adversely affect our business and financial condition.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

Our executive officers, directors and principal stockholders, together with their respective affiliates, currently own approximately 81% of our voting stock, including shares subject to outstanding options, and we expect that upon completion of this offering that same group will continue to hold at least a majority of our outstanding voting stock. Accordingly, even after this offering, these stockholders will likely be able to determine the composition of our board of directors, retain the voting power to approve all matters requiring stockholder approval and continue to have significant influence over our operations. This concentration of ownership could have the effect of delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the market value of our common stock.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission and the Nasdaq National Market, have imposed various new requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations will increase 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.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, commencing in fiscal 2007, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management and our independent registered public accounting firm to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses.

Table of Contents

Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources.

Future sales of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market after this offering, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. After this offering, we will have 26,327,003 shares of common stock outstanding.

Substantially all of our existing stockholders are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders ability to transfer shares of our common stock for at least 180 days from the date of this prospectus. The lock-up agreements, together with restrictions under the securities laws described in Shares Eligible for Future Sale limit the number of shares of common stock that may be sold immediately following the public offering.

All of the shares of common stock sold in this offering will be freely tradable without restrictions or further registration under the Securities Act of 1933, as amended, except for any shares purchased by our affiliates as defined in Rule 144 under the Securities Act. Rule 144 defines an affiliate as a person that directly, or indirectly through one or more intermediaries, controls, or is controlled by, or is under common control with, us and would include persons such as our directors and executive officers. The remaining 21,327,003 shares of common stock outstanding after this offering will be available for sale as described in the Shares Eligible for Future Sale section of this prospectus.

If you purchase shares of common stock sold in this offering, you will experience immediate dilution. You will experience further dilution if we issue shares in future financing transactions or upon exercise of options or warrants.

If you purchase shares of common stock in this offering, you will experience immediate dilution of $10.50 per share because the price that you pay will be substantially greater than the net tangible book value per share of the shares you acquire. This dilution is due in large part to the fact that our earlier investors paid substantially less than the initial public offering price when they purchased their shares.

If we raise additional funds by issuing additional common stock, or securities convertible into or exchangeable or exercisable for common stock, our stockholders will experience additional dilution, and new investors could have rights superior to existing stockholders.

Pursuant to our 2006 Equity Incentive Plan, our management is authorized to grant stock options to our employees, directors and consultants, and following the completion of this offering, our employees will be eligible to participate in our 2006 Employee Stock Purchase Plan. In addition, we also have warrants outstanding to purchase shares of our common stock. You will incur dilution upon exercise of any outstanding stock options or warrants.

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management s attention and resources, which could harm our business.

Table of Contents

We have broad discretion to use the net proceeds from this offering and our investment of these proceeds may not yield a favorable return.

Our management has broad discretion as to how to spend and invest the proceeds from this offering, and we may spend or invest these proceeds in ways with which our stockholders may not agree. Accordingly, you will need to rely on our judgment with respect to the use of these proceeds, and you will not have the opportunity as part of your investment decision to assess whether they are being used or invested appropriately. We plan to invest the net proceeds of this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code, if a corporation undergoes an ownership change (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We believe that, with our initial public offering, our most recent private placement and other transactions that have occurred over the past three years, we have triggered an ownership change limitation. We have performed an analysis to determine to what extent our ability to utilize our net operating loss carryforwards is limited. We may also experience ownership change in the future as a result of subsequent shifts in our stock ownership. At December 31, 2005, the Company had approximately $67.9 million of net operating loss carryforwards and approximately $1.4 million of research and experimentation credits which may be used to offset future taxable income.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders.

Provisions in our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions include:

- authorizing the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. 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.

Table of Contents

FORWARD-LOOKING STATEMENTS

Some of the statements under Prospectus Summary, Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations , Business and elsewhere in this prospectus contain forward-looking statements. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, estimate, predict, project, potential, c negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- the success and timing of our pre-clinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates and the labeling under any approval we may obtain;
- our plans to develop and commercialize our product candidates;
- the loss of key scientific or management personnel;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the U.S. and foreign countries;
- the rate and degree of market acceptance of any future products;
- our use of the proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the successful development of our sales and marketing capabilities;
- the success of competing drugs that are or become available; and
- the performance of third party manufacturers.

In addition, you should refer to the Risk Factors section of this prospectus for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933 do not protect any forward-looking statements that we make in connection with this offering.

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where 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 any sale of our common stock. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of our common stock in this offering will be approximately $68.2 million, or approximately $78.6 if the underwriters exercise their over-allotment option in full, based upon an assumed initial public offering price of $15.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses. A $1.00 increase (decrease) in the assumed initial public offering price of $15.00 per share would increase (decrease) the net proceeds to us from this offering by $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently expect to use our net proceeds from this offering as follows:

- approximately $33.0 million to fund clinical trials and other research and development activities for Orapem;
- approximately $21.0 million to fund future clinical trials for REP8839;
- approximately $8.0 million to fund activities in preparation for the potential commercial launch of Orapem; and
- the remainder, along with our available cash and cash equivalents, short-term investments and interest earned, to fund working capital and other general corporate purposes, including sales, general and administrative expenses and potential further expansion of our employee base and facilities, as well as amounts due to Daiichi Asubio under our license agreement, which amounts are uncertain as to timing and dependent on the achievement of milestones.

We may also use a portion of the proceeds for the potential acquisition of, or investment in, other product candidates, intellectual property rights or companies that complement our business, although we have no current understandings, commitments or agreements to do so.

This expected use of net proceeds of this offering represents our current intentions based upon our present plans and business conditions. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering. Accordingly, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the proceeds of this offering. Pending their uses, we plan to invest the net proceeds of this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

We do not expect the net proceeds from this offering alone to be sufficient to fully support commercial scale operations if we successfully commercialize Orapem or to fund the completion of development of our REP8839 product candidate, any product candidates generated from our discovery research program or our Orapem product candidate for certain indications. We intend to use our cash and cash equivalents, short-term investments, funding received or made available under our collaboration agreement with Forest Laboratories and interest earned on these balances toward the additional funding necessary to support these activities. If the funds provided by these sources are insufficient to satisfy our future capital needs, or if we develop additional products or pursue additional applications for our products, or conduct additional clinical trials beyond those currently contemplated, we may seek to sell additional equity or debt securities or acquire a credit facility. Any such required additional capital may not be available on reasonable terms, if at all. If we are unable to obtain additional financ