REPLIDYNE INC
Form S-1
April 05, 2006

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As filed with the Securities and Exchange Commission on April 5, 2006
Registration No. 333-

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

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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Cooley Godward LLP	**Wilson Sonsini Goodrich & Rosati**
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	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee
Common Stock, $0.001 par value per share	$100,000,000	$10,700

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended.

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.

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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 , 2006

Shares
Common Stock

We are offering 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 $ and $ per share.

We have applied to have our common stock approved for quotation on the Nasdaq National Market under the symbol RDYN.

Investing in our common stock involves risks. See Risk Factors beginning on page 6.

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 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 & Company **Pacific Growth Equities, LLC**

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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.

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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. Forest Laboratories is our partner for the development and commercialization of Orapem in the U.S. Orapem is a member of the penem family within the beta-lactam class of 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, expert treatment guidelines recommend the use of beta-lactams as first-line therapy in many respiratory and skin infections in adult and pediatric patients. In December 2005, we submitted an NDA to the 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 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 expect to file an IND for the clinical development of our second product candidate, REP8839, in 2006. We are developing REP8839 for topical use for skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of MRSA infections in hospital settings. We are also pursuing the development of other novel anti-infective products based on our in-house discovery research platform and library of proprietary compounds.

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. Although the efficacy data for acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections may be 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

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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 a member of a novel class of selective inhibitors of methionyl tRNA synthetase. REP8839 has exhibited promising activity against *S. aureus,* including MRSA, in pre-clinical studies. We expect to file an IND application in 2006 for the clinical development of a REP8839/mupirocin combination product for topical use for skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of 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 in-house discovery research platform and library of proprietary compounds. We are using our proprietary bacterial DNA replication inhibitor technology to develop novel products to treat bacterial infections. 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 in lead optimization in this program. We have also selected from a proprietary library several potential compounds for development to treat infections in hospital settings caused by *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 $190.0 million in development and 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 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.

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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 three indications: treatment of skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of 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.

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.

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THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding after this offering	shares
Use of proceeds	To fund clinical trials and other research and development activities; for future milestone payments to licensors; 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 shares of common stock outstanding as of and excludes:

shares of common stock issuable upon the exercise of outstanding options, with a weighted average exercise price of $ per share;

shares of common stock reserved for future issuance under our benefit plans; and

shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of $ per share.

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

a one-for- reverse stock split of our common stock;

the conversion of all our outstanding shares of preferred stock into shares of common stock;

the issuance of 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 , 2006 and the initial public offering price is $ 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.

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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. 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 December 31, 2005 as adjusted for the sale of shares of our common stock in this offering at an assumed initial offering price to the public of $ 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,		
	2003	**2004**	**2005**
	(in thousands, except share and per share amounts)		
Statement of Operations Data:			
Revenue	$ 726	$ 834	$ 441
Costs and expenses:			
Research and development	12,331	16,282	29,180
Sales, general and administrative	2,155	2,994	5,329
Total costs and expenses	14,486	19,276	34,509
Loss from operations	(13,760)	(18,442)	(34,068)
Other (expense) income, net	(190)	(797)	399
Net loss	(13,950)	(19,239)	(33,669)
Preferred stock dividends and accretion	(1,294)	(3,560)	(7,191)
Net loss attributable to common stockholders	$ (15,244)	$ (22,799)	$ (40,860)
Basic and diluted net loss attributable to common stockholders per share(1):			
Historical	$ (4.25)	$ (6.23)	$ (7.99)
Pro forma (unaudited)			$
Weighted average shares outstanding(1):			
Historical	3,589,945	3,659,885	5,111,873
Pro forma (unaudited)			

As of December 31, 2005

	Actual	Pro Forma As Adjusted
		(unaudited)
	(in thousands)	
Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 59,420	
Working capital	50,755	
Total assets	63,579	
Deficit accumulated during the development stage	(83,114)	
Preferred stock	136,815	
Total stockholders deficit	(82,632)	

(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.

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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 not be successful. We need approval of the U.S. Food and Drug Administration, or FDA, prior to marketing our product candidates in the U.S. In December 2005, we submitted our first New Drug Application, or 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. If any such approval 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 the initial FDA approval. Also, an approval might contain significant limitations in the form of narrow indications, warnings, precautions or contra-indications with respect to conditions of use. 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 applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our applications or any particular indication for which we are seeking approval. If any of these outcomes occur, we may be forced to abandon our applications 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 the 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 their facility in Takaoka, Japan, we expect to have to demonstrate to the satisfaction of the FDA the comparability of the active compound we are sourcing from Nippon Soda s new facility in Nihongi, Japan.

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. The FDA has recently indicated 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. The FDA may also require placebo-controlled trials before considering the approval of Orapem for other indications, including for one or more 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 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.

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 Holdings Limited, or 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

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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.

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.

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

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meaningful revenue. Our commercial opportunity will also be reduced or eliminated if our competitors develop and commercialize antibiotics that are safer, more effective, have fewer side effects or are less expensive than our product candidates.

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 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.

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.

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

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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;
- 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.

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.

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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

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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 $ 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.

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.

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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 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.

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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, or CROs, to provide monitors for and to manage data for our on-going clinical programs. We and our CROs 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 CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials 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 CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs 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

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

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 proposals in recent years to change the healthcare system in ways that could impact our ability to sell our products profitably. These proposals include prescription drug benefit proposals for Medicare beneficiaries and measures that would limit or prohibit payments for certain medical treatments or subject the pricing of drugs to government control. Legislation creating a prescription drug benefit and making certain changes in Medicaid reimbursement has recently been enacted. In particular, in December 2003, President Bush signed into law new Medicare prescription drug coverage legislation that changes the methodology used to calculate reimbursement for drugs such as Orapem. In addition, the legislation directs the Secretary of Health and Human Services to contract with procurement organizations to purchase physician-administered drugs from the manufacturers and provides physicians with the option to obtain drugs through these organizations as an alternative to purchasing from the manufacturers, which some physicians may find advantageous. In addition, the Centers for Medicare and Medicaid Services, or CMS, the agency within the Department of Health and Human Services that administers Medicare and will be responsible for reimbursement of the cost of Orapem, has asserted the authority of Medicare not to cover particular drugs if it determines that they are not reasonable and necessary for Medicare beneficiaries, or to cover them at a lesser rate, comparable to that for drugs already reimbursed that CMS considers to be therapeutically comparable. The availability of numerous generic antibiotics at lower prices than branded antibiotics such as Orapem, if it were approved for commercial introduction, can be expected to substantially reduce the likelihood of reimbursement for Orapem. Further federal and state proposals and healthcare reforms are likely.

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. 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.

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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, 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.

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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 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 rights related to Orapem under two issued U.S. patents and one issued foreign patent, as well as to one pending U.S. patent application. 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.

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;
- 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.

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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 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.

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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;
- 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.

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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. 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 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.

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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. The remaining shares of common stock outstanding after this offering will be available for sale, with shares of common stock, plus an additional shares issuable upon the exercise of outstanding options and shares issuable upon the exercise of outstanding warrants, available for sale after the expiration of contractual lock-up period, subject to volume limitations under Rule 144 under the Securities Act. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Morgan Stanley & Co. Incorporated, consenting together, could release all or some portion of the shares subject to lock-up agreements prior to expiration of the lock-up period.

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 $ 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.

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

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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. As of December 31, 2005 we had net operating loss carryforwards of approximately $24.9 million and $2.2 million for federal and state income tax purposes, respectively.

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. 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.

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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.

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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 $ million, or approximately $ if the underwriters exercise their over-allotment option in full, based upon an assumed initial public offering price of $ 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 $ per share would increase (decrease) the net proceeds to us from this offering by $ 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 $ million to fund clinical trials and other research and development activities;
- approximately $ million in future milestone payments to licensors;
- approximately $ million to fund activities in preparation for the potential commercial launch of Orapem; and
- the remainder to fund working capital, capital expenditures and other general corporate purposes.

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.

The amount and timing of our expenditures will depend on several factors, including the progress of our research and development efforts and the amount of cash used by our operations. 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 believe that the net proceeds from this offering, together with our existing cash and cash equivalents, short-term investments, funding received from our collaboration agreements and interest earned on these balances, will be sufficient to satisfy our anticipated cash needs for working capital and capital expenditures through at least the next 18 months.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

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CAPITALIZATION

The following table sets forth our capitalization as of December 31, 2005:

- on an actual basis,
- on a pro forma as adjusted basis to reflect:
  - the filing of a restated certificate of incorporation to authorize shares of common stock and shares of undesignated preferred stock;
  - the sale of shares of common stock in this offering at an assumed initial offering price of $ per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses;
  - the conversion of all of our outstanding shares of preferred stock into shares of common stock upon the closing of this offering; and
  - the issuance of shares of common stock upon the closing of this offering in satisfaction of accumulated dividends on our Series A, B, C and D convertible preferred stock, assuming an initial public offering price of $ per share, and the closing of this offering occurs on , 2006.

You should read the information in this table together with our financial statements and accompanying notes and Management s Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus.

	As of December 31, 2005	
	Actual	Pro Forma As Adjusted
	(unaudited)	
	(in thousands, except share data)	
Cash, cash equivalents and short-term investments	$ 59,420	$
Preferred stock, $0.01 to $0.001 par value: 88,862,226 authorized, 88,522,222 issued and outstanding shares, actual; no authorized, issued and outstanding shares, as adjusted	136,815	
Stockholders deficit:		
Common stock, $0.001 par value: 115,000,000 authorized shares; 9,306,129 issued shares and 9,156,129 outstanding shares, actual; authorized shares; issued shares and outstanding shares, as adjusted	9	
Additional paid-in capital		
Treasury stock, $0.01 par value; 150,000 shares	(2)	
Deferred stock-based compensation	(4)	
Accumulated other comprehensive income	479	
Deficit accumulated during the development stage	(83,114)	

Total stockholders (deficit) equity	(82,632)	
Total capitalization	$ 54,183	$

The outstanding share information in the table above excludes:

shares of common stock issuable upon the exercise of outstanding options, with a weighted average exercise price of $ per share;

shares of common stock reserved for future issuance under our benefit plans; and

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shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of $ per share.

We expect to complete a one-for- reverse stock split of our common stock before the completion of this offering. All share amounts have been retroactively adjusted to give effect to this stock split.

The terms of our existing Series A, B, C and D convertible preferred stock require us, upon the closing of this offering, to issue additional shares of common stock to the preferred stockholders in satisfaction of accumulated dividends on the preferred stock. The accumulated dividends were $12.7 million at December 31, 2005 and continue to accumulate at the rate of approximately $843 per month thereafter. The common stock issued in satisfaction of those dividends will be valued at the public offering price per share in this offering. Accordingly, the actual amount of shares we issue upon the closing of this offering in satisfaction of the accumulated dividends will depend both upon the timing and the pricing of this offering.

A $1.00 increase in the assumed initial public offering price above $ per share would decrease the number of shares of common stock to be issued to the holders of Series A, B, C and D convertible preferred stock in satisfaction of accumulated dividends on such preferred stock by approximately shares and a $1.00 decrease in the assumed initial public offering price below $ per share would increase the number of shares of common stock to be issued to the holders of Series A, B, C and D convertible preferred stock in satisfaction of accumulated dividends on such preferred stock by approximately shares.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the initial public offering price per share and the pro forma net tangible book value per share of our common stock after this offering. The historical net tangible book value (deficit) of our common stock as of , 2006 was approximately $ million, or approximately $ per share, based on the number of shares outstanding as of , 2006, as adjusted to reflect the one-for- reverse split of our common stock to be effected prior to the completion of this offering. Historical net tangible book value per share is determined by dividing the number of outstanding shares of our common stock into our total tangible assets (total assets less intangible assets) less total liabilities.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to the sale of common stock offered in this offering at an assumed initial public offering price of $ per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and after giving effect to the conversion of all outstanding shares of preferred stock into shares of common stock upon completion of this offering and the assumed issuance of shares of common stock upon the closing of this offering in satisfaction of accumulated dividends on our Series A, B, C and D convertible preferred stock, our pro forma as adjusted net tangible book value as of , 2006 would have been approximately $ million, or approximately $ per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of $ per share to existing stockholders, and an immediate dilution of $ per share to investors participating in this offering. The following table illustrates this per share dilution:

Assumed initial public offering price per share		$
Historical net tangible book value per share as of , 2006	$	
Decrease in net tangible book value per share attributable to conversion of convertible preferred stock and issuance of shares of common stock in satisfaction of accumulated dividends on convertible preferred stock		
Pro forma net tangible book value per share before this offering	$	
Increase in net tangible book value per share attributable to investors participating in this offering		
Pro forma as adjusted net tangible book value per share after this offering		$
Dilution per share to investors participating in this offering		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the pro forma net tangible book value before this offering by $ per share, the pro forma net tangible book value after this offering by $ per share and the dilution to investors in this offering by $ per share, 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.

If the underwriters exercise their over-allotment option in full to purchase additional shares of common stock in this offering, the pro forma as adjusted net tangible book value after the offering would be $ per share, the increase in the pro forma net tangible book value attributable to investors in this offering would be $ per share and the dilution to new investors purchasing common stock in this offering would be $ per share.

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The following table summarizes, on a pro forma as adjusted basis as of , 2006, the differences between the number of shares of common stock purchased from us, the total consideration and the average price per share paid by stockholders and by investors participating in this offering, after deducting underwriting discounts and commissions and estimated offering expenses, at an assumed initial public offering price of $ per share:

	Shares Purchased		Total Consideration		
	Number	Percent	Amount	Percent	Average Price Per Share
Existing stockholders before this offering		%	$	%	$
Investors participating in this offering					
Total		100%	$	100%	

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the total consideration paid by new investors by $ million, or increase (decrease) the percent of total consideration paid by new investors by %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The number of shares of common stock outstanding in the table above is based on the number of shares outstanding as of , 2006 and assumes no exercise of the underwriters over-allotment option. If the underwriters over-allotment option is exercised in full, the number of shares of common stock held by existing stockholders will be reduced to % of the total number of shares of common stock to be outstanding after this offering and the number of shares of common stock held by investors participating in this offering will be increased to shares or % of the total number of shares of common stock to be outstanding after this offering.

The above discussion and tables also assume no exercise of any outstanding stock options or warrants. As of , 2006, there were:

- shares of common stock subject to outstanding options, having a weighted average exercise price of $ per share;
- shares of common stock reserved for future issuance under our benefit plans as of the completion of this offering; and
- shares of common stock subject to outstanding warrants, having a weighted average exercise price of $ per share.

Effective upon the completion of this offering, an aggregate of shares of our common stock will be reserved for issuance under our benefit plans, and these share reserves will also be subject to automatic annual increases in accordance with the terms of the plans. To the extent that any of these options or warrants are exercised, new options are issued under our benefit plans or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

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SELECTED FINANCIAL DATA

The following selected financial data should be read together with our financial statements and accompanying notes and Management s Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus. The selected financial data in this section is not intended to replace our financial statements and the accompanying notes. Our historical results are not necessarily indicative of our future results.

The consolidated statements of operations data for the years ended December 31, 2003, 2004 and 2005 and the consolidated balance sheet data as of December 31, 2003, 2004 and 2005 are derived from our audited financial statements appearing elsewhere in this prospectus, which have been audited by KPMG LLP. The statements of operations data for the period from December 6, 2000 (date of inception) to December 31, 2001 and for the year ended December 31, 2002 and the consolidated balance sheet data as of December 31, 2001 and 2002 are derived from our unaudited financial statements not included in this prospectus.

The pro forma basic and diluted net loss per common share data for the year ended December 31, 2005 reflect the mandatory conversion, upon the closing of this offering, of the Series A, B, C and D convertible preferred stock at their respective conversion rates into our common stock and the issuance of shares of common stock in satisfaction of the accumulated dividends on the Series A, B, C and D convertible preferred stock through the end of the applicable period based on an assumed initial public offering price of $ per share, as if the conversion had occurred at December 31, 2005.

	For the Period from December 6, 2000 (Date of Inception) to December 31, 2001	Years Ended December 31,			
		2002	2003	2004	2005
	(in thousands, except share and per share amounts)				
	(unaudited)	(unaudited)			
Statement of Operations Data:					
Revenue	$ 49	$	$ 726	$ 834	$ 441
Costs and expenses:					
Research and development	125	2,517	12,331	16,282	29,180
Sales, general and administrative	397	1,275	2,155	2,994	5,329
Total costs and expenses	522	3,792	14,486	19,276	34,509
Loss from operations	(473)	(3,792)	(13,760)	(18,442)	(34,068)
Other (expense) income, net	(12)	30	(190)	(797)	399
Net loss	(485)	(3,762)	(13,950)	(19,239)	(33,669)
Preferred stock dividends and accretion		(915)	(1,294)	(3,560)	(7,191)
Net loss attributable to common stockholders	$ (485)	$ (4,677)	$ (15,244)	$ (22,799)	$ (40,860)

Basic and diluted net loss attributable to common stockholders per share(1):					
Historical	$ (0.15)	$ (1.34)	$ (4.25)	$ (6.23)	$ (7.99)
Pro forma (unaudited)					$
Weighted average shares outstanding(1):					
Historical	3,308,238	3,479,725	3,589,945	3,659,885	5,111,873
Pro forma (unaudited)					

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	As of December 31,				
	2001	2002	2003	2004	2005
	(unaudited)				
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 80	$ 8,549	$ 692	$ 27,018	$ 59,420
Working capital	(498)	7,400	(1,657)	24,409	50,755
Total assets	412	11,988	4,169	30,067	63,579
Long-term debt, net of current portion and discount		1,688	1,208	84	
Deficit accumulated during the development stage	(485)	(4,963)	(20,108)	(42,238)	(83,114)
Preferred stock		13,764	20,058	69,447	136,815
Total stockholders deficit	(428)	(4,918)	(20,115)	(42,202)	(82,632)

(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.

Effective April 12, 2005, KPMG LLP was engaged as our independent registered public accounting firm and replaced PricewaterhouseCoopers LLP, who were dismissed as our independent registered public accounting firm. The decision to change independent registered public accounting firms was approved by our Audit Committee of the Board of Directors. PricewaterhouseCoopers LLP reported on our financial statements as of and for the years ended December 31, 2002 and 2003, and cumulatively for the period from December 6, 2000 (date of inception) to December 31, 2003. Except for an explanatory paragraph expressing significant doubt about the ability of Replidyne to continue as a going concern, the report of PricewaterhouseCoopers LLP on those financial statements did not contain an adverse opinion or disclaimer of opinion and was not qualified or modified as to uncertainty, audit scope or accounting principles. During the years ended December 31, 2002 and 2003 and through April 12, 2005, we did not have any disagreements with PricewaterhouseCoopers LLP on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedure, which disagreements, if not resolved to their satisfaction, would have caused them to make reference thereto in connection with their report on the financial statements for such years. PricewaterhouseCoopers LLP has not audited or reported on any financial statements or information included in this prospectus. For purposes of this filing, the financial statements for the years ended December 31, 2003, 2004 and 2005 (and for the period from December 6, 2000 through December 31, 2005) have been audited by KPMG LLP. Prior to retaining KPMG LLP, we had not consulted with KPMG LLP on items that involved our accounting principles or the form of audit opinion to be issued on our financial statements. PricewaterhouseCoopers LLP s letter to the Securities and Exchange Commission stating its agreement with the statements in this paragraph is filed as an exhibit to the registration statement of which this prospectus is a part.

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MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis together with our financial statements and the notes to those statements included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. As a result of many factors, such as those set forth under Risk Factors and elsewhere in this prospectus, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a biopharmaceutical company initially focused on discovering, developing, in-licensing and commercializing innovative anti-infective products. Our lead product, Orapem, is a novel oral community antibiotic for which we have filed an NDA. In December 2005, we submitted to the FDA our NDA for Orapem for four indications: acute bacterial sinusitis, community-acquired pneumonia, acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections. Although the efficacy data for acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections may be 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 have entered into a collaboration and commercialization agreement with Forest Laboratories to co-develop and co-market Orapem in the U.S. We and Forest Laboratories 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 seeking clinical indications for the two largest pediatric indications: acute otitis media and tonsillitis/pharyngitis.

Our second product candidate is REP8839, which we are developing for topical use for skin and wound infections, eradication of *Staphylococcus aureus,* or *S. aureus,* in hospital settings and prevention of methicillin-resistant *S. aureus,* or MRSA, infections in hospital settings. REP8839 is a member of a novel class of selective inhibitors of methionyl tRNA synthetase and, in pre-clinical studies, has shown promising activity. We expect to file an investigational new drug application, or IND, for the development of a REP8839/mupirocin combination product in 2006.

We are also pursuing the development of other novel anti-infective products based on our in-house discovery research platform and library of proprietary compounds. We are using our proprietary bacterial DNA replication inhibitor technology to develop novel products to treat bacterial infections. We have also selected from a proprietary library several potential compounds for development to treat infections in hospital settings caused by *C. difficile* and are in late pre-clinical testing.

We were incorporated on December 6, 2000 in Delaware. Prior to inception, we had not commenced any significant activity to develop our technology. On December 6, 2000, an affiliated entity contributed certain assets and liabilities to us, which we recorded at their historical cost at that time, and we commenced development activity. Since our inception, we have focused on the in-license and acquisition of technology and acquisition of our technology acquired as in-process research and development, the selection of pre-clinical testing of product candidates and the manufacture of clinical trial supplies. The majority of our activities have been in support of the development of Orapem and REP8839.

We have incurred significant operating losses since our inception on December 6, 2000, and, as of December 31, 2005, we had an accumulated net loss of $71.1 million and accumulated net loss attributable to common stockholders of $84.1 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, subsequent to December 31, 2005, from payments by Forest Laboratories under our collaboration and commercialization agreement. We expect to continue to incur substantial operating losses for the next several years as we pursue our clinical trials and research and development efforts.

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Our Collaboration with Forest Laboratories

In February 2006, we entered into a collaboration and commercialization agreement with Forest Laboratories to be our exclusive partner for the development and marketing of Orapem in the U.S. We granted Forest Laboratories a right of first refusal to extend the territory to include Canada. We received an up-front payment of $50.0 million in February 2006 and $10.0 million in milestone payments in March 2006 from Forest Laboratories. We may receive up to an additional $190.0 million in development and commercial milestones for both adult and pediatric indications, which will be reduced by $25.0 million if we exercise our option to directly market and promote Orapem to pediatricians on an exclusive basis, which we expect to do. These milestone payments are largely dependent on the acceptance of additional NDA filings, FDA approvals and achieving certain sales levels of adult and pediatric formulations of Orapem. Forest Laboratories will book all Orapem sales and pay us a co-promotion fee, reimburse our marketing expenses and pay us royalties on all sales, milestones on development of the liquid oral formulation and, provided we exercise our option to market Orapem directly to pediatricians, a portion of the commercialization milestones. Product development activities under the agreement are a joint responsibility between us and Forest Laboratories, although Forest Laboratories is responsible for a substantial portion of development expenses. We maintain access to all data generated in our joint development efforts for use in territories outside the U.S. Forest Laboratories has agreed to assume responsibility for supply chain management in the territory 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. Forest Laboratories is responsible for sales and marketing activities and associated costs.

We will perform marketing and promotion activities directed toward targeted specialists, such as otolaryngologists (ear, nose and throat specialists). With respect to these activities, Forest Laboratories will reimburse us for our sales force expenses incurred during the one year period prior to commencement of these marketing and promotion activities, up to a maximum amount as provided in our agreement. For the five year period after commencement of such marketing and promotion activities, Forest Laboratories will reimburse us for certain marketing and sample expenses (subject to an approved annual budget) and for certain sales force expenses. As to sales forces expenses during this period, Forest Laboratories will reimburse us for all of such expenses incurred during the first two years after commencement of our marketing and promotion activities up to a maximum amount as provided in our agreement, and for the remaining three years Forest Laboratories will reimburse us for such sales force expenses up to a certain percentage of the maximum amount as provided in our agreement. We have the right to retain the majority of the sales margin, defined as net sales less cost of goods and marketing expenses, from the oral liquid formulation of Orapem prescribed by pediatricians, provided we exercise this option at least six months before this formulation is submitted for regulatory approval. If the sales margin is negative, we will bear the majority of the losses in the period they are generated. If we exercise this option, we and Forest Laboratories will jointly determine the product launch and marketing and selling strategies for the oral liquid formulation of Orapem. Further, if we exercise this option, Forest Laboratories will extend us a $60.0 million line of credit to support our promotional efforts to pediatricians.

In accordance with our revenue recognition policy for up-front and milestone payments received under collaboration and commercialization agreements, we intend to recognize revenue for the payments received to date on a straight-line basis over a period of 13.5 years, which is the period of estimated benefit to us. The up-front payment and milestone payment received are non-refundable. We anticipate accounting for amounts received as reimbursements from Forest Laboratories for research and development and sales and marketing activities as revenue. This treatment reflects our role as principal in these transactions whereby we are responsible for selecting vendors, performing significant duties and bearing credit risk.

Financial Operations Overview

Revenue. Through December 31, 2005, we have generated revenue from a research and license agreement. Under the terms of this agreement, to date, we have received up-front license payments and

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periodic, non-refundable milestone payments. As of December 31, 2005, we have no additional obligations under this agreement and no further milestone payments are currently due.

Research and Development Expense. Research and development expense consists primarily of expenses incurred to acquire in-process research and development and to develop and test our product candidates. Such expenses include:

- external research and development expenses, including the costs of materials relating to our pre-clinical studies and clinical trials;
- third party supplier, consultant and employee related expenses, including compensation and benefits;
- license fees associated with acquiring in-process research and development; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, information technology, laboratory and office supplies and depreciation of capital assets used to research and develop our product candidates.

Through December 31, 2005, we have incurred approximately $60.4 million in research and development expenses. Prior to 2003, all research and development activities were related to discovery research activities.

In March 2004, we licensed all rights to Orapem from Daiichi Asubio in the U.S. and Canada. In addition, we have the sole negotiation right to license such rights for the rest of the world, except Japan. Orapem was in development at the time we entered into the license and we accounted for the license of the technology as acquired in-process research and development. Since March 2004, we have focused our efforts on completing the clinical program, establishing commercial scale manufacturing capability and completing other regulatory steps to support the NDA for Orapem that we submitted to the FDA in December 2005. We are in the process of conducting an additional Phase III clinical trial using a higher dose therapy to treat acute exacerbation of chronic bronchitis. We are also seeking to expand the expected labeled indication of Orapem into pediatric markets for treatment of acute otitis media using an oral liquid formulation. To be accepted in the pediatric market, in addition to an excellent safety and efficacy profile, an oral liquid formulation must have a taste that is acceptable to children. We are continuing development work to improve the taste of our oral liquid formulation of Orapem.

We acquired the worldwide rights to the methionyl tRNA synthetase inhibitor program from GlaxoSmithKline PLC, or GSK, in June 2003 in exchange for 4,000,000 shares of our Series B convertible preferred stock at a deemed fair value of $1.25 per share. Because this program was in pre-clinical development at the time we acquired the worldwide rights, we accounted for the acquisition as acquired in-process research and development in 2003. Using this acquired technology, we have continued the development of our product candidate REP8839 for the treatment of skin and wound infections and eradication of *S. aureus* in the hospital setting. We anticipate filing an IND for REP8839 in combination with mupirocin in 2006, and if the IND is approved, to commence a Phase I clinical trial of REP8839/mupirocin in late 2006. Mupirocin is a widely used generic antibiotic that is indicated for treatment of skin infections and nasal decolonization of *S. aureus*.

Our 2005 and current year research and development activities are primarily focused on the clinical development of Orapem. We expect our research and development expense to increase as we advance Orapem, REP8839 and new product candidates into further clinical and pre-clinical development. We are unable to estimate with any certainty the costs we will incur in the continued development of Orapem, REP8839 and our other product candidates. We expect to continue to expand our research and development activities relating to the clinical development of our product candidates and pre-clinical research of treatments in the anti-infective area. If we acquire or in-license additional technologies or product candidates in the clinical or pre-clinical development stage, we also expect to expand our research and development activities to develop these technologies or product candidates.

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Clinical development timelines, likelihood of success and associated costs are uncertain and therefore vary widely. Although we are currently focused primarily on Orapem for the treatment of community-acquired respiratory tract and skin infections and have commenced the clinical trials program for an oral liquid formulation of Orapem for treatment of acute otitis media in pediatric patients, we anticipate that we will make determinations as to which research and development projects to pursue and how much funding to direct toward each project on an on-going basis in response to the scientific and clinical success of each product candidate and each additional indication for Orapem.

Due to the risks inherent in the clinical trial process, development completion dates and costs will vary significantly for each product candidate and are difficult to estimate. The lengthy regulatory approval process requires substantial additional resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals for our product candidates could cause the costs of our research and development to increase and have a material adverse effect on our results of operations. We cannot be certain when any cash flows from our current product candidates will commence.

Sales, General and Administrative Expense. Sales, general and administrative expense consist principally of compensation and related costs for personnel in executive, sales, marketing, corporate development, legal, finance, accounting and human resource functions. Other sales, general and administrative costs include professional fees, costs of insurance and market research.

Interest and Other Income. Interest income consists of interest earned on our cash and cash equivalents and short-term investments. Other income consists primarily of realized gains on short-term investments available-for-sale.

Interest Expense. Interest expense consists of interest incurred on equipment loans and convertible promissory notes.

Loss on Extinguishment of Convertible Notes Payable. Loss on extinguishment of convertible notes payable represents a charge equal to the difference between the carrying amount of our convertible promissory notes on the date the notes were converted to Series C redeemable convertible preferred stock and the fair value of the stock received on conversion in 2004.

Preferred Stock Dividends and Accretion. Preferred stock dividends and accretion consists of cumulative but undeclared dividends payable and accretion of issuance costs on preferred stock. The issuance costs on the shares of Series A, C and D redeemable convertible preferred stock were recorded as a reduction to the carrying amount of the stock when issued, and are accreted to preferred stock ratably through July 31, 2014 by a charge to additional paid-in capital and loss attributable to common stockholders. Upon the completion of this offering, the cumulative but unpaid dividends on Series A, B, C and D preferred stock are payable in shares of common stock at the price of the common stock sold in the offering. Upon closing of this offering, we will no longer record preferred dividends and accretion on the preferred stock, which will convert into common shares upon completion of this offering. As of December 31, 2005, the cumulative dividends payable on our preferred stock totaled $12.7 million.

Critical Accounting Policies and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. Actual results may differ from these estimates. Our significant accounting policies are described in the Note 1 of Notes to Financial Statements appearing elsewhere in this prospectus. We believe the following accounting policies affect our more significant judgments and estimates used in the preparation of our financial statements.

Revenue Recognition. We generate revenue through research, license, collaboration and commercialization agreements. These agreements can contain multiple elements, including non-refundable up-front fees, payments for reimbursement of research and commercialization costs, non-refundable

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payments associated with achieving specific milestones, promotion fees based on marketing margins defined in our agreement with Forest Laboratories and royalties based on specified percentages of net product sales.

In determining when to recognize revenue related to up-front and milestone payments under these agreements we apply the revenue recognition criteria as outlined in EITF Issue 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). In applying these criteria, we consider a variety of factors to determine the appropriate method of revenue recognition, including whether the elements of the agreement are separable, whether payments received are subject to refund or forfeiture, whether there are determinable fair values and whether there is a unique earnings process associated with each element of an agreement.

When a payment is specifically tied to a separate earnings process and the amount to be received is fixed and determinable, revenue is recognized when the performance obligation associated with the payment is completed. Performance obligations typically consist of significant and substantive milestones. Revenues from milestone payments may be considered separable from funding for research, development or commercial activities because of the uncertainty surrounding the achievement of the milestones. Accordingly, these payments could be recognized as revenue when the performance milestone is achieved as described in EITF 00-21. In circumstances where we cannot identify a separate earnings process related to an upfront or milestone payment, we record deferred revenue and recognize revenue ratably over the period of expected benefit, which is generally the unexpired contract term.

Revenues derived from reimbursement of expenses for research, development and commercial activities under our collaboration and commercialization agreements are recorded in compliance with EITF Issue 99-19, *Reporting Revenue Gross as Principal Versus Net as an Agent* (EITF 99-19). In accordance with the criteria established by EITF 99-19, in transactions where we act as principal, with discretion to choose suppliers, bear credit risk and perform a substantive part of the services, revenue is recorded at the gross amount of the reimbursement. Costs associated with these reimbursements are reflected as a component of operating expenses in our statements of operations.

Under our agreement with Forest Laboratories entered into in February 2006, we intend to record the initial $50 million upfront payment received in February 2006 as deferred revenue and recognize this amount into revenue ratably over a 13.5 year period. In addition, we have and may continue to receive payments upon the achievement of certain development and commercial milestones. The first milestone was achieved and a payment of $10 million was received in March 2006. Due to this milestone being achieved within one month of entering into the collaboration and commercialization agreement with Forest Laboratories, we could not identify a separate earnings process related to this milestone payment and will recognize revenue related to this payment over 13.5 years, the expected term of the agreement. In assessing the remaining milestone payments contemplated in our agreement with Forest Laboratories we have reviewed the criteria for achievement of future milestones. Based on this review, we believe that achievement is uncertain and dependent upon a number of factors which will involve substantive effort. We further believe that a unique earnings process has been identified for each of the remaining development and commercial milestones, the amounts received will be fixed and determinable and, therefore, we intend to recognize revenue related to these milestones upon achievement.

We also anticipate receiving amounts from Forest Laboratories as reimbursement for certain research and development and sales and marketing activities under our agreement. We believe that, as it relates to these activities, we will act as the principal, performing a substantive part of the services directly, having the discretion to choose our suppliers and bearing all credit risk associated with the performance of these activities. We therefore intend to record these amounts as revenue in accordance with our revenue recognition policy. See Note 1 to our financial statements for more information about our revenue recognition policies.

Stock-Based Compensation. Through December 31, 2005, we have accounted for employee stock options using the intrinsic-value method in accordance with Accounting Principles Board (APB), Opinion No. 25, *Accounting for Stock Issued to Employees,* Financial Accounting Standards Board (FASB),

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Interpretation No. 44, *Accounting for Certain Transactions Involving Stock Compensation, an interpretation of APB No. 25*, and related interpretations. We have adopted the disclosure-only provisions of Statement of Financial Accounting Standards (SFAS), No. 123, *Accounting for Stock-Based Compensation,* as amended.

Under APB No. 25, we recognized stock-based compensation expense, which is a non-cash charge, when we issued employee stock option grants at exercise prices that, for financial reporting purposes, are deemed to be below the estimated fair value of the underlying common stock on the date of grant. Given the absence of an active market for our common stock, our board of directors determined the estimated fair value of our common stock on the dates of grant based on several factors, including progress against regulatory, clinical and product development milestones; sales of redeemable convertible preferred stock and the related liquidation preference associated with such preferred stock; our progress toward establishing a collaborative development and commercialization partnership for Orapem; changes in valuation of comparable publicly-traded companies; overall equity market conditions; and the likelihood of achieving a liquidity event such as an initial public offering or sale of our company. Based on these factors, during 2005 we valued our common stock and set exercises prices for common stock options at each date of grant within the range of $0.13 to $0.45.

In connection with the preparation of the financial statements necessary for our initial public offering, we obtained an independent valuation of our common stock at September 8, 2005, November 30, 2005 and December 30, 2005. These independent valuations supported the fair value of our common stock established by our board of directors during the year ended December 31, 2005.

While our financial statements account for stock option grants pursuant to APB No. 25, in accordance with SFAS No. 123, we disclose in the notes to our financial statements the pro forma impact on our net loss had we accounted for stock option grants using the fair value method of accounting. This information is presented as if we had accounted for our employee stock options at fair value using the minimum value option-pricing model. Our use of the minimum value model was primarily due to our determination as to its appropriateness as well as its general acceptance as an option valuation technique for private companies. We will not utilize the minimum value method subsequent to our adoption of SFAS 123R on January 1, 2006, and the fair value of our options will be higher as a result. Stock-based compensation expense under APB No. 25 for stock options granted to employees and directors has been determined as the difference between the exercise price and the fair value of our common stock on the date of grant, as estimated by us for financial reporting purposes, on the date those options were granted. It also includes stock-based compensation for options granted to consultants that has been determined in accordance with SFAS No. 123, and Emerging Issues Task Force (EITF) Issue No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring or in Conjunction with Selling Goods and Services,* as the fair value of the equity instruments issued and is periodically revalued as the options vest. Stock-based compensation expense depends on the amount of stock options and other equity compensation awards we grant to our employees, consultants and directors and the exercise price of those options. See Notes 1 and 9 to our financial statements.

Deferred Tax Asset Valuation Allowance. In establishing an allowance on the valuation of our deferred tax assets we are required to make significant estimates and judgments about our future operating results. Our ability to realize deferred tax assets depends on our future taxable income as well as limitations on utilization primarily of net operating losses and tax credits. We are required to reduce our deferred tax assets by a valuation allowance if it is more likely than not that some portion or all of our deferred tax asset will not be realized. As we have historically incurred significant operating losses, it is difficult to conclude with certainty that any of our deferred tax assets will be realized. Accordingly, we have recorded a full valuation allowance on our net deferred tax assets since inception due to uncertainties related to our ability to realize deferred tax assets in the foreseeable future. See Note 10 to our financial statements.

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Results of Operations

Comparison of Years Ended December 31, 2005 and 2004

Revenue. Revenue was $0.4 million for the year ended December 31, 2005, as compared to $0.8 million for the year ended December 31, 2004. The decrease was primarily due to the completion of a research and development project in 2005.

Research and Development Expense. Research and development expenses were $29.2 million for the year ended December 31, 2005 compared to $16.3 million for the year ended December 31, 2004. The increase was primarily due to:

- the commencement of clinical trials for Orapem higher dose therapy for acute exacerbation of chronic bronchitis and an oral liquid formulation for pediatric use;
- activities related to completing our NDA for Orapem that was submitted in December 2005;
- expenses of $2.1 million payable to Daiichi Asubio upon submission of our NDA for Orapem in accordance with the terms of our license agreement;
- expanded pre-clinical development spending on REP8839; and
- increased personnel related costs to support our pre-clinical studies, clinical trials and other discovery efforts.

Research and development expenditures made to advance our product candidates and other research efforts during the years ended December 31, 2005 and 2004 were as follows:

	Years Ended December 31,		Change	
	2004	2005	$	%
	(in thousands)			
Orapem	$ 12,626	$ 24,689	$ 12,063	96%
REP8839	2,629	3,634	1,005	38
Other research and development	1,027	857	(170)	(17)
	$ 16,282	$ 29,180	$ 12,898	79%

Overall, our total external clinical trial and pre-clinical development expenditures increased by $7.4 million and $1.3 million, respectively, in 2005 compared to 2004 related to our clinical and pre-clinical trial activity. The cost of our internal research and development personnel and related costs increased by $3.5 million in 2005 compared to 2004 as we increased our clinical and regulatory head count in support of our clinical development activities. During 2004, our clinical and pre-clinical efforts were focused primarily on preparing to file our Orapem NDA in 2005 and designing clinical studies on Orapem in additional areas, including higher dose therapy for acute exacerbation of chronic bronchitis.

Research and development expenses are expected to increase in 2006 as we:

- advance our Phase III clinical trials for a higher dose adult Orapem therapy;

complete our Phase II clinical trials for an oral liquid formulation of Orapem among pediatric patients; and

initiate clinical development of REP8839.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $5.3 million for the year ended December 31, 2005, as compared to $3.0 million for the year ended December 31, 2004. The increase was primarily due to increased staffing necessary to support our growth, costs of recruiting and relocating personnel and conducting market research, as well as professional service expenses, principally legal expenses related to patent filings and general corporate and licensing activities. We expect increases in sales, general and administrative expense as we add employees, prepare for

commercialization of our product candidates and increase consulting, legal, accounting, insurance and investor relations activities associated with being a public company.

Marketing and sales costs are expected to increase substantially in 2006 as we expand our sales and marketing organization to support the potential commercialization of Orapem. General and administrative costs are expected to increase as a result of increased compensation costs, as well as higher legal, accounting, insurance and other professional service costs relating to compliance obligations associated with being a public company.

Interest and Other Income. Interest and other income was $0.7 million for the year ended December 31, 2005, as compared to $0.2 million for the year ended December 31, 2004. The increase was due to higher overall cash available for investing throughout 2005 as compared to 2004. We sold shares of our Series C redeemable convertible preferred stock in preferred stock financings that were completed in April, August, September and November 2004 with net proceeds of $38.8 million and therefore did not have a full year of interest and other income on the proceeds from that financing in 2004. We sold shares of our Series D redeemable convertible preferred stock in a preferred stock financing that we completed in August 2005 with net proceeds of $60.2 million, which increased our average cash balance available for investment in 2005 compared to 2004.

Interest and Other Expense. Interest expense was $0.3 million for the year ended December 31, 2005, as compared to $0.5 million for the year ended December 31, 2004. The decrease was due to a lower overall debt balance throughout 2004 as compared to 2005. Additionally, we ceased to incur interest expense on our convertible notes payable when the notes were converted to Series C redeemable convertible preferred stock in 2004.

Loss on Extinguishment of Convertible Notes Payable. In 2004, our convertible notes payable were converted into Series C redeemable convertible preferred stock. We recorded a loss of $0.5 million, which amount is equal to the difference between the carrying value of the convertible notes payable and the fair value of the Series C redeemable convertible preferred stock received on conversion.

Comparison of Years Ended December 31, 2004 and 2003

Revenue. Revenue was $0.8 million for the year ended December 31, 2004, as compared to $0.7 million for the year ended December 31, 2003. The increase was primarily due to the timing of scheduled milestone payments under a research and development project.

Research and Development Expense. Research and development expenses were $16.3 million for the year ended December 31, 2004, as compared to $12.3 million for the year ended December 31, 2003. The increase was primarily due to the in-license of Orapem in 2004 and related costs. In 2004, we incurred expenditures of $3.2 million to complete the acquisition of the U.S. and Canadian rights to Orapem and the sole negotiation right to acquire rights to Orapem from Daiichi Asubio for the rest of the world, except Japan. In 2003, we initiated discussions with Daiichi Asubio for these Orapem product rights and incurred expenditures of $0.6 million to enter into a letter of intent. As Orapem was in clinical development at the time we entered into the license agreement, we accounted for the acquisition of the license as in-process research and development. In addition, once we acquired the rights to Orapem, we began preparations to file our NDA for Orapem and design clinical studies to pursue additional indications including higher dose therapies for treatment of acute exacerbation of chronic bronchitis and pediatric indications. In 2003, we acquired the rights that included technology used in our REP8839 program in exchange for 4,000,000 shares of our Series B convertible preferred stock valued at $5.0 million. The full amount was accounted for as acquisition of in-process research and development expenses in 2003.

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Research and development expenditures made to advance our product candidates and other research efforts during the years ended December 31, 2004 and 2003 were as follows:

	Years Ended December 31,		Change	
	2003	2004	$	%
	(in thousands)			
Orapem	$ 634	$ 12,626	$ 11,992	1,891%
REP8839	6,239	2,629	(3,610)	(58)
Other research and development	5,458	1,027	(4,431)	(81)
	$ 12,331	$ 16,282	$ 3,951	33%

Prior to the acquisition of the in-process research and development programs that provided us with Orapem and REP8839, our research and development efforts were focused principally on discovery.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $3.0 million for the year ended December 31, 2004, as compared to $2.2 million for the year ended December 31, 2003. The increase was primarily due to increased personnel and related costs to support our increased research and business development activities, including market research related to assessing the market potential of our product candidates, and professional service expenses, principally legal expenses related to patent filings and general corporate governance and licensing activities.

Interest and Other Income. Interest and other income was $0.2 million for the year ended December 31, 2004, as compared to $0.1 million for the year ended December 31, 2003. This increase was due to higher overall cash available for investing throughout 2004 as compared to 2003. We sold shares of our Series C redeemable convertible preferred stock in financings that we completed in April, August, September and November 2004 with net proceeds of $38.8 million, increasing our cash and cash equivalents and short term investments balances available for investment.

Interest and Other Expense. Interest expense was $0.5 million for the year ended December 31, 2004, as compared to $0.3 million for the year ended December 31, 2003. The increase was due primarily to interest expense on our convertible notes payable that ceased during 2004 upon conversion of the notes into Series C redeemable convertible preferred stock.

Loss on Extinguishment of Convertible Notes Payable. In 2004, outstanding convertible notes were converted into Series C redeemable convertible preferred stock, in connection with which we recorded a loss of $0.5 million, equal to the difference between the carrying value of the convertible notes and the fair value of the Series C redeemable convertible preferred stock issued upon conversion.

Liquidity and Capital Resources

We have incurred losses since our inception in 2000. As of December 31, 2005, we had an accumulated deficit of $83.1 million. We have funded our operations to date principally from private placements of equity securities and convertible notes totaling $121.5 million through December 31, 2005 and, subsequent to December 31, 2005, from payments by Forest Laboratories under our collaboration and commercialization agreement. As of December 31, 2005, we had $59.4 million in cash, cash equivalents and short-term investments classified as securities available-for-sale.

In February 2006, we entered into a collaboration and commercialization agreement with Forest Laboratories for the right to be our development and marketing partner of Orapem in the U.S. We also granted Forest Laboratories a right of first refusal to extend the territory to include Canada. Under our agreement, in February 2006 we have received an up-front payment of $50.0 million and in March 2006 we received a $10.0 million development milestone

payment from Forest Laboratories. We may receive up to an additional $190.0 million in development and commercial milestones for both adult and pediatric indications, which will be reduced by $25.0 million if we exercise our option to directly market and promote Orapem products to pediatricians, which we currently expect to do. These milestone payments are

largely dependent on the acceptance of additional NDA filings, FDA approvals and achieving certain sales levels of adult and pediatric formulations of Orapem. Product development activities under the agreement are a joint responsibility between us and Forest Laboratories although Forest Laboratories is responsible for the substantial portion of development expenses. We will perform marketing and promotion activities directed toward targeted specialists, such as otolaryngologists, for which we will be reimbursed by Forest Laboratories up to established limits in the first year of the agreement. For the following five years, we will be reimbursed up to established limits in accordance with our direct marketing and selling activities. We have the right to retain the majority of the sales margin, defined as net sales less cost of goods and marketing expense, from the oral liquid formulation of Orapem prescribed by pediatricians, provided we exercise this option at least six months before this formulation is submitted for regulatory approval. If we exercise this option, we and Forest Laboratories will jointly determine the product launch and marketing and selling strategies for any approved pediatric formulation of Orapem. Further, if we exercise this option, Forest Laboratories will extend us a $60.0 million line of credit to support our promotional efforts to pediatricians.

In 2002, we entered into an equipment loan and security agreement that provided a line of credit of up to $3.5 million for the purchase of equipment, tenant improvements and software licenses. Through December 31, 2005, we borrowed $3.4 million under this arrangement. The line of credit bears interest at a weighted-average rate of 8.97% and is collateralized by the assets purchased with borrowed funds. As of December 31, 2005, we had $0.2 million in payments remaining on our equipment loan, which was repaid in full by March 31, 2006, and no amounts remain available for additional borrowing under this facility.

In 2005, we entered into interest bearing loans with two of our officers for the purpose of exercising stock options in accordance with the provisions of our equity incentive plan and their option agreements. The loans plus accrued interest, which totaled $0.4 million and bore interest at a market rate, were repaid in full in cash on February 28, 2006.

In 2004, we entered into a license agreement with Daiichi Asubio to develop and commercialize Orapem in the U.S. and Canada and we have the sole negotiation right to license such rights for the rest of the world except Japan. In consideration for the license, we paid an initial license fee of $3.8 million comprising $0.6 million paid in 2003 and paid in $3.2 million in 2004. In December 2005, we recorded research and development expense for a milestone payable of $2.1 million in accordance with the terms of the license agreement following submission of the NDA to the FDA in December 2005. In February 2006, in conjunction with our entering into the license agreement with Forest Laboratories, this milestone payment was increased to ¥375 million (approximately $3.2 million using the U.S. dollar to Japanese yen exchange rate as of December 31, 2005). The increased milestone amount was accounted for as research and development expense in 2006 when the modified terms of the license were finalized. Under the modified license agreement we are further obligated to future payments of (i) up to ¥375 million (approximately $3.2 million as of December 31, 2005) upon filing of an additional NDA in the U.S. or Canada, (ii) up to ¥375 million (approximately $3.2 million as of December 31, 2005) upon initial FDA approval, (iii) ¥500 million (approximately $4.3 million as of December 31, 2005) upon a product launch and (iv) up to ¥875 million (approximately $7.4 million as of December 31, 2005) in subsequent milestone payments for Orapem. Additionally, we are responsible for royalty payments to Daiichi Asubio based upon net sales of Orapem. The license term extends to the later of: (i) the expiration of the last to expire of the licensed patents owned or controlled by Daiichi Asubio or (ii) 12 years after the first commercial launch of Orapem. We have recorded payments made to date as research and development expense, as Orapem has not yet been approved by the FDA.

Under a supply agreement entered into in December 2004 between Daiichi Asubio, Nippon Soda and us, we are obligated to purchase, and Nippon Soda is obligated to supply, all our commercial requirements of the Orapem active pharmaceutical ingredient. At the time of full commercial launch, we are obligated to make certain annual minimum purchase commitments. If the full commercial launch is delayed, we may be obligated for certain delay compensation to Nippon Soda up to ¥280 million (approximately $2.4 million as of December 31, 2005). Under the agreement with Forest Laboratories entered into in February 2006, we are responsible for only the delayed compensation that may accrue for any period ending on or prior to December 31, 2007. Thereafter, Forest Laboratories will be responsible for

any delayed compensation. If we terminate the Orapem program, under certain circumstances we may be obligated to reimburse Nippon Soda for up to ¥65 million (approximately $0.6 million as of December 31, 2005) in engineering costs.

In April 2005, we entered into a supply agreement for production of adult tablets of Orapem with Tropon, which was amended as to certain terms in March 2006. Beginning in 2006, we are obligated to make minimum purchases of Tropon s product of 2.3 million (approximately $2.7 million as of December 31, 2005) annually. An amount equal to 50% of these minimum purchase commitments, if applicable, may be credited against future drug product purchases. Under our agreement with Forest Laboratories, we are responsible for only the minimum purchase commitments in 2006 that may not be credited against future purchases. We are required to buy all of our requirements for adult oral Orapem tablets from Tropon until cumulative purchases exceed a specified amount. If the agreement is terminated, under certain circumstances we may be obligated to pay up to 1.7 million (approximately $2.0 million as of December 31, 2005) in decontamination costs.

In June 2003, we acquired certain intellectual property and supporting material from GSK in exchange for the issuance of 4,000,000 shares of our Series B convertible preferred stock at a fair value of $5.0 million. The acquisition was accounted for as a research and development expense. Under this agreement, we have an obligation to pay GSK $1.5 million upon filing of an IND in cash or equity, at our option. This payment would be due upon filing of an IND for our product candidate REP8839.

In 2006, we anticipate that capital expenditures will total approximately $4.0 million.

We have not yet commercialized our products or achieved profitability. We anticipate that we will continue to incur substantial net losses for the next several years as we develop our products, conduct and complete clinical trials, pursue additional product candidates, expand our clinical development team and corporate infrastructure and prepare for the potential commercial launch of Orapem. We do not anticipate generating any product related revenue until we obtain FDA approval for Orapem and Forest Laboratories launches the product.

We believe that the net proceeds from this offering, together with our current cash and cash equivalents, securities available-for-sale, funding received from our collaboration agreement with Forest Laboratories and interest earned on these balances, will be sufficient to satisfy our anticipated cash needs for working capital and capital expenditures through at least the next 18 months. This forecast of the period in which our financial resources will be adequate to support operations is a forward-looking statement and involves risks, uncertainties and assumptions. Our actual results and the timing of selected events may differ materially from those anticipated as a result of many factors, including but not limited to those discussed under Risk Factors and elsewhere in this prospectus.

Our future capital uses and requirements depend on a number of factors, including but not limited to the following:

- the rate of progress and cost of our pre-clinical studies, clinical trials and other research and development activities;
- the scope and number of clinical development and research programs we pursue;
- the costs, timing and outcomes of regulatory approvals;
- the costs of establishing or contracting for marketing and sales capabilities, including the establishment of our own sales force;
- the extent to which we acquire or in-license new products, technologies or businesses;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and

the terms and timing of any additional collaborative, strategic partnership or licensing agreements that we may establish.

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If our available cash and cash equivalents, securities available-for-sale, funding received or made available under our collaboration agreement with Forest Laboratories, net proceeds from this offering and interest earned on these balances are insufficient to satisfy our liquidity requirements, or if we develop additional products or pursue additional applications for our products, we may seek to sell additional equity or debt securities or acquire an additional credit facility. The sale of additional equity and debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities, these securities could have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Any such required additional capital may not be available on reasonable terms, if at all. If we are unable to obtain additional financing, we may be required to modify our planned research, development and commercialization strategy, which could adversely affect our business.

Our future contractual obligations, including financing costs, at December 31, 2005, include the following:

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	Over 5 Years
			(in thousands)		
Operating lease obligations	$ 3,592	$ 712	$ 1,213	$ 1,256	$ 411
Equipment financing obligations	172	172			
	$ 3,764	$ 884	$ 1,213	$ 1,256	$ 411

The table above reflects only payment obligations that are fixed and determinable. Our commitments for operating leases primarily relate to the lease for our office and laboratory facilities in Colorado and Connecticut.

The table above does not include information with respect to the following contractual obligations because the amounts of the obligations are not currently determinable:

- contractual obligations for clinical trials that are payable on a per patient basis;
- royalty obligations, which would be payable based on sales of Orapem in future periods; and
- amounts due to Daiichi Asubio and GSK under our license agreements, which amounts are uncertain as to timing and dependent on the achievement of milestones.

Redeemable Convertible Preferred Stock

Our redeemable convertible preferred stock is classified on the balance sheet between liabilities and stockholders deficit as the holders of the redeemable convertible preferred stock have the right to request redemption in the future if certain classes of stockholders vote in favor of such redemption. Our Series B convertible preferred stock is also classified on the balance sheet between liabilities and stockholders deficit as the holders of Series B convertible preferred stock have certain rights in liquidation. Immediately prior to the closing of this offering, all of our outstanding shares of preferred stock will convert into shares of common stock and the redemption right and rights in liquidation will terminate.

Recent Accounting Pronouncements

In December 2004, the FASB issued SFAS No. 123(R), *Share-based Payment*. SFAS No. 123(R) revises SFAS No. 123, supersedes APB No. 25 and amends SFAS No. 95, *Cash Flows*. SFAS No. 123(R) applies to transactions in which an entity exchanges its equity instruments for goods or services and also applies to liabilities an entity may incur for goods or services that are based on the fair value of those equity instruments. Under

SFAS No. 123(R), we will be required to follow a fair value approach using an option valuation model, such as the Black-Scholes option-pricing model, at the

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date of stock option grants. The deferred compensation amount calculated under the fair value method will then be recognized over the respective vesting period of the stock options.

We adopted the provisions of SFAS No. 123(R) as of January 1, 2006. Due to our use of the minimum value method for valuing employees stock options during prior periods, we are required to adopt SFAS No. 123(R) using the prospective method. Pursuant to the prospective method of adoption, we will continue to account for options granted before adoption under the current APB No. 25 accounting. All grants issued or modified subsequent to adoption will be accounted for pursuant to SFAS No. 123(R). Since the adoption of SFAS No. 123(R) relates only to future grants or modifications under the prospective method of adoption, the adoption of the new guidance will only impact future periods to the extent we grant or modify options in the future. As such, the impact of the adoption of SFAS No. 123(R) cannot be predicted at this time because it will depend on levels of share based payments granted or modified in the future.

Off-Balance Sheet Arrangements

Since inception, we have not engaged in material off-balance sheet activities, including the use of structured finance, special purpose entities or variable interest entities.

Qualitative and Quantitative Disclosures About Market Risk

Our exposure to market risk is confined to our cash, cash equivalents that have original maturities of less than three months and investment securities. The primary objective of our investment activities is to preserve our capital for the purpose of funding operations while at the same time maximizing the income we receive from our investments without significantly increasing risk. To achieve these objectives, our investment policy allows us to maintain a portfolio of cash equivalents and investments in a variety of marketable securities, including U.S. government and mortgage backed securities, money market funds and under certain circumstances, derivative financial instruments. Our cash and cash equivalents as of December 31, 2005 included liquid money market accounts. The securities in our investment portfolio are classified as available for sale and are, due to their short-term nature, subject to minimal interest rate risk. We currently hedge exposure to foreign currency fluctuations on current and forecasted expenses denominated in Japanese Yen. The risk that counterparties to our derivative contracts will default and not settle according to the terms of the agreements is a credit risk. Although these instruments are considered derivatives, their economic risks have historically been insignificant and managed on the same basis as risks of other securities we hold.

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BUSINESS

Overview

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 for which we have submitted an NDA. Orapem is a member of the penem family within the beta-lactam class of 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, expert treatment guidelines recommend the use of beta-lactams as first-line therapy in many respiratory and uncomplicated skin and skin structure infections in adult and pediatric patients. 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 in the indications for which we are seeking approval and safety data for over 5,000 patients who have been treated with Orapem. We expect to file an IND for the clinical development of our second product candidate, REP8839, in 2006. REP8839 is being developed for topical use for skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of MRSA infections in hospital settings. We are also pursuing the development of other novel anti-infective products based on our in-house discovery research platform and library of proprietary compounds.

According to IMS Health, the annual worldwide market for antibiotics was $25.0 billion in 2005, which includes $8.5 billion of U.S. sales 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 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.

In December 2005, we submitted our NDA for Orapem for four indications: acute bacterial sinusitis; community-acquired pneumonia; acute exacerbation of chronic bronchitis; and uncomplicated skin and skin structure infections. Although the efficacy data for acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections may be 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 have licensed all rights to Orapem from Daiichi Asubio in the U.S. and Canada. In addition, we have the sole negotiation right to license such rights for the rest of the world, except Japan. 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 granted Forest Laboratories a first refusal right to market Orapem in Canada. We believe that Forest Laboratories experience in successfully launching branded primary care products and the fact that Forest Laboratories has no competing community antibiotics in its current product portfolio make it a strong partner for us in the development and commercialization of Orapem. We received an upfront payment of $50.0 million in February 2006 and a milestone payment of $10.0 million March 2006. We may receive up to an additional $190.0 million in development and 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 physicians. We intend to build our own marketing and sales force to promote Orapem to otolaryngologists (ear, nose and throat physicians) 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.

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

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formulation among pediatric patients with acute otitis media. We intend to conduct Phase III clinical trials seeking clinical indications 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.

Our second product candidate, REP8839, has exhibited promising activity in pre-clinical studies against *S. aureus,* including MRSA. We are developing REP8839 for topical use for skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of MRSA infections in hospital settings. We expect to file an IND application for the clinical development of a REP8839/mupirocin combination product in 2006. Mupirocin is a widely used topical antibiotic. 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.

We are also pursuing the development of other novel anti-infective products based on our in-house discovery research platform and library of proprietary compounds. We are using our proprietary bacterial DNA replication inhibitor technology to develop novel products to treat bacterial infections. 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 in lead optimization in this program. We have also selected from a proprietary library several potential compounds for development to treat infections in hospital settings caused by *C. difficile*. We are currently in pre-clinical testing for these compounds. We retain worldwide rights to all of these programs.

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. If approved, we intend to establish Orapem as a leading community antibiotic and a preferred branded oral beta-lactam in adult and pediatric markets. We believe that Orapem s safety profile and spectrum of activity make it suitable for use against a wide variety of common bacterial infections. Forest Laboratories will market Orapem in the U.S. to primary care physicians using its established primary care sales force. We will seek to commercialize Orapem outside the U.S. and Canada through additional strategic collaborations.

Develop specialty sales and marketing capabilities. We intend to build our own sales and marketing capabilities to target specialist physicians in major metropolitan areas. If Orapem is approved for adult use, we intend to promote Orapem directly to otolaryngologists (ear, nose and throat physicians) and Forest Laboratories will reimburse us for most of the related marketing and sales force costs. If Orapem is approved for pediatric use, we intend to expand our sales force to market Orapem to pediatricians. We plan to leverage this sales force to market other products that we may develop, acquire or in-license.

Develop REP8839 to treat S. aureus infections. We are developing REP8839 for topical use in three target indications: treatment of skin and wound infections; eradication of *S. aureus* in hospital settings; and prevention of MRSA infections in hospital settings. Our pre-clinical studies have shown promising activity in each of these target indications. We expect to file an IND application for the development of a REP8839/mupirocin

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combination product in 2006 and to aggressively pursue clinical development if the IND is approved.

Discover and develop novel anti-infective products. We intend to expand our pipeline of novel anti-infective product candidates by continuing to pursue our discovery research programs. We plan to use our DNA replication inhibitor expertise to develop anti-infective products with novel mechanisms of action based on inhibition of bacterial DNA replication, which we believe may limit development of resistance to those products. We also have an active program to develop a treatment for *C. difficile,* a growing medical problem in hospital settings for which existing therapies have significant limitations, and are conducting pre-clinical testing of several small molecules to treat *C. difficile*.

Acquire or in-license additional products or product candidates. We plan to leverage our development, regulatory and commercial resources by acquiring or in-licensing additional products or product candidates. These may include anti-infective products or other products that are prescribed by the physicians targeted by our sales force.

Antibiotic Market Background and Opportunity

Bacterial infections occur when bacteria that naturally exist in the body or that are inhaled, ingested or otherwise acquired are not controlled by our immune systems. The antibiotics used to treat these infections are classified as either broad spectrum or narrow spectrum. The broad spectrum antibiotics are typically oral antibiotics used to treat community-acquired infections, whereas the narrow spectrum antibiotics are typically intravenous antibiotics used to treat specific bacteria in the hospital setting with the exception of penicillin. 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.

The two primary factors that drive a physician s choice of a particular oral antibiotic to treat community-acquired infections are the drug s effectiveness against a particular type of bacterial infection and the safety profile of the drug. We believe that an antibiotic with good efficacy and an excellent safety profile may be used in preference to a more powerful antibiotic that has the risk of serious side effects, especially in non life-threatening infections. As a patient s condition becomes more serious, the physician may be more willing to expose a patient to a potentially increased risk of side effects and safety issues in order to obtain the benefit of a drug that may be more potent against the bacteria that caused that infection.

Oral antibiotics are classified as either first- or second-line therapies for each disease state by the key opinion leader physicians who write the adult and pediatric antibiotic treatment guidelines, such as those published by the Sinus and Allergy Health Partnership and American Academy of Pediatrics. First-line therapy includes both branded and generic antibiotics and constitutes a larger market than second-line therapy which currently includes primarily branded products.

According to IMS Health, over 90% of all bacterial infections that occurred in 2005 were classified as upper respiratory tract infections, lower respiratory tract infections and uncomplicated skin and skin structure infections. There are three primary classes of oral antibiotics that are prescribed to treat respiratory tract and skin infections. These include the beta-lactam, macrolide/ketolide and quinolone classes. Each class has a distinctive chemical structure that is shared by the various antibiotics included in that class.

Beta-lactam antibiotics have been the most widely prescribed antibiotics for more than 50 years. This class of antibiotics is well known for favorable efficacy, safety and tolerability. Since the introduction of penicillin in 1942, only two other sub-classes of beta-lactams have been introduced: cephalosporins (1974) and carbapenems (1985). Carbapenems are only available in intravenous form for use in the hospital setting. Therefore, if approved, the introduction of the penem sub-class will represent the first oral community beta-lactam sub-class introduction in the past 30 years.

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The penem subclass of beta-lactam antibiotics have structural features that resemble a fusion of the penicillin and cephalosporin core structures. An advantage of penems is their ability to resist degradation by commonly encountered beta-lactamase enzymes. Bacteria commonly become resistant to beta-lactam antibiotics by producing beta-lactamase enzymes which inactivate the antibiotic. Beta-lactamase enzymes are known to destroy some of the penicillin and cephalosporin antibiotics, which can result in resistance to those subclasses of beta-lactam antibiotics.

Beta-lactam antibiotics are effective against a range of common bacterial infections and do not exhibit many of the safety issues common with the macrolide/ketolide and quinolone classes. The beta-lactam class is recommended as first-line therapy and is the leading antibiotic class for treating acute bacterial sinusitis and uncomplicated skin and skin structure infections in adults. According to the Infectious Disease Society of America, or IDSA, macrolides are a preferred treatment for acute exacerbation of chronic bronchitis while quinolones are a preferred treatment for community-acquired pneumonia. In more serious conditions, the benefit of using antibiotics with greater potency may outweigh the risks of increased side effects and safety issues.

The following table shows the prescriptions and percentage use of each class of oral antibiotics in 2005 for common adult indications:

			Drug Class Share of Indication			
Bacterial Infection Type	**Indication**	**Adult Oral Market Prescriptions (in millions)**	**Beta-Lactams**	**Macrolides/ Ketolides**	**Quinolones**	**Other Antibiotics**
Upper Respiratory Tract Infections	Acute Bacterial Sinusitis	34.4	49.3%	32.7%	13.2%	4.8%
	Acute Otitis Media	9.0	68.2%	21.4%	6.8%	3.6%
	Tonsilitis/ Pharyngitis	19.0	70.8%	25.4%	2.4%	1.3%
Lower Respiratory Tract Infections	Acute Exacerbation of Chronic Bronchitis	33.5	21.5%	50.5%	19.2%	8.9%
	Community-Acquired Pneumonia	6.6	11.5%	35.5%	49.6%	3.4%
Skin Infections	Uncomplicated Skin & Skin Structure Infections	34.2	62.8%	6.7%	14.3%	16.1%
Total			42.9%	26.1%	19.9%	11.1%

Source: IMS Health

The safety profile of the beta-lactam class has been particularly important in the pediatric market. The beta-lactam class is recommended by the American Academy of Pediatrics as first-line therapy for acute otitis media, tonsillitis/pharyngitis and acute bacterial sinusitis in the pediatric market. Ketolides and quinolones are not currently approved for pediatric indications.

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The following table shows the prescriptions and percentage use of each class of oral antibiotics in 2005 for common pediatric indications:

			Drug Class Share of Indication			
Bacterial Infection Type	**Indication**	**Pediatric Oral Market Prescriptions (in millions)**	**Beta-Lactams**	**Macrolides**	**Quinolones**	**Other Antibiotics**
Upper Respiratory Tract Infections	Acute Bacterial Sinusitis	4.8	84.8%	14.0%	0.0%	1.1%
	Acute Otitis Media	22.7	88.9%	9.2%	0.0%	1.9%
	Tonsillitis/Pharyngitis	9.3	89.0%	10.0%	0.0%	1.0%
Lower Respiratory Tract Infections	Acute Exacerbation of Chronic Bronchitis	3.5	43.0%	53.7%	0.0%	3.3%
	Community-Acquired Pneumonia	1.5	49.3%	50.7%	0.0%	0.0%
Skin Infections	Uncomplicated Skin & Skin Structure Infections	2.8	81.8%	8.6%	0.0%	9.6%
Total			82.0%	14.6%	0.0%	3.4%

Source: IMS Health

We believe that in addition to efficacy and safety, the prescribing decisions in the pediatric market are also significantly affected by the tolerability and taste of the antibiotic. Diarrhea is the leading tolerability issue for the currently marketed oral antibiotics in the pediatric market which can cause therapy to be discontinued early. Because the efficacy of many antibiotics depends on the patient taking the full course of therapy at the prescribed times, a patient s discontinuation of therapy or refusal to take the drug can result in prolongation of the infection and possibly serious complications.

We believe that three key factors are creating significant opportunities for new branded antibiotics that are more effective, better tolerated and safer than existing therapies:

Emergence of Drug-resistant Bacteria. Over the past several decades, many of the most prevalent bacteria that cause adult and pediatric respiratory and skin infections have developed resistance to currently marketed antibiotics. If bacteria are resistant, the infection can become difficult or impossible to treat and may lead to serious complications, including death. The two most prevalent bacteria in respiratory infections include *Streptococcus pneumoniae*, or *S. pneumoniae* and *Haemophilus influenzae*, or *H. influenzae*. According to the 2006 PROTEKT U.S. surveillance study, designed to track antibiotic resistance, more than 29% of the Streptococcus species are resistant to at least one of the drugs most commonly used to treat these infections. The rate of *H. influenzae* resistance to at least one of the drugs most commonly used to treat infections caused by this bacteria has reached 30%, as reported in the 2005 Journal of Clinical Infectious Disease. The U.S. Centers for Disease Control has stated that antibiotic resistance is now among that organization s top concerns.

Tolerability Issues. Many current oral antibiotics have been associated with tolerability issues that cause patients extreme discomfort and compliance issues that can lead to product failures. The most

widely reported adverse event among leading oral antibiotics is diarrhea. The prescribing label for two of the leading oral beta-lactam antibiotics for use in adults, Augmentin and Omnicef, list diarrhea incidence levels that are approximately 15%.

Safety Issues. Many of the common oral antibiotics in the quinolone and macrolide/ketolide classes are burdened with safety issues such as hepatotoxicity (drug related liver damage), heart rhythm abnormalities, photosensitivity (increased sensitivity to sunlight), hypoglycemia (low blood sugar), hyperglycemia (high blood sugar) or rash. Macrolide and ketolide class antibiotics are also associated with clinically meaningful drug

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interaction issues with frequently prescribed drugs such as cholesterol lowering agents. To date, four of the nine quinolone antibiotics that have been marketed have been withdrawn from the market due to safety issues.

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. Our current product candidate portfolio consists of the following:

			Commercial Rights	
Product Candidate (Dosage Form)	**Target Indications**	**Development Status**	**Replidyne**	**Partner**
Orapem				
300 mg tablet	Acute bacterial sinusitis Community-acquired pneumonia Acute exacerbation of chronic bronchitis Uncomplicated skin and skin structure infections	NDA submitted December 2005; currently under review	U.S.: specialists; co-promote option to exclusively promote to pediatricians Canada Sole negotiation right in rest of world, except Japan	Forest: U.S. primary care physicians and other non- specialists First refusal right in Canada
600 mg tablet	Acute exacerbation of chronic bronchitis	Phase III		
Oral liquid formulation	Acute otitis media (pediatric)	Phase II		
REP8839	Skin and skin structure infections Eradication of *S. aureus* in hospital settings Prevention of MRSA infections in hospital settings	Pre-clinical	Worldwide	Not applicable

Orapem Program

Orapem is a member of the penem class of beta-lactam antibiotics. If approved by the FDA, it would be the first oral penem available outside of Japan. We believe that with its broad spectrum of activity, increased potency and safety and tolerability profile, Orapem would be appropriate for use as a first-line therapy. Promotional efforts by us and Forest Laboratories will be concentrated on this market.

We believe that, if approved, Orapem will be well-positioned to capitalize on market opportunities within the oral antibiotic arenas of adult and pediatric community-acquired respiratory tract and skin infections. The following characteristics differentiate Orapem from existing beta-lactam antibiotics:

First oral penem available in the U.S. If approved by the FDA, Orapem would represent the first new sub-class of beta-lactams (penems) to be introduced in oral form for community use in more than 30 years. According to IMS Health, beta-lactams are the most widely used first-line therapy; however, over the years many bacteria have developed resistance to older beta-lactam antibiotics. Penems are intrinsically able to resist degradation by beta-lactamase enzymes. Because Orapem is a first product in a new class of

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antibiotics, its introduction should not be burdened with the resistance issues at the levels associated with other existing antibiotics.

Potency Profile. In vitro studies have indicated that Orapem is four times more active than Augmentin (amoxicillin/clavulanate) against *S. pneumoniae,* including those strains that have evolved resistance to penicillin or amoxicillin. Orapem is also generally twice as active as Augmentin against *H. influenzae,* including those strains that have evolved resistance to other beta-lactam antibiotics. *In vitro* potency does not always correlate to clinical efficacy.

Safety profile consistent with other beta-lactam antibiotics. Due to its safety profile, we believe that Orapem would be appropriate as a first-line treatment for common respiratory and skin infections in the primary care setting. We believe that Orapem would allow physicians to reserve quinolones for second-line therapy, reducing quinolone resistance and improving the risk-to-benefit ratio for individual patients. Unlike carbapenems, Orapem has a low potential for neurotoxicity. In Phase III clinical testing, Orapem did not exhibit the potentially serious safety issues that affect the macrolide/ketolide and quinolone classes of antibiotics. Due to the safety issues previously listed for the ketolide and quinolone antibiotics, we do not anticipate competitive activity from products in these classes in the leading pediatric disease states (i.e. acute otitis media).

Tolerability Profile. In the Phase II and Phase III clinical studies referenced in our NDA, the overall incidence of diarrhea was less than 5% in over 5,000 patients treated with Orapem. This rate of incidence compares favorably with the incidence of diarrhea reported in other commonly used beta-lactam antibiotics. Further, in two Phase III clinical studies in which Orapem was compared directly to Augmentin, the incidence of diarrhea was two to three times lower in the Orapem-treated patients.

Orapem (faropenem medoxomil) is a prodrug form of the active moiety faropenem and was initially discovered by Suntory Limited, now known as Daiichi Asubio. Faropenem medoxomil is metabolized by the body to release faropenem sodium, a drug that has been approved and sold in Japan by Daiichi Asubio since 1997. Since then, it is estimated that approximately 68.5 million prescriptions have been written. Prodrugs are designed to improve the amount of drug reaching the bloodstream in which the prodrug molecule is separated by the body s natural metabolic enzymes into its active component and an inactive component. In clinical pharmacology studies, approximately 72% to 84% of an orally administered dose of Orapem was absorbed into the bloodstream and then rapidly converted to the active parent compound faropenem, resulting in three to four times greater bioavailability compared to faropenem sodium.

Pre-clinical Data

In pre-clinical studies, Orapem has exhibited broad spectrum activity that includes bacteria commonly associated with respiratory infections (*S. pneumoniae, H. influenzae* and *Moraxella catarrhalis*, or *M. Catarrhalis*) and uncomplicated skin structure and skin infections (methicillin-susceptible *S. aureus* and *Streptococcus pyogenes*, or *S. pyogenes*).

The following table shows the antibacterial activities of Orapem and other antibiotics against these common respiratory and skin bacterial pathogens in *in vitro* studies. The MIC_{90} value shown is the minimum inhibitory concentration of drug required to inhibit growth of 90% of the bacterial isolates within a given population. The lower the MIC_{90} value for a given drug the more potent it is against the population of bacteria. In these studies, Orapem was the most active agent against *S. pneumoniae*, including penicillin-resistant isolates, where it was four-fold more active than Augmentin. Among *H. influenzae,* the activity of Orapem did not appear to be compromised by the ability of the bacteria to produce beta-lactamase enzymes. Orapem showed equivalent activity to Augmentin against beta-lactamase producing strains of *M. catarrhalis* and was active against methicillin-susceptible *S. aureus* but was inactive against methicillin-resistant isolates. *S. pyogenes,* the other major skin pathogen, was also

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susceptible to Orapem. Collectively, these data indicate the potent activity of Orapem against the important respiratory and skin pathogens.

	MIC_{90} (Ug/mL)				
	Orapem	**Augmentin**	**Omnicef**	**Zithromax**	**Levaquin**
Respiratory Pathogens					
S. pneumoniae					
Penicillin-susceptible	0.008	0.03	0.12	0.25	1
Penicillin-intermediate	0.25	1	4	≥512	1
Penicillin-resistant	1	4	>4	≥512	1
H. influenzae					
b-Lactamase-positive	0.5	2	0.5	4	0.015
b-Lactamase-negative	1	1	1	4	0.015
M. catarrhalis					
b-Lactamase-positive	0.5	0.5	0.25	≤0.06	0.06
b-Lactamase-negative	0.12	0.03	0.12	≤0.06	0.06
Skin Pathogens					
S. aureus					
Methicillin-susceptible	0.12	1	0.5	>64	0.25
Methicillin-resistant	>32	>32		>64	
S. pyogenes	0.03	≤0.015	≤0.03	0.25	1

Orapem for the Adult Market

We submitted our NDA for Orapem to the FDA in December 2005 and requested approval for four indications: acute bacterial sinusitis, community-acquired pneumonia, acute exacerbation of chronic bronchitis and uncomplicated skin and skin structure infections. The FDA accepted the NDA for review in February 2006. The anticipated 10 month review period by the FDA will include among other data, review of the clinical data and manufacturing related issues. Unless there is a regulatory extension of the review period, we expect that the FDA will provide us with an assessment of the NDA by the end of October 2006. We believe that the Phase III studies used to support regulatory approval that were designed and carried out by Bayer after conferring with the appropriate FDA review division met all the applicable clinical trial guidelines that were in place at the time the studies were conducted.

One study submitted in the NDA in uncomplicated skin and skin structure infections showed statistical non-inferiority to a FDA-approved comparator treatment regimen, while a second study did not show statistical non-inferiority. When we pool the data from the two studies, clinical outcomes were similar and microbiological eradication rates were similar and greater than 90%. When presented with the data at a meeting in April 2005, the FDA review division advised that these data would be carefully scrutinized but that an additional Phase III clinical trial will likely be required for approval of this indication.

Regulatory requirements for approval of new drugs can change over time. In September 2005, the FDA informed us that it will likely require a placebo-controlled trial prior to approving Orapem for acute exacerbation of chronic bronchitis. Nevertheless, the FDA agreed to review our application for this indication and accepted the NDA for filing. Placebo-controlled trials may also become required by the FDA for other indications, including other indications covered by our NDA, during the FDA review period of Orapem and thereafter.

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Clinical Overview. The trials that supported our NDA filing were conducted by Bayer when it was a previous licensee of Orapem and were generally designed to support approval in the U.S. and also in major international markets other than Japan. As has been the norm in antimicrobial drug development, the primary study objective in most of these studies was to demonstrate that Orapem was non-inferior to a control antibiotic treatment approved for use in the U.S. Orapem was demonstrated to be non-inferior in eight of the nine randomized controlled studies and similar efficacy was demonstrated in the two uncontrolled studies. The definition of statistical non-inferiority was met if there was less than 5% probability (a 95% confidence interval, or CI) that Orapem was 10% worse than the standard treatment. The choice of a delta of 10% conforms to current standards for establishing non-inferiority of antimicrobial agents; in past decades a less stringent 15% delta was commonly accepted. Efficacy evaluation, including clinical and microbiological responses, was determined by physician assessment and bacterial cultures. The clinical outcome analysis was first conducted for subjects who met all the protocol defined criteria or rules (the clinically evaluable population) and subsequently on all treated subjects (the intent-to-treat population). The references to N/N in the tables below represent the number of patients who had a clinical response compared to the total number of patients included in the study population. For all non-inferiority studies, the intent-to-treat analysis supported the per protocol analysis. In this extensive Phase III clinical testing, Orapem exhibited the activity and safety profile typical of beta-lactam antibiotics with improved tolerability.

Clinical Studies for Acute Bacterial Sinusitis. The efficacy of Orapem in subjects with acute bacterial sinusitis was evaluated in three Phase III studies. In two comparative studies, where seven-day and 10-day courses of Orapem were compared to cefuroxime axetil, the primary endpoints were met and statistical non-inferiority was demonstrated. The third study (Study 100287) was an open-label (no comparative control treatment) trial in which all subjects received Orapem after undergoing a needle aspiration of the sinus cavity in order to obtain a direct sinus specimen to culture for bacterial pathogens. The clinical and microbiological outcomes were consistent with the comparative studies and we believe the microbiological results support approval of Orapem to treat acute bacterial sinusitis caused by all three of the major respiratory pathogens. We believe the results of the three studies demonstrate that seven-day treatment with Orapem is effective in the treatment of subjects with acute bacterial sinusitis. The following table summarizes the clinical results of the acute bacterial sinusitis studies:

Study Population	**Orapem 300 mg 2x/day** n/n	**Orapem 300 mg 2x/day** n/n	**Cefuroxime Axetil 250 mg 2x/day** n/n	**Statistical Result 95% CI** %
Study 100288	**7 days**	**10 days**	**10 days**	**Clinically Non-Inferior**
Clinically Evaluable	237/295(80%)	229/280(82%)	213/286(74%)	0.1, 13.6 (7 day) 1.7, 15.2 (10 day)
Intent-to-Treat	262/366(72%)	255/363(70%)	250/370(68%)	-2.7, 10.5 (7 day) -3.9, 9.5 (10 day)
Study 10186	**7 days**		**7 days**	**Clinically Non-Inferior**
Clinically Evaluable	203/228(89%)		198/224(88%)	-5.2, 6.4
Intent-to-Treat	237/274(86%)		239/273(88%)	-7.0, 4.0
Study 100287	**7 days**			**Open Label**
Clinically Evaluable	246/300(82%)			Not relevant
Intent-to-Treat	269/353(76%)			Not relevant

Clinical Studies for Community-Acquired Pneumonia. Community-acquired pneumonia is the most serious type of bacterial respiratory infection and can be life threatening. The efficacy of Orapem in subjects with community-acquired pneumonia was evaluated in four Phase III studies. In the three comparative studies, the primary endpoints were met and non-inferiority was demonstrated for 10-day

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therapy with Orapem compared to 10-day therapy with amoxicillin/clavulanate, 14-day therapy with cefpodoxime and 10-day therapy with amoxicillin. The fourth study (Study 100289) was an open-label (no comparative control treatment) trial in which bacterial samples were collected for culture. The clinical and microbiological outcomes were consistent with the comparative studies and we believe the results of this study support approval of Orapem for community-acquired pneumonia caused by all three major respiratory pathogens. Overall, we believe the results of the four studies demonstrate that 10-day treatment with Orapem is effective in the treatment of subjects with community-acquired pneumonia. The following table summarizes the clinical results of the community-acquired pneumonia studies:

Study Population	**Orapem** **300 mg 2x/day 10 days** n/n	**Comparator** n/n	**Statistical Result** **95% CI** **%**
Study 10188		**Amoxicillin** **1g 3x/day 10 days**	**Clinically** **Non-Inferior**
Clinically Evaluable	260/284 (92%)	237/268 (88%)	-1.9, 8.1
Intent-to-Treat	289/314 (92%)	270/304 (89%)	-1.4, 7.8
Study 10189		**Amoxicillin/Clavulanate** **625 mg 3x/ day 10 days**	**Clinically** **Non-Inferior**
Clinically Evaluable	222/257 (86%)	223/253 (88%)	-7.6, 3.9
Intent-to-Treat	242/305(79%)	242/309(78%)	-5.4, 5.9
Study 100290		**Cefpodoxime** **200 mg 2x/day 14 days**	**Clinically** **Non-Inferior**
Clinically Evaluable	205/229 (90%)	203/229 (89%)	-4.1, 7.1
Intent-to-Treat	223/304 (73%)	224/298 (75%)	-7.4, 6.3
Study 100289			**Open Label**
Clinically Evaluable	252/294 (86%)		Not relevant
Intent-to-Treat	287/388 (74%)		Not relevant

Clinical Studies for Acute Exacerbation of Chronic Bronchitis. The efficacy of Orapem in acute exacerbation of chronic bronchitis was evaluated in two comparative, non-inferiority Phase III studies. The primary endpoints were met in both studies and statistical non-inferiority was demonstrated for five-day Orapem compared to five-day azithromycin and seven-day clarithromycin, both macrolide antibiotics. Overall, we believe the results of both studies demonstrate that five-day treatment with Orapem is effective in the treatment of subjects with acute exacerbation of chronic bronchitis. The following table summarizes the clinical results of the acute exacerbation of chronic bronchitis studies:

Study Population	**Orapem** **300 mg 2x/day 5 days** n/n	**Comparator** n/n	**Statistical Result** **95% CI** %
Study 100291		**Azithromycin** **500 mg 1 day,** **200 mg 4 days**	**Clinically** **Non-Inferior**
Clinically Evaluable	225/278 (81%)	236/279 (85%)	-9.5, 2.6
Intent-to-Treat	277/410 (68%)	283/405 (70%)	-8.5, 4.0
Study 10187		**Clarithromycin**	**Clinically** **Non-Inferior**

		500 mg 2x/day 7days	
Clinically Evaluable	262/299 (88%)	288/318 (91%)	-7.9, 2.0
Intent-to-Treat	316/369 (86%)	337/379 (89%)	-7.2, 2.0

Clinical Studies for Uncomplicated Skin and Skin Structure Infections. 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. When we pooled the data from the two studies, results indicated that Orapem was not less effective than the control treatments. The eradication rates for the key pathogens in this indication, *S. aureus* and *S. pyogenes,* were high (greater than 90%) and were similar for Orapem and the comparators. We believe that these findings show that Orapem is effective in the treatment of subjects with uncomplicated skin and

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skin structure infections. The following table summarizes the clinical results of the uncomplicated skin and skin structure infections studies:

Study Population	Orapem 300 mg 2x/day 7 days n/n	Comparator n/n	Statistical Result 95% CI %
Study 100292		**Cephalexin 500 mg 2x/day 7 days**	**Clinically Inferior**
Clinically Evaluable	210/246 (85%)	226/246 (92%)	-12.3, -1.3
Intent-to-Treat	220/290 (76%)	228/283 (81%)	-11.5, 2.1
Study 10190		**Amoxicillin/Clavulanate 625 mg 3x/day 7 days**	**Clinically Non-Inferior**
Clinically Evaluable	224/246 (91%)	207/227 (91%)	-5.1, 5.3
Intent-to-Treat	258/298 (87%)	254/295 (86%)	-4.7, 6.4

Other Studies. Three Phase III studies for other indications were also initiated, two in tonsillitis/pharyngitis and one in uncomplicated urinary tract infections. One study in each indication did not meet the primary efficacy criteria for non-inferiority, and the second study in tonsillitis/pharyngitis was halted shortly after enrollment began. Although the safety data from all treated subjects are included in the overall safety analysis of Orapem submitted with the NDA, we are not seeking approval of the specific treatment indications explored in these studies.

The efficacy of five-day treatment with Orapem in subjects with tonsillitis/pharyngitis was evaluated in one Phase III study. The comparator was 10-day treatment with penicillin VK. Another study was discontinued shortly after enrollment began. In the completed study, a five-day treatment with Orapem did not demonstrate non-inferiority relative to the comparator. The bacteriological cure rate was 87% in the Orapem treated patients and 94% in the penicillin VK patients. We believe that this difference may be related to the shorter course of therapy in the Orapem arm. Multiple published reports suggest that shorter course therapy with penicillin is associated with lower bacteriological cure rates in this indication. We currently do not intend to conduct additional studies in adults for this indication and are not seeking approval of this indication in our pending NDA.

The efficacy of five-day treatment with Orapem in subjects with uncomplicated urinary tract infections was studied in one Phase III study. The comparator was five-day treatment with trimethoprim-sulfamethoxazole. In this study, five-day treatment with Orapem did not demonstrate non-inferiority relative to the comparator. The clinical cure rate was 86% in the Orapem treated patients and 96% in the trimethoprim-sulfamethoxazole patients. We believe that this difference may be related at least in part to factors specific to the kidneys. There is an enzyme in the kidneys known to degrade carbapenem antibiotics and also Orapem, resulting in decreased drug concentrations in the region of the infection. We do not consider this indication to be an important commercial opportunity for a beta-lactam antibiotic such as Orapem. We currently do not intend to conduct additional studies in this indication and we are not seeking approval of this indication in our pending NDA.

Safety and Tolerability Data

We believe that Orapem has a favorable safety and tolerability profile. The pharmacokinetics of faropenem following oral administration of Orapem were evaluated in 27 Phase I studies, three Phase II studies and one Phase III study. Orapem was well absorbed, rapidly converted to faropenem and reached maximum plasma concentrations approximately one hour after administration. Single doses of Orapem up to 3,000 mg and multiple doses up to 3,750 mg per day were administered without notable safety issues.

At the request of the FDA, we evaluated Orapem in a Phase I study to determine whether there was any potential of Orapem to prolong QT interval, a measure of electrocardiac function, which has been problematic for the quinolone and macrolide (including telithromycin) classes of antibiotics. This Thorough QT study, now required for

all new drug applications, demonstrated that Orapem does not cause any electrocardiographic abnormalities, including QT interval prolongation.

In Phase III clinical testing, Orapem exhibited the activity and safety profile typical of beta-lactam antibiotics with improved tolerability. The Phase III studies have accrued a safety database comprising 3,461 patients in respiratory tract infection indications and 4,863 patients in all Phase III studies. Orapem has been administered to over 5,000 people including all Phase I, Phase II and Phase III studies. The most common adverse events involved the gastrointestinal tract, including diarrhea, nausea or abdominal pain, or the central nervous system, including headaches and dizziness.

We believe that the safety profile of Orapem is similar to that of penicillins and cephalosporins. Unlike some carbapenems, Orapem showed no proconvulsant effects in animal models. There was only one incident of convulsion in the Orapem clinical studies (a rate of 0.02%), which the treating physician did not attribute to Orapem. In comparison with amoxicillin/clavulanate, Orapem produced lower rates of adverse events, including gastrointestinal events and liver enzyme abnormalities. Unlike macrolides/ketolides and quinolones, Orapem was not associated with hepatotoxicity, heart rhythm abnormalities, photosensitivity, hypoglycemia or hyperglycemia.

In the Phase II and Phase III clinical studies referenced in our NDA, the overall incidence of diarrhea was less than 5% in over 5,000 patients treated with Orapem. Further, in two Phase III clinical studies in which Orapem was compared directly to Augmentin, the incidence of diarrhea was two to three times lower in the Orapem-treated patients. We believe the safety and tolerability profile of Orapem make it a promising agent to be used as a first-line antibiotic in the community setting.

Ongoing Clinical Development. We and Forest Laboratories are committed to conducting additional clinical studies to expand the indications for which we will seek approval, including higher dose therapy and pediatric indications.

Placebo-controlled Acute Exacerbation of Chronic Bronchitis Study. We are currently conducting another Phase III trial in acute exacerbation of chronic bronchitis. The comparators include both placebo and Ketek (telithromycin), an approved ketolide antibiotic. Our primary purpose in conducting this study is to demonstrate the benefit of treatment with Orapem over placebo because the FDA has communicated to us that it may begin requiring such data before approving an antibiotic for this indication.

In this study, we are using a higher dose of Orapem than in previous Phase III studies; 600 mg twice per day rather than 300 mg twice per day. Study subjects are taking two 300 mg tablets at each dose. However, we may develop a single 600 mg tablet for commercial use, which will require that we demonstrate bioequivalence of the two dosage forms. The duration of therapy is five days, as it was in previous studies in this indication. We believe that this higher dose may offer the potential for even greater efficacy than the current dose, particularly in short course therapy. Beta-lactam antibiotics have typically been used for seven to 14 days for acute exacerbation of chronic bronchitis.

We have corresponded with the FDA regarding our ongoing development work in this indication. Based on this correspondence, we believe that the results of this single study may support filing for approval of the higher dose to treat this indication. Because the FDA has not issued formal guidance regarding the design or conduct of placebo-controlled studies for this indication, there can be no assurance that the FDA will accept such a filing or grant approval even if the results obtained from our study meet the primary endpoint(s) defined in our protocol.

We have previously evaluated the potential for adverse events with the 600 mg dose in a Phase I study and a Phase II study conducted in 2005. In the Phase I study, the 600 mg twice per day dose was directly compared to a 300 mg two times per day regimen, both administered for seven days. In the Phase II study, a 300 mg two times per day seven day treatment course was compared to a 600 mg two times per day regimen in patients with acute bacterial sinusitis. In both trials, the adverse events were similar in both type and frequency. Based on the results of these two studies, together with prior Phase I studies that included increased doses of Orapem, we believe that the incidence and severity of adverse events may prove not to be substantially higher with the 600 mg two times per day dose than previously observed with the 300 mg two times per day dose.

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We currently anticipate that enrollment in the ongoing Phase III acute exacerbation of chronic bronchitis study will continue into 2007.

Orapem for the Pediatric Market

We are developing an Orapem oral liquid formulation for pediatric use in conjunction with our strategic partner, Forest Laboratories. Under our agreement with Forest Laboratories, we have an option to exclusively promote 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.

Orapem has performed well *in vitro* against many common pediatric pathogens. We believe that the well-known safety of beta-lactam antibiotics and the tolerability profile of Orapem demonstrated in extensive clinical testing in adults make Orapem a promising candidate for the pediatric market.

Interactions with the FDA. We met with the FDA on January 18, 2006 to discuss the filing of our IND in the U.S. for the oral liquid formulation for pediatric use and our ongoing Phase II clinical trial. We also began a discussion with the FDA regarding pediatric Phase III clinical design. We will have ongoing interactions with the FDA to finalize the design of our Phase III clinical trials.

Formulation Development. For pediatric indications, it is important that Orapem be available as an oral liquid formulation since the majority of patients being treated for acute otitis media are less than three years old. Any oral liquid formulation should have both a competitive taste profile and the requisite stability. Like many other medications, the active ingredient in Orapem is bitter. We have developed a prototype oral liquid formulation that has been used to complete a bioavailability study in healthy adults. We have also initiated a Phase II trial in acute otitis media described further below. Additional work to optimize the taste and stability of the oral liquid formulation is ongoing.

Clinical Studies Completed or Ongoing. We have completed a bioavailability study in healthy adults that showed similar drug absorption for the tablet and oral liquid formulation. We also have a Phase II clinical trial that began enrolling patients in January 2006 for acute otitis media. The Phase II trial is designed to determine the dosage for our planned Phase III clinical trials. We anticipate that the results of the Phase II clinical trial will be available in 2006.

Clinical Studies Planned or Under Consideration. We expect to conduct additional bioavailability studies with an improved oral liquid formulation. Upon successful completion of such bioavailability studies and following assessment of the Phase II clinical trial, we and Forest Laboratories plan to conduct Phase III clinical trials to support an NDA for two pediatric indications, acute otitis media and tonsillitis/pharyngitis. The details of the study design will be determined through an interactive process involving the FDA, Forest Laboratories and external advisors.

REP8839 Program

We are developing REP8839 for topical use for skin and wound infections, eradication of *S. aureus* in hospital settings and prevention of MRSA infections in hospital settings. Aminoacyl tRNA synthetases represent a promising platform for the potential development of new antibacterial agents having no cross-resistance to currently marketed antibiotics. There are aminoacyl tRNA synthetases for 19 of the 20 different amino acids and these enzymes play an essential role in protein synthesis. Inhibition of tRNA synthetases results in reduced protein synthesis and attenuation of bacterial growth. Mupirocin, an isoleucyl tRNA synthetase inhibitor, has proved to be a successful topical antibiotic with activity against both *S. aureus* and *S. pyogenes* and serves as a precedent for the development of aminoacyl tRNA synthetases as topical antibiotics. REP8839 is a member of a novel class of selective inhibitors of methionyl tRNA synthetase, another class of aminoacyl tRNA synthetase, which is a novel and unexploited target that is essential and well conserved in clinically important Gram-positive bacteria. Pre-clinical studies have indicated that REP8839 exhibits potent activity against major skin pathogens such as

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S. aureus and *S. pyogenes,* including strains of *S. aureus* that are resistant to methicillin, vancomycin, linezolid or mupirocin.

We are currently conducting pre-clinical testing of REP8839 to evaluate its suitability for use in humans. We expect to file an IND application for the development of a REP8839/mupirocin combination product in 2006. Mupirocin is a widely used topical antibiotic. We believe that the distinctive mechanisms of action of the two drugs greatly reduce the likelihood that *S. aureus* will develop resistance to this combination. We retain worldwide rights to REP8839.

Market Opportunity

MRSA is a significant and growing public health threat. The IDSA has published a series of reports entitled Bad Bugs, No Drugs that highlights the severity of this and other infectious disease concerns related to increasing bacterial resistance to antibiotics and decreasing investment in antibiotic development by the pharmaceutical industry. MRSA infections have been a recognized problem in hospitals for a number of years. Recently, MRSA has become a significant concern in the community setting, appearing in groups such as sports teams and child care facilities. There are a number of approved antibiotics to treat MRSA in the hospital and more are in development. However, as indicated in the March 2006 update of IDSA s report, a need exists for oral or topical antibiotics that can be used for MRSA infection prevention, where infection may be suspected but not confirmed.

Mupirocin is the most widely prescribed topical antibiotic, indicated for the treatment of skin infections, wound infection prevention and eradications of *S. aureus* in hospital outbreaks of MRSA. Some strains of MRSA have also begun to exhibit resistance to mupirocin. It is well documented that widespread use of mupirocin can lead to a marked rise in the number of mupirocin-resistant strains of *S. aureus,* including MRSA strains. For example, mupirocin was made available without a prescription in the early 1990s in New Zealand. Resistance increased dramatically within just a few years and the product was taken off the over-the-counter market. We believe there is a need in the medical community for an antibiotic that offers the advantages of mupirocin, is effective against mupirocin-resistant strains and is less likely to develop resistance when used widely in the community or as a prophylactic.

Oral antibiotics also can be used to treat skin infections. The leading oral antibiotic used to treat skin infections has been cephalexin for many years. The limitations associated with cephalexin include a requirement for dosing three or four times per day and concerns regarding resistance, efficacy and the treatment of a skin infection with a systemic agent that has the potential to cause adverse events. We believe an opportunity exists to convert some use of oral cephalexin in this indication to a new and more effective topical agent.

Differentiating Characteristics

We observed the following characteristics that we believe may make the combination of REP8839 and mupirocin a promising topical treatment option for bacterial skin infections and for eradication of *S. aureus* from the nasal passages:

Novel mechanism of action. REP8839 is a synthetic antibiotic with a distinct mechanism of action from mupirocin and other marketed antibiotics. REP8839 is a selective inhibitor of methionyl tRNA synthetase, a previously unexploited drug target. REP8839 showed potent antibacterial activity *in vitro* against important skin pathogens such as *S. aureus* and *S. pyogenes* and is more potent than mupirocin *in vitro* against these skin pathogens.

Low rate of spontaneous resistance emergence. Antibiotics are sometimes used in combination to prevent or delay the emergence of drug-resistant strains of bacteria. When drugs that act on different molecular targets are used in combination, the probability of emergence of strains resistant to both drugs is substantially reduced. Since REP8839 and mupirocin act on two distinct essential enzymes (tRNA synthetases), the probability that bacterial resistance will develop during therapy is low.

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REP8839/mupirocin combination is unlikely to compromise the effectiveness of antibiotics used for the treatment of systemic infections. Because REP8839 and mupirocin have different mechanisms of action from the systemic antibacterial agents that are commonly used to treat more serious hospital infections, development of resistance to mupirocin or REP8839 would not jeopardize the efficacy of these systemic agents.

Pre-Clinical Data and Clinical Development Strategy

In pre-clinical studies, REP8839 has exhibited low dermal irritancy potential, low genotoxicity potential, low systemic toxicity following intravenous administration and low systemic exposure following application to skin. Taken together, the pre-clinical studies we have conducted to date suggest a safety profile that is suitable for the initiation of Phase I clinical trials.

We plan to pursue the following three clinical indications for the combination of REP8839 and mupirocin:

treatment of uncomplicated skin and skin structure infections, including secondarily infected traumatic skin lesions caused by *S. aureus,* MRSA and *S. pyogenes;*

eradication of *S. aureus*, including MRSA, in hospital settings from nasal passages; and

prevention of infections with *S. aureus* in hospital settings through eradication from nasal passages.

A pre-IND meeting with the FDA is scheduled on April 12, 2006 to discuss our plans for the clinical development of a REP8839/mupirocin combination product. Four Phase I studies are proposed to be carried out in the second half of 2006 to support further clinical development of all three indications. FDA approval of a combination drug product requires demonstration that the combination is superior to the individual components. We expect that our clinical strategy will evolve as our discussions with the FDA continue.

Research Capabilities and Discovery Programs

We maintain an active internal research effort that is currently focused on identifying novel antibiotics. We have built a research organization that includes expertise in biochemistry, microbiology, medicinal chemistry, process chemistry, pharmacology and toxicology. We believe it is important to have expertise in these areas not only for discovery programs, but also for developing later stage products and evaluating new product opportunities. Our research organization was initially responsible for evaluating the Orapem and REP8839 programs as in-license opportunities and has continued with the development of both programs. The research organization also pursues our own internal discovery activities. Our discovery activities at this time include the following programs:

DNA Replication Inhibitors Program. Bacterial DNA replication is an attractive target system for new antibacterial drugs since it is an essential process and stalled DNA replication can trigger cell death. However, to date, this is an underexploited drug target. We have reconstituted nine high-throughput assays targeting the central DNA replication complex from the following bacteria: *Escherichia coli, S. pyogenes, Pseudomonis aeruginosa, S. aureus* and *Bacillus subtilis.* Each high-throughput assay includes at least six protein components and many include twelve or more proteins that constitute the replication system of bacteria that need to work together in highly cooperative DNA replication reactions. These assays simultaneously target multiple sites that are amenable to inhibition by small molecules. We have screened a library of approximately 250,000 compounds assembled from various sources that are currently at the stage of lead optimization.

Clostridium difficile Program. Another one of our discovery programs is focused on the identification of novel antibacterial drugs that are active against *C. difficile.* In recent years, *C. difficile* associated diarrhea (CDAD) has emerged as a major public health threat among

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elderly patients in health care or long-term care institutions. Oral vancomycin is the only antibiotic that is currently approved by the FDA for the treatment of CDAD. Metronidazole is also used extensively in clinical practice following early reports of its efficacy in CDAD. However, recent studies have noted relatively high and growing incidence of treatment failure and relapse following both vancomycin and metronidazole therapy. Furthermore, widespread vancomycin use raises resistance concerns. Overall, options for the treatment of CDAD are currently limited and a need exists for the development of new agents to address this emerging problem.

An ideal drug for treating CDAD would have good activity against *C. difficile* but limited activity against normal intestinal flora, low oral bioavailability and a mechanism-of-action that is distinct from antibiotics currently used for the treatment of systemic infections. We have recently identified a class of compounds with *in vitro* activity against *C. difficile* that may meet the above criteria. To date, we have synthesized and tested approximately 140 structurally related compounds and identified several compounds that have considerably improved antibacterial activity against *C. difficile.* We are currently studying pharmacology, toxicology and animal efficacy of several representative compounds.

Our Collaboration with Forest Laboratories

In February 2006, we entered into a collaboration and commercialization agreement with Forest Laboratories to be our exclusive partner for the development and marketing of Orapem in the U.S. We believe that Forest Laboratories is particularly well suited to help us develop and commercialize Orapem in the U.S. for a number of reasons. In recent years, Forest Laboratories has successfully launched new products into primary care markets, particularly mature markets with many product alternatives. We believe that Forest Laboratories commercial success with Celexa®, Lexapro® and Benicar®, for example, are indicative of its strong capabilities in this area. We also believe that the timing of an Orapem launch complements Forest Laboratories portfolio of other products. Forest Laboratories presently has no competing community antibiotics in their product portfolio. Finally, we believe that Forest Laboratories core competencies complement ours by combining their strength in executing major launches with our expertise in antibacterial development and marketing.

Forest Laboratories will make payments to us upon the achievement of certain development and commercial milestones and royalty payments to us based upon Orapem sales. We have received $60.0 million in upfront and milestone payments. We may receive up to an additional $190.0 million in development and commercial milestones, which will be reduced by $25.0 million if we exercise our option to directly market and promote Orapem to pediatricians on an exclusive basis, which we expect to do. We will oversee the development and regulatory approval of the products through a joint development committee with Forest Laboratories. A substantial portion of development and regulatory expenses are paid by Forest Laboratories.

Under the collaboration and commercialization agreement, Forest Laboratories is required, subject to certain conditions, to launch Orapem within six to nine months after approval of our NDA by the FDA, provided that the FDA approval includes at least two respiratory tract infection indications, the approved products have a shelf life of at least 18 months and that adequate product supply is available. Forest Laboratories is generally responsible for all sales and marketing activities related to primary care physicians and has agreed to certain minimum commitments for sales and marketing efforts. We have the right to promote to targeted specialists, such as otolaryngologists. Forest Laboratories will reimburse us for most expenses associated with such marketing and selling efforts. We may terminate our promotion activities upon 12 months notice to Forest Laboratories. Similarly, Forest Laboratories may terminate our specialist promotion to target specialists if it ceases to promote Orapem entirely, or if our sales force fails to substantially perform as provided in the marketing plan for two consecutive years.

We also have an option to market and promote Orapem products to pediatricians on an exclusive basis in the U.S. for the life of the products. This option must be exercised at least six months before an

NDA for a liquid oral formulation is projected to be submitted. If we exercise this option, all joint marketing committee decisions with respect to the liquid oral formulation will be by mutual agreement, including the approval of launch strategy and commitments by each party for marketing and selling efforts. Forest Laboratories will extend us a line of credit in the amount of $60.0 million which we may elect to draw against to support our promotional efforts. Forest Laboratories will book all Orapem sales and, under certain circumstances, pay us a co-promotion fee, reimburse our marketing expenses and pay us royalties on all sales, milestones on development of the liquid oral formulation and a portion of the commercialization milestones. We may terminate our promotion activities to pediatricians upon 18 months notice to Forest Laboratories. Similarly, Forest Laboratories may terminate our promotion to pediatricians if it ceases to promote Orapem entirely, or if we fail to meet our promotional commitments under the agreement. Unless terminated earlier, the term of the pediatrician promotion option ends upon the earlier of the expiration of the last to expire of the applicable patents regarding the liquid oral formulation, including extended commercial exclusivity, and the commercial introduction by a third party of a generic liquid oral formulation containing faropenem medoxomil.

We have a reciprocal agreement with Forest Laboratories that restricts either of us from developing, marketing or selling certain competing products for a period of time. Forest Laboratories has no rights to other of our current product candidates or to our future products, if any. Forest Laboratories has a right of first refusal to extend the territory for Orapem to include Canada if we decide to commercialize Orapem in Canada through a third party.

The agreement with Forest Laboratories extends until the later of (a) the expiration of the last to expire of the applicable patents, including extended commercial exclusivity, (b) 12 years after the first commercial sale of a product under the agreement and (c) the commercial introduction by a third party of a generic product, unless terminated earlier. Forest Laboratories may also terminate our agreement upon 90 days written notice if safety or efficacy issues arise that could prevent or materially delay regulatory approval of Orapem or substantially negatively impact Orapem s marketing potential. Each party has the right to terminate the agreement upon 60-days prior written notice in the case of the other party s bankruptcy or dissolution or a material breach of the agreement.

We have agreed to a reciprocal standstill provision whereby neither we nor Forest Laboratories will acquire any interest in the other without the party s consent. Either we or Forest Laboratories may assign this agreement to an affiliate or in connection with a transfer or sale of the business related to Orapem, provided that the third party has no competing products or a firewall is created to protect promotion and sales of Orapem.

Sales and Marketing

Our collaboration agreement with Forest Laboratories provides that Forest Laboratories will be responsible for the sales and marketing efforts of Orapem within the U.S. primary care market, which includes the family practice, general practice and internal medicine physicians, physician assistants and nurse practitioners.

We plan to build an initial sales organization of 50 to 75 specialty representatives geographically-focused in major metropolitan areas to promote Orapem tablets to relevant specialists, principally otolaryngologists. We are also currently building a marketing group to initially market this product to all relevant specialists, including key opinion leaders in the infectious disease and otolaryngology communities and other physician groups. Forest Laboratories will reimburse us for a majority of the expenses we incur for our sales force and marketing activity relating to specialists promotion in the near term. In addition, we intend to evaluate additional products for in-licensing or acquisition that our specialty sales organization could promote and sell outside the context of our collaboration with Forest Laboratories.

We plan to grow the size of our specialty sales organization if and when additional Orapem indications are approved by the FDA or if our other product candidates are successfully developed, approved and launched. In particular, we may elect to exercise our option to promote Orapem to pediatricians if an oral liquid formulation can be successfully developed. In this case, we plan to

substantially increase the size of our specialty sales organization to address this physician group. Sales organizations designed to market to pediatricians are typically comprised of 200 to 400 representatives. If we make the election to promote Orapem to pediatricians, we plan to acquire or develop additional pediatric products for such an organization to promote and sell to pediatricians.

We do not anticipate building sales capabilities outside the U.S. and expect to enter into strategic collaborations with respect to any of these sales activities.

Our License Agreement with Daiichi Asubio

We entered into a license agreement with Daiichi Suntory Pharma (now Daiichi Asubio Pharma Co., Ltd.) that was effective in March 2004. Under this agreement, we have an exclusive license to, with the right to sublicense, Daiichi Asubio s patent rights and know-how to develop and commercialize all forms of Orapem for adult and pediatric use in the U.S. and Canada. The license includes rights to all clinical and other data related to Orapem generated by Daiichi Asubio and prior licensees, other than rights to manufacture Orapem. Bayer was a prior licensee of Orapem and conducted Phase III studies in multiple indications, including the studies that form the basis of our pending NDA.

We also have a sole negotiation right to develop and commercialize Orapem in the rest of the world, excluding Japan, until two years following the commercial introduction of Orapem in the U.S. or Canada. Our license does not include the rights to other forms of faropenem, such as faropenem sodium, but Daiichi Asubio has agreed not to license or market any other form of faropenem for use in the U.S. or Canada.

In consideration for our licenses, we paid Daiichi Asubio an up-front license fee. We will also be obligated to pay Daiichi Asubio additional sums upon the occurrence of development and commercial milestone events and royalties on all Orapem sales.

Our license agreement with Daiichi Asubio extends until the last relevant patent expires or 12 years after the first commercial sale of a Orapem in the territory, whichever is later. Each party has the right to terminate the agreement in the event of the bankruptcy or dissolution of the other party or a material breach of the agreement. We may also terminate the license agreement upon six months written notice in the event that the development program indicates significant issues of safety or efficacy for an indication or it becomes no longer commercially reasonable to commercialize the product.

If we substantially fail to meet our goals under our sales and marketing plan over a period of two years, then we must make certain payments to Daiichi Asubio or Daiichi Asubio may convert our license to a non-exclusive license, in which case we would be required to grant Daiichi Asubio a license to use the information and know-how we have developed under this agreement. Under certain circumstances, we may be required to make certain payments to Daiichi Asubio upon termination of the agreement.

Manufacturing

We obtain the drug substance, or active pharmaceutical ingredient, faropenem medoxomil, from Nippon Soda and the finished Orapem tablet from Tropon. These contract manufacturers are the sole manufacturing sources for Orapem. Under our collaboration agreement with Forest Laboratories, Forest Laboratories will assume sole responsibility for managing the supply chain for Orapem for the U.S. market. We will cooperate with Forest Laboratories and manage the supply of Orapem for the rest of the world. As a penem antibiotic, Orapem requires dedicated manufacturing facilities for the manufacture of drug substance and drug product. For many years, beta-lactams have been produced separately in segregated facilities due to concerns about allergic reactions to these types of antibiotics. During development, faropenem medoxomil was manufactured by Nippon Soda in a segregated building at its Takaoka facility in Japan and Bayer manufactured the Orapem tablet internally for its clinical studies.

In anticipation of commercial production, Nippon Soda expanded and equipped a new facility located in Nihongi, Japan. The Nihongi facility is presently being used for the manufacture of faropenem sodium for the Japanese market. Faropenem medoxomil is produced from faropenem sodium by converting

it into an ester prodrug form. We have a requirements contract for the supply of faropenem medoxomil at the Nihongi facility. Nippon Soda is obliged to supply all of our requirements of faropenem medoxomil and we and Forest Laboratories are obligated to purchase all faropenem medoxomil requirements from Nippon Soda. We have the right to transfer manufacturing to a third party, with Nippon Soda s cooperation, if Nippon Soda cannot assure supply and in certain other circumstances. In the case of such a transfer, Nippon Soda will be required to grant us the necessary licenses, including the right to sublicense, under its intellectual property to manufacture faropenem medoxomil. Nippon Soda has patent protection for certain aspects of the manufacturing process through 2014. Nippon Soda has agreed to complete preparations necessary at its Nihongi facility for FDA regulatory approval and launch of Orapem in accordance with an agreed timeline. Nippon Soda recently added a quality control facility at its Nihongi plant specifically for GMP compliant products, including Orapem. After launch, the parties have agreed to certain minimum purchase requirements and pricing. The term of this agreement is for the life of the Daiichi Asubio patents on faropenem medoxomil or 12 years after launch, whichever is longer. We believe that the capacity of this plant is sufficient to provide commercial quantities of faropenem medoxomil for the next several years.

Forest Laboratories has contracted with Tropon to complete and equip an existing building as a commercial drug product facility for Orapem. The facility consists of a stand-alone building encompassing all aspects of the tablet manufacturing process including manufacturing, packaging, labeling and warehousing. This facility was built specifically for the manufacture of Orapem tablets. We believe that the capacity of this plant will be sufficient to supply all requirements for adult tablet dosage forms of Orapem to Forest Laboratories for the next several years. The parties have agreed to certain minimum purchase requirements and pricing. The initial term of Forest Laboratories agreement with Tropon is 10 years. If our agreement with Forest Laboratories terminates for any reason, the Tropon obligations will revert to us directly.

We have built a small scale drug product manufacturing facility at our Louisville, Colorado site. The facility is used for the manufacture of development batches (oral tablets and liquid suspensions) and for the manufacture of clinical supplies. The facility is dedicated exclusively for Orapem manufacturing and will not be used for other product classes.

We currently have a small internal manufacturing group that we intend to expand to manage both internal manufacturing and external contract manufacturers. For the REP8839 program and other discovery programs, we generally conduct research and development scale manufacturing in-house or use contract manufacturers. We use contract manufacturers for scale up of pre-clinical and clinical quantities of product. We anticipate using contract manufacturers for commercial scale quantities of product when this is commercially feasible.

Government Regulation and Product Approval

Regulation by governmental authorities in the U.S. and other countries is a significant factor in the development, manufacture and marketing of pharmaceuticals and antibiotics. All of our products will require regulatory approval by governmental agencies prior to commercialization. In particular, pharmaceutical drugs are subject to rigorous preclinical testing and clinical trials and other premarketing approval requirements by the FDA and regulatory authorities in other countries. In the U.S., various federal, and, in some cases, state statutes and regulations, also govern or impact the manufacturing, safety, labeling, storage, record-keeping and marketing of pharmaceutical products. The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources. Regulatory approval, if and when obtained for any of our product candidates, may be limited in scope, which may significantly limit the indicated uses for which our product candidates may be marketed. Further, approved drugs and manufacturers are subject to ongoing review and discovery of previously unknown problems that may result in restrictions on their manufacture, sale or use or in their withdrawal from the market.

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Before testing any compounds with potential therapeutic value in human subjects in the U.S., we must satisfy stringent government requirements for pre-clinical studies. Pre-clinical testing includes both *in vitro* and *in vivo* laboratory evaluation and characterization of the safety and efficacy of a drug and its formulation. Pre-clinical testing results obtained from studies in several animal species, as well as data from *in vitro* studies, are submitted to the FDA as part of an IND and are reviewed by the FDA prior to the commencement of human clinical trials. These pre-clinical data must provide an adequate basis for evaluating both the safety and the scientific rationale for the initial trials in human volunteers.

In order to test a new drug in humans in the U.S., an IND must be filed with the FDA. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concern or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed.

Clinical trials are typically conducted in three sequential phases, phases I, II and III, with phase IV trials potentially conducted after initial marketing approval. These phases may be compressed, may overlap or may be omitted in some circumstances.

Phase I. After an IND becomes effective, Phase I human clinical trials may begin. These trials evaluate a drug s safety profile and the range of safe dosages that can be administered to healthy volunteers and/or patients, including the maximum tolerated dose that can be given to a trial subject with the target disease or condition. Phase I trials also determine how a drug is absorbed, distributed, metabolized and excreted by the body and the duration of its action.

Phase II. Phase II clinical trials are typically designed to evaluate the potential effectiveness of the drug in patients and to further ascertain the safety of the drug at the dosage given in a larger patient population.

Phase III. In Phase III clinical trials, the drug is usually tested in one or more controlled, randomized trials comparing the investigational new drug to an approved form of therapy or placebo in an expanded and well defined patient population and at multiple clinical sites. The goal of these trials is to obtain definitive statistical evidence of safety and effectiveness of the investigational new drug regimen as compared to a placebo or an approved standard therapy in defined patient populations with a given disease and stage of illness.

Phase IV. Clinical trials are studies required of or agreed to by a sponsor that are conducted after the FDA has approved a product for marketing. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase IV clinical trial requirement. These clinical trials are often referred to as Phase III/ IV post approval clinical trials. Failure to promptly conduct Phase IV clinical trials could result in withdrawal of approval for products approved under accelerated approval regulations.

After completion of Phase I, II and III clinical trials, if there is substantial evidence that the drug is safe and effective, an NDA is prepared and submitted for the FDA to review. The NDA must contain all of the essential information on the drug gathered to that date, including data from preclinical and clinical trials, and the content and format of an NDA must conform to all FDA regulations and guidelines. Accordingly, the preparation and submission of an NDA is a significant undertaking for a company.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information from the sponsor rather than accepting an NDA for filing. In this case, the NDA must be re-submitted with the additional information and, again, is subject to review before filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Most NDAs are reviewed by the FDA within 10 months of submission. The review process is often significantly extended by the FDA through requests for additional information and

clarification. The FDA may refer the

application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation but typically gives it great weight. If the FDA evaluations of both the NDA and the manufacturing facilities are favorable, the FDA may issue either an approval letter or an approvable letter, the later of which usually contains a number of conditions that must be satisfied in order to secure final approval. If the FDA s evaluation of the NDA submission or manufacturing facility is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter.

Any products we manufacture or distribute under FDA approvals are subject to pervasive and continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the products. Drug manufacturers and their subcontractors are required to register with the FDA and, where appropriate, state agencies, and are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMPs regulations which impose procedural and documentation requirements upon us and any third party manufacturers we utilize.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product s labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer s communications on the subject of off-label use.

The FDA s policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or approval of new indications after the initial approval of our existing products. We cannot predict the likelihood, nature or extent of adverse governmental regulations that might arise from future legislative or administrative action, either in the U.S. or abroad.

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

Intellectual Property

The proprietary nature of, and protection for, our product candidates, processes and know-how are important to our business. We seek patent protection in the U.S. and internationally for our product candidates and other technology. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. In addition, we use license agreements to selectively convey to others rights to our own intellectual property. We also rely on trade secrets, know-how and continuing innovation to develop and maintain our competitive position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

We have licensed two U.S. patents from Daiichi Asubio covering the faropenem medoxomil composition of matter and a process for making faropenem medoxomil. Both of these patents expire on November 3, 2015. The Canadian and European equivalents of these patents expire in August 2011. The U.S. and Canadian patents are licensed to us and we have the sole negotiation right to license such rights in the rest of the world, excluding Japan. We believe that patent term extension under Hatch-Waxman

Act should be available to extend exclusivity to at least 2018 in the U.S. In Europe, we believe that patent term extension under a supplementary protection certificate should be available for an additional five years to 2016. Data exclusivity in Europe provides a period of up to 10 years from the date a product is granted marketing approval, during which the regulatory authorities are not permitted to cross-refer to the data submitted by the original applicant for approval when reviewing an application from a generic manufacturer of the same approved product. Data exclusivity does not prevent a generic manufacturer from filing for regulatory approval of the same or similar drug, even in the same indication for which that drug was previously approved in Europe, based upon data generated independently by that manufacturer. We plan to pursue development of alternative formulations of faropenem medoxomil, such as a pediatric formulation. We have not controlled and do not control the prosecution of the patents licensed from Daiichi Asubio. 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.

Daiichi Asubio also owns patents related to faropenem sodium composition of matter that expire in 2008 in the U.S. and have expired in the rest of the world. We do not have a license to the faropenem sodium patents but our agreement with Daiichi Asubio specifies that they will not license any form of faropenem for use in the U.S. or Canada. Even upon expiration of the patents, a generic competitor would be required to conduct complete clinical development in order to bring a faropenem sodium product to the market in the U.S. because that active molecule has not received regulatory approval previously in the U.S.

We acquired worldwide rights to the methionyl tRNA synthetase inhibitor program from GSK in June 2003. Our agreement with GSK included the assignment of patents and patent applications to us relating to small molecule MRS inhibitors and the targets initially used to identify the inhibitors. We have filed additional patent applications directed to small molecule methionyl tRNA synthetase, uses, production methods and the like. We have one issued U.S. patent that covers REP8839 generically and additional patent applications directed to REP8839 composition of matter and combinations of REP8839 and mupirocin. As of March 31, 2006, we have eight issued U.S. patents, 10 pending U.S. patent applications and 23 pending foreign patent applications related to the REP8839 program. These patents expire from 2017 to 2025. There are no royalty or other ongoing financial obligations to GSK, except for a $1.5 million milestone payment due upon IND filing.

We have begun to file patent applications directed to compounds that inhibit DNA replication that have been identified through our in-house screening efforts. We also own a portfolio of patents related to the DNA replication targets and drug screening methods to identify inhibitors of DNA replication. As of March 31, 2006, we have one issued U.S. patent, five pending U.S. patent applications and 14 pending foreign patent applications related to our bacterial DNA replication program. These patents expire from 2021 to 2025.

Competition

The oral anti-infective marketplace has traditionally been one of the most competitive within the pharmaceutical industry due to the large number of products competing for market share and significant levels of commercial resources being utilized to promote brands. In addition, our ability to compete may be affected because in some cases insurers and other third-parties may seek to encourage the use of generic products. This may have the effect of making branded products less attractive, from a cost perspective, to buyers. Among the products with which we will directly compete, we expect to differentiate on the basis of greater potency, improved resistance profile, enhanced safety and tolerability. Although we expect to face competition in the future, we do not expect the level of competition from branded products to be as intense as it has been in prior years due to the recent and ongoing exclusivity expiration of many major brands. Furthermore, we believe the pipeline of new oral antibiotics to treat community-acquired respiratory tract infections in development is weak, with a limited number of products currently in Phase III development. Several pharmaceutical and biotechnology companies are actively engaged in research and development related to new generations of antibiotics. We cannot predict the basis upon

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which we will compete with new products marketed by others. Many of our competitors have substantially greater financial, operation, sales and marketing and research and development resources than we have.

Legal Proceedings

We are not currently a party to any legal proceeding.

Facilities

Our facilities currently consist of approximately 42,000 square feet of laboratory and office facilities located at our headquarters in Louisville, Colorado, which is leased until September 2011, and approximately 8,000 square feet of office facilities for our clinical and regulatory group located in Milford, Connecticut, which is leased until May 2010.

We believe that these facilities are adequate to meet our current needs. We have an option to lease more space at our Louisville, Colorado facility should we need additional space. We believe that if additional space beyond that is needed in the future, such space will be available on commercially reasonable terms as needed.

Employees

As of March 31, 2006, we employed 61 persons, 18 of whom hold Ph.D., M.D. or Pharm.D. degrees. 28 employees were engaged in discovery research, 15 in clinical research and regulatory affairs, eight in commercial and corporate development and 10 in support administration, including finance, information systems, facilities and human resources. We consider our relationship with our employees to be good.

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MANAGEMENT

Executive Officers and Directors

Our directors and executive officers and their respective ages and positions are as follows:

Name	Age	Position
Kenneth J. Collins(1)	59	President, Chief Executive Officer and Director
Roger M. Echols, M.D.(1)	58	Chief Medical Officer
Nebojsa Janjic, Ph.D.(1)	45	Chief Scientific Officer and Secretary
Peter W. Letendre, Pharm.D.(1)	48	Chief Commercial Officer
Donald J. Morrissey, Jr.(1)	40	Senior Vice President, Corporate Development
Mark L. Smith(1)	44	Chief Financial Officer and Treasurer
Kirk K. Calhoun(2)	61	Director
Ralph E. Christoffersen, Ph.D.(4)	68	Director
Geoffrey Duyk, M.D., Ph.D.(3)	46	Director
Christopher D. Earl, Ph.D.(2)	49	Director
Augustine Lawlor(2)(3)	49	Director
Daniel J. Mitchell(3)(4)	49	Director
Henry Wendt(4)	72	Director

(1) Executive officer.

(2) Member of the audit committee.

(3) Member of the compensation committee.

(4) Member of the corporate governance and nominating committee.

Executive Officers

Kenneth J. Collins has served as our President, Chief Executive Officer and a member of the board of directors since January 2002. From 1997 to 2001, Mr. Collins served as President of Pegasus Technology Ventures, a firm that advised and raised seed capital for early stage life sciences companies. From 1995 to 1996, Mr. Collins served as Chief Financial Officer and a member of the board of directors of Quark, Inc., a developer of desktop publishing software. Mr. Collins served as an Executive Vice President from 1992 to 1994 and Chief Financial Officer from 1983 to 1994 of Synergen, Inc., a biotechnology company. Mr. Collins holds a B.S. from the University of Notre Dame and an M.B.A. from the Harvard Business School.

Roger M. Echols, M.D. has served as our Chief Medical Officer since January 2005. From 1997 to 2004, Dr. Echols served as Vice President of Infectious Disease Clinical Research and Development at Bristol Myers Squibb. He served as Medical Director at Immunex Corporation from 1996 to 1997 and as Medical Director at Bayer Corporation from 1989 to 1996. Prior to joining the pharmaceutical industry, Dr. Echols was Head of the Division of Infectious Diseases at Albany Medical College and an attending physician at Albany Medical College. Dr. Echols holds a B.A. from Yale University and an M.D. from Tufts University School of Medicine and trained in internal medicine and infectious diseases at the University of New Mexico.

Nebojsa Janjic, Ph.D. has served as our Secretary since December 2000 and as our Chief Scientific Officer since June 2005. Dr. Janjic joined us at inception and served as our Vice President, Research and Development until June 2005. From 1992 to 1999, Dr. Janjic served as Senior Director, Drug Discovery at NeXstar Pharmaceuticals, Inc., a biotechnology company. Dr. Janjic holds B.S. and Ph.D. degrees from the University of Washington and completed postdoctoral training at the Scripps Research Institute.

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Peter W. Letendre, Pharm.D. has served as our Chief Commercial Officer since March 2005. From October 2002 until February 2005, Dr. Letendre held various positions at Abbott Laboratories, most recently as Vice President and General Manager of the anti-infective division from October 2002 until July 2004. From August 1990 to September 2002, Dr. Letendre held a number of marketing positions with SmithKline Beecham and GlaxoSmithKline Pharmaceuticals, including marketing director for the diabetes and metabolism division from 1998 to 2000. From 1988 to 1990, Dr. Letendre served as the Associate Dean of Clinical Practice at Southeastern University of the Health Sciences. Dr. Letendre holds B.S. and Doctor of Pharmacy degrees from the Massachusetts College of Pharmacy and Allied Health Sciences.

Donald J. Morrissey, Jr. has served as our Senior Vice President, Corporate Development since March 2006 and, prior to that, as Vice President, Corporate Development since 2002. From 1997 to 2002, Mr. Morrissey held various positions with Caliper Technologies, most recently as Vice President, Legal Affairs and Business Development from September 2001 to November 2002. From 1992 to 1997, Mr. Morrissey was a business attorney with Cooley Godward llp . Mr. Morrissey holds a B.A. from the University of Colorado and a J.D. from the University of Southern California Law School.

Mark L. Smith has served as our Chief Financial Officer and Treasurer since March 2006. From August 1999 to March 2006, Mr. Smith held financial executive capacities at Nabi Biopharmaceuticals, including serving as Senior Vice President, Finance, Chief Financial Officer and Chief Accounting Officer from 2001 to March 2006. From 1998 to 1999, Mr. Smith served as Vice President of Finance and Administration and Chief Financial Officer of Neuromedical Systems, Inc. From 1996 to 1998, Mr. Smith served in various financial executive capacities at Genzyme Corporation. From 1991 to 1996, Mr. Smith held various positions at Genetrix, Inc., most recently as its Chief Financial Officer. Before joining Genetrix, Inc., Mr. Smith practiced with the accounting firm of PricewaterhouseCoopers LLP in both the U.S. and Australia. Mr. Smith holds a B.A. in Accounting from the Canberra College of Advanced Education in Australia.

Directors

Kirk K. Calhoun has served as a Director since March 2006. Mr. Calhoun joined Ernst & Young, LLP, a public accounting firm, in 1965 and served as a partner of the firm from 1975 until his retirement in 2002. His responsibilities included both area management and serving clients in a variety of industries, including biotechnology. Mr. Calhoun is a Certified Public Accountant with a background in auditing and accounting. He is currently on the Board of Directors of Adams Respiratory Therapeutics, Inc., American Pharmaceutical Partners, Inc., Aspreva Pharmaceuticals Corporation and Myogen, Inc. and the Board of Governors of the California State University Foundation. Mr. Calhoun received a B.S. in Accounting from the University of Southern California.

Ralph E. Christoffersen, Ph.D. has served as a Director since December 2003. Dr. Christoffersen has been a partner at Morgenthaler Ventures since August 2001. From 1992 to 2001, Dr. Christoffersen was the President and Chief Executive Officer of Ribozyme Pharmaceuticals, Inc. From 1981 to 1992, he was the Senior Vice President of Research at SmithKline Beecham, Vice President of Discovery Research at The Upjohn Company, and President of Colorado State University. Dr. Christoffersen is a member of the Board of Directors of Serologicals Corp. Dr. Christoffersen holds a B.S. from Cornell College and a Ph.D. from Indiana University.

Geoffrey Duyk, M.D., Ph.D. has served as a Director since June 2004. Dr. Duyk is a partner at Texas Pacific Group Ventures. From 1996 to 2003, Dr. Duyk was President of Research & Development and a director of Exelixis Inc. From 1993 to 1996, he was one of the founding scientific staff at Millennium Pharmaceuticals. Prior thereto, Dr. Duyk was an Assistant Professor at Harvard Medical School in the Department of Genetics and Assistant Investigator of the Howard Hughes Medical Institute. Dr. Duyk holds a B.A. from Wesleyan University and a Ph.D. and M.D. from Case Western Reserve University.

Christopher D. Earl, Ph.D. has served as a Director since September 2004. Dr. Earl is President and Chief Executive Officer of BIO Ventures for Global Health. From 1997 to 2005, he served as

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Managing Director at Perseus Capital and of Perseus-Soros Management, LLC, an affiliate of the Perseus-Soros BioPharmaceutical Fund, LP, a private equity fund. Prior to that, Dr. Earl was President and Chief Executive Officer of Avitech Diagnostics, Inc. and a General Partner of Plant Resources Venture Funds. Dr. Earl serves on the Board of Governing Trustees of the Jackson Laboratory. Dr. Earl holds a B.A. from the University of Pennsylvania and a Ph.D. from Harvard University.

Augustine Lawlor has served as a Director since March 2002. Mr. Lawlor has been a Managing Director of HealthCare Ventures LLC since 2000. Mr. Lawlor was previously Chief Operating Officer of LeukoSite, Inc. and has also served as a management consultant with KPMG Peat Marwick. Mr. Lawlor is a member of the Board of Directors of Human Genome Sciences Inc. Mr. L