VICURON PHARMACEUTICALS INC
Form 10-K
March 16, 2005
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

x **Annual report pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934**

for the fiscal year ended December 31, 2004

OR

¨ **Transition report pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934**

for the transition period from to .

Commission file number: 000-31145.

VICURON PHARMACEUTICALS INC.

(Exact name of registrant as specified in its charter)

Delaware	**04-3278032**
(State or Other Jurisdiction of Incorporation)	**(I.R.S. Employer Identification Number)**
455 South Gulph Road, Suite 305	
King of Prussia, PA 19406	**(610) 205-2300**
(Address of principal executive offices) (Zip Code)	**(Telephone number)**

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	**Nasdaq National Market and**
	Nuovo Mercato

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes x No ¨

On June 30, 2004, which was the last business day of our most recently completed second fiscal quarter, our public market value was approximately $683.1 million (based on 54.4 million shares of our common stock then held by non-affiliates and a closing price that day of $12.56 per share of our common stock on the Nasdaq National Market). These public market value calculations exclude shares held on the stated dates by our executive officers and directors and persons filing a Schedule 13D with the Securities and Exchange Commission in respect to our common stock. (Exclusion from these public market value calculations does not imply affiliate status for any other purpose).

On February 23, 2005, we had 60,631,269 shares of our common stock outstanding.

Documents Incorporated By Reference: Portions of the Proxy Statement for the 2005 Annual Meeting of Stockholders (the Proxy Statement), to be filed within 120 days of the end of the fiscal year ended December 31, 2004, are incorporated by reference in Part III hereof. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part hereof.

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Cautionary Note Regarding Forward-Looking Statements

In addition to historical information, this Annual Report on Form 10-K, including the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations, contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical facts included in this Annual Report on Form 10-K, regarding our strategy, future operations, financial position, projected costs, prospects, plans and objectives of management are forward-looking statements. As contained herein, the words expects, anticipates, believes, intends, will, and similar types of expressions identify forward-looking statements, although not all forward-looking statements contain these identifying words. These statements are based on information that is currently available to us, speak only as of the date hereof, and are subject to certain risks and uncertainties. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or to reflect any change in events, conditions, or circumstances on which any such forward-looking statement is based, in whole or in part. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to, those discussed in the sections in this Annual Report on Form 10-K entitled Risk Factors. Readers should carefully review the risk factors described in other documents the Company files from time to time with the Securities and Exchange Commission, including the Quarterly Reports on Form 10-Q that we will file in 2005.

All references to dollars or $ in this Annual Report on Form 10-K are references to United States dollars; all references to euros or are references to European Union, or EU, euros. On February 23, 2005, the median 4 p.m. Greenwich Mean Time spot rate for the euro expressed in

dollars per euro was $1.32 to 1.00.

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PART I

ITEM 1. BUSINESS

In this Annual Report on Form 10-K, references to the Company, Vicuron, and we, throughout this Form 10-K shall all refer to Vicuron Pharmaceuticals, Inc. and its subsidiaries. This Annual Report contains trademarks and trade names of other entities.

Overview

We are a biopharmaceutical company focused on discovering, developing, manufacturing and commercializing vital medicine for seriously ill patients. We focus on seeking to develop antibiotics and antifungals that may have competitive advantages over existing products, such as greater potency, improved effectiveness against difficult to treat strains and reduced toxicity. Because the development process for anti-infective products is relatively efficient and well-defined, we believe the costs and time required to bring new anti-infective products to market can be significantly less than the time required to bring products to market in other major therapeutic categories.

In early 2003, we submitted a new drug application, or NDA, for our lead antifungal product candidate, anidulafungin, to the U.S. Food and Drug Administration, or FDA. Anidulafungin belongs to the first new class of antifungal agents, called echinocandins, introduced in more than 40 years. In May 2004, we received an approvable letter from the FDA for anidulafungin. Based on the approvable letter and our discussions with the FDA, we intend to pursue two paths for approval of anidulafungin, as follows:

amending our existing NDA for the treatment of esophageal candidiasis; and

submitting an additional NDA for the treatment of invasive candidiasis/candidemia.

In December 2004, we submitted an NDA for dalbavancin, a novel antibiotic for the treatment of complicated skin and soft tissue infections, or cSSTIs. In February 2005, we received from the FDA the acceptance file notification and were granted priority review status by the FDA for the NDA for dalabanvin for the treatment of complicated skin and soft tissue infections. Dalbavancin is a unique, once weekly IV lipoglycopeptide for the treatment of cSSTIs caused by Gram-positive bacteria, including the difficult-to-treat strains of Staphylococcus-methicillin-resistant Staphylococcus aureus, or MRSA. Dalbavancin is a second-generation lipoglycopeptide antibiotic belonging to the same class as vancomycin, a widely-used injectable antibiotic for Staphylococcal infections. The current Prescription Drug User Fee Act, or PDUFA date is June 21, 2005.

We have a two-fold approach to product discovery, development and marketing. Our primary strategy is to focus on the discovery and development of proprietary products, concentrating on injectable antibiotic and antifungal products for the hospital market. We expect to market these products in certain markets through a targeted and cost-effective sales and marketing infrastructure, including a direct sales force, that we plan to establish. Our product candidates target disease indications that represent markets where there is demand for new therapies.

Our secondary strategy is to collaborate with major pharmaceutical companies to discover and develop orally administered antibiotic and antifungal products for the community market. Major pharmaceutical companies are generally better suited to market these products, as these products require substantial expenditures for sales and marketing to reach their full market potential. Under our typical collaboration agreements, we are responsible for discovering the compounds and our collaborators are responsible for developing and marketing them. We expect to receive a combination of research funding, milestone payments and equity investments from our collaborators, as well as royalty fees if any products are commercialized.

Our discovery platform combines our proprietary expertise in the critical areas of functional genomics, mechanism-based rational drug design, high-throughput screening of our diversified library of microbial extracts, combinatorial chemistry, lead optimization and medicinal chemistry. We intend to leverage our technology

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platform to discover and supply lead compounds both for internal development and commercialization, in the case of hospital products, and for our pharmaceutical collaborations, in the case of community products.

Our revenues in the near term are expected to consist primarily of collaborative research payments, license fees and milestone payments to be received from our collaborators. Certain of these payments are dependent on the achievement of specified milestones. We expect these revenues to decrease in 2005. If the development efforts result in clinical success, regulatory approval and successful commercialization of our products, we will generate revenues from sales of proprietary products and from receipt of royalties on sales of collaboration products.

Our expenses have consisted primarily of costs incurred in research and development of new product candidates when in-licensing existing product candidates, and in connection with our collaboration agreements, and from general and administrative costs associated with our operations. We expect licensing costs to increase as development milestones are achieved, and our research and development expenses to increase as we continue to develop our product candidates. We expect to incur sales and marketing expenses during 2005 as we establish our sales and marketing organization.

Since our inception we have incurred significant losses. As of December 31, 2004, we had an accumulated deficit of $405.2 million. We anticipate incurring additional losses, which may increase for the foreseeable future, including at least through December 31, 2006.

We anticipate that our quarterly results of operations will fluctuate for the foreseeable future due to several factors, including payments made or received pursuant to licensing or collaboration agreements, progress of our research and development efforts, and the timing and outcome of regulatory approvals. The fluctuating nature of these factors makes predictions of our future operations difficult or impossible to ascertain.

Our Proprietary Products

Anidulafungin

Our lead antifungal product candidate, anidulafungin, is intended for the intravenous treatment of serious systemic fungal infections. Anidulafungin has potent activity against the principal yeasts, such as *Candida*, and molds, such as *Aspergillus*, that cause serious fungal infections. In addition, anidulafungin has fungicidal activity against yeast, which means that it kills the yeast. This is in contrast to many widely-used antifungal agents which only inhibit fungal growth. Because of anidulafungin s novel mechanism of action, it is active against strains resistant to other agents, such as fluconazole. We believe anidulafungin will have competitive advantages over existing therapies because it combines potent fungicidal activity with a good resistance profile to date.

In early 2003, we completed a Phase 3 clinical trial with anidulafungin for the treatment of esophageal candidiasis. Based in part on the results of that trial, in April 2003 we filed an NDA for anidulafungin for the treatment of esophageal candidiasis, which was accepted for review by the FDA in June 2003. In May 2004, we received an approvable letter from the FDA indicating that the NDA submission for anidulafungin did not currently support a labeling claim for the initial treatment of esophageal candidiasis. In the approvable letter, the FDA provided that its basis for this conclusion was that we had not presented sufficient efficacy and safety data to establish a satisfactory risk/benefit rationale for the use of anidulafungin in the initial treatment of esophageal candidiasis, including the relapse rate at the two-week post-therapy visit. We intend to address these matters with the submission of additional efficacy and safety data as described below.

We plan to file an amendment to the esophageal candidiasis NDA, which will provide supplemental efficacy and safety data largely at the 100 mg dose, including from our completed invasive candidiasis/candidemia Phase 3 clinical trial. We expect to submit the amendment in the second quarter of 2005. Under this timeline, the fourth quarter of 2005 is the earliest anidulafungin could be approved for this indication. In December 2003, we also announced the filing of our marketing authorization application, or MAA for anidulafungin for the treatment of esophageal candidiasis with the European Agency for the Evaluation of Medicinal Products, or EMEA. We requested, and the EMEA granted us, a 90 day extension for submitting responses to the EMEA. Subsequently,

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we requested the withdrawal of the anidulafungin MAA for esophageal candidiasis from the EMEA in March 2005. We intend to resubmit a new MAA for anidulafungin in invasive candidiasis.

We intend to file a new NDA for anidulafungin for the treatment of invasive candidiasis/candidemia with updated efficacy and integrated safety data, including data from our completed Phase 3 clinical trial, the top line results of which were released on February 7, 2005. We plan to submit the NDA for this indication in the third quarter of 2005.

We began the Phase 3 clinical trial of anidulafungin for invasive candidiasis/candidemia in December 2002 and announced the completion of enrollment in September 2004. This double-blind, multi-center, randomized Phase 3 trial studied a 100 mg daily dose of anidulafungin versus a 400 mg daily dose of fluconazole in 256 patients with invasive candidiasis/candidemia. Patients received daily intravenous, or IV infusions of either anidulafungin or fluconazole for 10 to 42 days. The primary endpoint was the global response at the end of IV therapy, which required a successful clinical and a successful microbiological response.

Success in the global response at the end of IV therapy in the microbiological intent-to-treat, or ITT population was 75.6% (96/127) of patients with anidulafungin and 60.2% (71/118) with fluconazole. These results demonstrate statistical superiority (95% confidence interval of the difference: 3.85, 26.99) in favor of anidulafungin.

The secondary endpoint of successful global response at the two-week follow up visit in the microbiological ITT population was observed in 64.6% (82/127) of patients in the anidulafungin arm and 49.2% (58/118) of patients in the fluconazole arm, again demonstrating statistical superiority (95% confidence interval of the difference: 3.14, 27.68).

The secondary endpoint of successful global response at the six-week follow-up visit in the microbiological ITT population was observed in 55.9% (71/127) of patients in the anidulafungin arm and 44.1% (52/118) of patients in the fluconazole arm demonstrating non-inferiority (95% confidence interval of the difference: -0.6, 24.28). Anidulafungin demonstrated comparable tolerability to fluconazole in the study.

We also began a Phase 2/3 clinical trial of anidulafungin in combination with liposomal amphotericin for the treatment of invasive aspergillosis in the fourth quarter of 2001 and released results of this trial in March 2004. This open-label, non-comparative trial enrolled 30 hospitalized patients with a diagnosis of invasive aspergillosis. A single daily intravenous infusion of anidulafungin and a single daily intravenous infusion of a lipid-complexed formulation of amphotericin B was administered to patients for up to 90 days. We believe that the results of this clinical trial demonstrate that anidulafungin and liposomal amphotericin can be combined without increasing side effects.

Dalbavancin

Our lead antibiotic product candidate, dalbavancin, is a second-generation lipoglycopeptide antibiotic belonging to the same class as vancomycin, a widely-used injectable antibiotic for Staphylococcal infections. Dalbavancin is intended for the treatment of serious systemic infections, particularly those caused by Staphylococci. Dalbavancin is more potent than vancomycin *in vitro*, in particular against methicillin-resistant Staphylococci, a common and difficult-to-treat bacterium. Dalbavancin has bactericidal activity, which means that it kills the bacteria rather than merely inhibiting their growth, as shown in both the laboratory and in infected animals. Because of its unique pharmacokinetic properties and the tolerability profile seen to date, dalbavancin has the potential to be dosed weekly, which may be a significant competitive advantage over other products that are typically dosed once or multiple times each day. We have completed Phase 3 clinical trials

with dalbavancin for the treatment of both complicated and uncomplicated skin and soft tissue infections, or SSTIs. The results of the Phase 3 clinical trials met the primary endpoint of non-inferiority in evaluable patients clinical response at two weeks following therapy when compared to linezolid, cefazolin or vancomycin, three of the standard-of-care agents for SSTIs. Dalbavancin was also shown to be well tolerated. Based on these data, we filed in December 2004 an NDA for dalbavancin for

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the treatement of cSSTIs. In February 2005, we received the acceptance to file notification from the FDA and were granted priority review status by the FDA for the NDA for dalbavancin. The current PDUFA date is June 21, 2005.

In December 2002, we began two pivotal Phase 3 clinical trials evaluating weekly dosing of dalbavancin for treatment of SSTIs, the first in complicated skin and soft tissue infections, or cSSTIs, versus linezolid (Zyvox) and the second in uncomplicated skin and soft tissue infections, or uSSTIs, versus intravenous cefazolin followed by oral cephalexin. In August 2004, we announced the results of these trials. The cSSTI trial was a randomized, double-blind trial involving 854 patients randomized in a 2:1 ratio for dalbavancin:linezolid. The primary endpoint was clinical response at the follow-up visit in the evaluable patient population. Evaluable patients taking dalbavancin demonstrated an 88.9% response versus 91.2% for linezolid patients (95% confidence interval -7.3, 2.9), which met the pre-determined criterion for non-inferiority delta. In the ITT, group dalbavancin patients showed a 76.5% response versus 82.7% for linezolid (95% confidence interval -12.0, -0.3) demonstrating non-inferiority. Dalbavancin was well tolerated in this trial. The uSSSI trial was a randomized, double-blind trial involving 553 patients randomized in a 2:1 ratio for dalbavancin:intravenous cefazolin followed by oral cephalexin. The primary endpoint was clinical response at the follow-up visit in the evaluable patient population. Evaluable patients taking dalbavancin demonstrated an 89.1% response versus 89.1% for cefazolin (95% confidence interval -6.8, 6.8), which met the pre-determined criterion for non-inferiority. In the ITT group, dalbavancin patients showed a 76.0% response versus a 75.8% response for cefazolin (95% confidence interval -7.7, 8.2) demonstrating non-inferiority. Dalbavancin was well tolerated in this trial.

In addition, in October 2003, we initiated another Phase 3 clinical trial to evaluate the safety and efficacy of dalbavancin versus vancomycin in SSTIs in patients at risk for methicillin-resistant *Staphylococcus aureus*, or MRSA. In August 2004, we announced the results from this randomized, controlled, open-label trial of 156 patients randomized in a 2:1 ratio versus vancomycin in SSTIs suspected or confirmed to be caused by MRSA. The primary endpoint was clinical response at the follow-up visit in the evaluable patient population. Evaluable patients taking dalbavancin demonstrated an 89.9% response versus 86.7% for vancomycin (95% confidence interval -13.0, 19.4). In the ITT group, dalbavancin patients showed an 86.0% response versus 65.3% for vancomycin (95% confidence interval 4.3, 37.0). Dalbavancin was well tolerated in this trial. This trial is not pivotal, but was included with the NDA submission.

In addition to the SSTI trials, we have completed a Phase 2 clinical trial of dalbavancin administered weekly versus vancomycin for the treatment of catheter-related blood stream infections, or CR-BSI. In January 2004, we released results of this trial, which demonstrated the superiority of dalbavancin over vancomycin, a standard of care for this disease. This randomized, comparative, open-label trial enrolled 67 patients with CR-BSI due to a Gram-positive organism. The primary endpoint was the combined clinical and microbiological response at follow-up. The overall response rate was 87% for dalbavancin which was statistically superior to 50% for vancomycin.

Ramoplanin

Our third product candidate, ramoplanin, is an oral non-absorbable form of antibiotic called a lipopeptide. Ramoplanin selectively inhibits Gram-positive bacteria, including MRSA, and all types of vancomycin-resistant enterococci, or VRE, and Clostridia, including *Clostridium difficile*. Ramoplanin does not show a propensity to select resistant mutants *in vitro* and does not have cross-resistance with known antibiotics. Oscient Pharmaceuticals Corporation, formerly Genome Therapeutics Corp., our licensee in North America, is developing ramoplanin. Oscient Pharmaceuticals initiated a Phase 3 clinical trial for the reduction of VRE bloodstream infections in patients at risk in June 2000. However, our licensee announced in July 2004 that it prematurely terminated enrollment in this trial because of slow enrollment. Oscient Pharmaceuticals also recently completed a Phase 2 clinical trial of ramoplanin for the treatment of *Clostridium difficile*-associated diarrhea, or CDAD, and data have been publicly presented. Pending the completion of full analysis of the Phase 2 data and the outcome of planning discussions with the FDA, Oscient Pharmaceuticals has indicated that it expects to commence a Phase 3 clinical trial in CDAD by the end of this year.

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VIC-Acne

Our fourth product candidate, VIC-Acne, is a novel antibiotic which we are developing as a topical cream. VIC-Acne has a new mechanism of action and shows selective activity against *Propionibacterium acnes*, a bacteria associated with acne, including drug resistant strains, while it shows only modest activity against normal skin flora. As a result, it might have the potential to selectively eliminate the *Propionibacterium acnes* without significantly affecting the natural skin flora. We completed a Phase I clinical trial with VIC-Acne in the second quarter of 2003 which showed that the drug was safe and well-tolerated. We plan to out-license this product candidate to a company with a dermatology business who will agree to develop and commercialize the product candidate. We would expect to receive milestone payments and a royalty on our contemplated licensee s sales.

VIC-5555

VIC 5555 is the lead product candidate in our lincosamide research program. It is designed as an improvement of clindamycin, an antibiotic often used for anerobic bacterial infections. VIC-5555 has shown improved *in vivo* and *in vitro* activity when compared to clindamycin. We plan to file an IND for VIC-5555 in 2005.

Research Collaborations

Our most advanced collaboration is with Novartis Pharma AG and is designed to develop deformylase inhibitors as new antibacterial agents and to provide novel target-based screens. Deformylase is an essential enzyme in bacteria but not in human cells, and thus represents a good target for the discovery of selective inhibitors that can serve as broad spectrum antibacterial agents. We have identified several lead inhibitor molecules that are active against multi-drug resistant strains, as well as respiratory pathogens such as *S. pneumoniae*, *H. influenzae* and *M. catarrhalis*. Several lead compounds have demonstrated activity in pre-clinical *in vivo* studies when administered orally, representing an example of the *de novo* design of an active antibacterial agent. Our collaboration with Novartis began in April 1999. In January 2002, we received a fifth milestone payment as a result of our delivery of our fifth target-based screen, which we expect will be used in Novartis high-throughput screening laboratory to identify new anti-infectives. In March 2002, we amended the original agreement in order to extend the research term an additional year and to provide that Novartis will make an additional payment upon our achievement of a new milestone. In February 2003, we amended the original agreement in order to extend the research term through March 31, 2005. In September 2003, we announced that we received a milestone payment from Novartis for achieving a late-stage pre-clinical milestone and in December 2003, we received a further milestone payment associated with the entry into Phase 1 of a drug candidate stemming from the ongoing research collaboration with Novartis. In March 2005, we announced that Novartis has opted to suspend the Phase 1 compound and intends to advance a second compound. We received a milestone for the designation of this second compound as a late stage preclinical compound.

Our second most advanced collaboration is with Pfizer Inc. and is aimed at discovering second and third generation oxazolidinones. The oxazolidinones represent one of the first new major classes of antibacterial products to enter the market in over 30 years. In test tubes, our collaboration compounds are active against a broad range of bacteria, including multi-drug resistant Staphylococci, Streptococci and Enterococci. Pfizer received approval from the FDA, independent of us, for the first generation oxazolidinone called Zyvox. We have identified several structurally novel second generation oxazolidinone candidates, certain of which have either a broader spectrum of activity or improved potency as compared to Zyvox. Some of these compounds also show good activity in pre-clinical *in vivo* studies when administered orally. This collaboration began in April 1999 with Pharmacia Corporation, and continued when Pharmacia was acquired by Pfizer. In October 2000, Pfizer increased its research support payments to us by 30% and, in June 2002, we amended our agreement with Pfizer to extend the research term for an additional three years. In May 2003, we announced an agreement to continue this collaboration with Pfizer after their acquisition of Pharmacia, our original collaborator.

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Another collaboration program is called VITACHEM and is designed to investigate the pharmaceutical and non-pharmaceutical utility of our collection of microbial chemicals in markets outside of the anti-infectives market. We offer two types of collaborations under the VITACHEM program: fee-for-service collaborations, under which our collaborators pay us research fees, plus milestone payments and royalties calculated as a percentage of net sales; and equal collaborations, based on cost-sharing and reward-sharing. Currently, we have one equal collaboration with Myriad Genetics Inc. on oncology, cardiovascular and viral targets.

Internal Discovery Research

In addition to our external research collaborations, we have internal research programs both in the United States and in Italy. The objective of internal research is primarily to discover novel antimicrobials for hospital use for development by us. This effort combines our internal expertise in functional genomics-based target selection, novel assay development, mechanism-based rational drug design, combinatorial chemistry, high-throughput screening of our diversified library of microbial extracts and medicinal chemistry. We are currently investigating several *in vivo* active leads.

Our Strategy

Our objective is to be a leader in the discovery, development and marketing of pharmaceutical products for the treatment of bacterial and fungal infections in the hospital setting. We intend to achieve this goal through the implementation of four strategies:

Focus our discovery and development efforts on products to treat bacterial and fungal infections. We believe that anti-infective products have significant development advantages over products in some other therapeutic categories. These advantages include lower costs and shorter development cycles. In addition, product candidates in this area have a greater probability of clinical success due to the higher predictive value of clinical trials in this area. Finally, there is a growing demand for new anti-infective products. We believe that this demand is driven primarily by the aging of the population, the growing number of seriously ill patients in hospitals and an increase in immunosuppression and fungal and bacterial resistance to existing therapies.

Target our resources on products that have potential utility in the hospital setting. We believe that our efforts are best focused on developing products that would be administered in a hospital setting. Because of the increased number of elderly patients and the severity of illnesses among patients in intensive care units, we believe that hospitals present an addressable market with significant unmet needs. This strategy will also allow us to use a relatively small sales force, thereby allowing us to reach the greatest number of patients while still remaining cost-effective.

Focus on products that have a competitive advantage over currently marketed drugs. We intend to focus our development efforts on products that we expect to have potential advantages over currently marketed drugs. This strategy reduces the time and expense we will need to effectively educate physicians about new types of treatments and will allow us to market our relative benefits directly against our competitors products.

Pursue our twofold approach to product development. We have a twofold approach to product development and marketing. Our primary strategy is to internally develop anti-infective products with utility in a hospital setting and then to market these products to hospitals using our own focused sales force. For oral anti-infective products, which have utility in a broader community setting, we intend to collaborate in our development and marketing efforts with large pharmaceutical companies. This twofold approach allows us to pursue, on a proprietary basis, internal development and marketing of those products for which we feel the development and

marketing requirements are manageable, such as injectable anti-infectives, and to out-license products, such as orally administered anti-infectives, that require greater marketing resources than we are willing to commit.

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Our Proprietary Product Candidates

The table below summarizes our product candidates, their target infections, their nature of activity and their development status.

Product Candidate/Program	Target Infections	Development Status	Regulatory Status
	Proprietary		
Anidulafungin	*Esophageal Candidiasis (EC)*	Phase 3[(1)]	NDA Approvable Letter (EC)
	Invasive Candidiasis/Candidemia	Phase 3[(1)]	
	Invasive Aspergillosis	Phase 2-3[(1)]	
Dalbavancin	*Skin and Soft Tissue Infections*	Three Phase 3[(1)]	NDA cSSTI filed (File Accepted/Priority Review)
	Catheter Related Blood Stream Infections	Phase 2[(1)]	
VIC-Acne	*Acne*	Phase 1[(1)]	
VIC-5555	*Bacterial Infections*	Pre-clinical in vivo	
	Collaborations		
Ramoplanin (Oscient Pharmaceuticals)	*Clostridium difficile - associated Diarrhea*	Phase 2[(1)]	
Deformylase Inhibitors (Novartis)	*Bacterial Infections*	Pre-clinical *in vivo*	
Oxazolidinones (Pfizer)	*Bacterial Infections*	Pre-clinical *in vivo*	

(1) Clinical trial complete.

Anidulafungin A Novel Antifungal for the Treatment of Serious Infections

Clinical Experience

On the basis of Phase 1 dose ranging studies and a successful Phase 2 study, we began a pivotal Phase 3 trial of anidulafungin for the treatment of esophageal candidiasis in the first quarter of 2001 and completed enrollment in October 2002. In this randomized, double-blind, double-dummy trial involving 601 patients, we compared anidulafungin at a daily maintenance dose of 50 mg with oral fluconazole at a 100 mg daily dose. Treatment continued for between 14 and 21 days, with the primary assessment of response made at the end of therapy. Additional evaluations were made at a follow-up visit approximately two weeks later. Endoscopic response was the primary endpoint, with both clinical responses and eradication of fungi as secondary endpoints. In early 2003, we completed this clinical trial. The Phase 3 esphogeal candidiasis trial demonstrated a 97.2% endoscopic response for anidulafungin (N=249) versus a 98.8% endoscopic response for fluconazole (N=255) at the primary endpoint at end of treatment.demonstrating non-inferiority (95% confidence interval of the difference: -4.1, 0.8). The endoscopic response at follow-up, a secondary endpoint, was 64.4% for anidulafungin versus 89.5% for fluconazole which was statistically significant (95% confidence interval of the difference: -32.5%, -17.8%).

Based in part on the results of that trial, in April 2003 we filed an NDA for anidulafungin for the treatment of esophageal candidiasis, which was accepted for review by the FDA in June 2003. We received a 90-day review extension due to a major amendment. In May 2004, we received an approvable letter from the FDA indicating that the NDA submission for anidulafungin did not currently support a labeling claim for the initial

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treatment of esophageal candidiasis. In the approvable letter, the FDA provided that its basis for this conclusion was that we had not presented sufficient efficacy and safety data to establish a satisfactory risk/benefit rationale for the use of anidulafungin in the initial treatment of esophageal candidiasis, including the relapse rate at the two-week post-therapy visit. We intend to address these matters with the submission of additional efficacy and safety data as described below.

We plan to file an amendment to the esophageal candidiasis NDA, which will provide supplemental efficacy and safety data largely at the 100 mg dose, including data from our completed invasive candidiasis/candidemia Phase 3 clinical trial. We expect to submit the amendment in the second quarter of 2005. Under this timeline, the fourth quarter of 2005 is the earliest anidulafungin could be approved for this indication

We intend to file a new NDA for anidulafungin for the treatment of invasive candidiasis/candidemia with updated efficacy and integrated safety data, including data from our completed Phase 3 clinical trial, the results of which were released in February 2005. We plan to submit the NDA for this indication in the third quarter of 2005.

We began the Phase 3 clinical trial of anidulafungin for invasive candidiasis/candidemia in December 2002 and announced the completion of enrollment in September 2004. This double-blind, multi-center, randomized Phase 3 trial studied a 100 mg daily dose of anidulafungin versus a 400 mg daily dose of fluconazole in 256 patients with invasive candidiasis/candidemia. Patients received daily intravenous, or IV infusions of either anidulafungin or fluconazole for 10 to 42 days. The primary endpoint was the global response at the end of IV therapy, which required a successful clinical and a successful microbiological response.

Success in the global response at the end of IV therapy in the microbiological ITT population, the primary endpoint, was 75.6% (96/127) of patients with anidulafungin and 60.2% (71/118) with fluconazole. These results demonstrate statistical superiority (95% confidence interval of the difference: 3.85, 26.99) in favor of anidulafungin.

The secondary endpoint of successful global response at the two-week follow up visit in the microbiological ITT population was observed in 64.6% (82/127) of patients in the anidulafungin arm and 49.2% (58/118) of patients in the fluconazole arm, again demonstrating statistical superiority (95% confidence interval of the difference: 3.14, 27.68).

The secondary endpoint of successful global response at the six-week follow up visit in the microbiological ITT population was observed in 55.9% (71/127) of patients in the anidulafungin arm and 44.1% (52/118) of patients in the fluconazole arm demonstrating non-inferiority (95% confidence interval of the difference: -0.6, 24.28). Anidulafungin demonstrated comparable tolerability to fluconazole in the study.

Global Response

	Microbiological ITT			Evaluable		
	Anidulafungin	**Fluconazole**	**95% CI**	**Anidulafungin**	**Fluconazole**	**95% CI**
End of IV Therapy	75.6%	60.2%	(3.85,26.99)(1)(a)	87.4%	74.7%	(1.66,23.65)(a)
2 Week Follow-up	64.6%	49.2%	(3.14,27.68)(a)	80.7%	67.1%	(0.17,26.98)(a)

6 week Follow-up	55.9%	44.1%	(-0.6,24.28)(b)	74.7%	62.3%	(-2.56,27.29)(b)

(1) Primary
(a) Statistically Superior
(b) Stastically non-inferior

We began a Phase 2/3 trial of anidulafungin for the treatment of aspergillosis in the fourth quarter of 2001. Aspergillosis has a very high rate of mortality, therefore, new therapies are urgently needed. For this reason, and because our Phase 1 trial demonstrated that higher doses of anidulafungin were well-tolerated by volunteers, we have taken an anidulafungin dose of a 200 mg loading dose followed by daily maintenance doses of 100 mg directly into our Phase 2/3 trial. This open-label, non-comparative study enrolled 30 hospitalized patients with a

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diagnosis of invasive aspergillosis. A single daily intravenous infusion of anidulafungin and a single daily intravenous infusion of a lipid-complexed formulation of amphotericin B was administered to patients for up to 90 days. The primary endpoint was combined global response, *i.e.,* clinical and radiographic responses, at the conclusion of therapy. We believe that the results of this clinical trial demonstrate that anidulafungin and liposomal amphotericin can be combined without increasing side effects.

Characteristics of Anidulafungin

Anidulafungin, our lead antifungal product candidate, belongs to the echinocandin class of antifungal agents. It is being developed for the treatment of serious fungal infections, including disseminated or bloodstream infections, organ infections and esophagitis, or severe infections of the esophagus. The most serious fungal infections generally occur in individuals who have impaired immune systems. *In vitro* anidulafungin is fungicidal for *Candida*, which means that it kills, rather than just inhibits, the pathogen. Anidulafungin is active against candida and aspergillus strains resistant to azoles, such as fluconazole.

Anidulafungin is a chemically modified derivative of a natural product that was chosen for development because of its improved properties over existing treatments. In May 1999, we obtained an exclusive worldwide license for its development and commercialization from Eli Lilly.

As compared with current therapies, we believe that anidulafungin has a number of potential advantages, including the following:

Novel mechanism of action. Anidulafungin belongs to a new class of antifungal drug that only recently has been developed for human use. It selectively inhibits an enzyme, found only in fungi, which is critical for the production and integrity of the fungal cell wall. This mechanism is completely different from that of the polyenes, such as Amphotericin B, and the azoles, such as fluconazole. The mechanism of action of anidulafungin has advantages, including fungicidal activity and lack of cross-resistance with traditional therapies. In addition, this novel mechanism of action may allow for synergistic combinations with polyenes or azoles and may result in better outcomes for patients with the most difficult-to-treat infections.

Potent broad spectrum. Anidulafungin has shown highly potent *in vitro* activity against diverse groups of fungi, both yeasts and molds, that cause life-threatening infections. Anidulafungin is particularly potent against *Candida,* including fluconazole-resistant strains, and *Aspergillus,* the two most common types of fungi causing serious human infections. Anidulafungin also shows activity against non-albicans species of *Candida*, which are important causative agents for systemic infections and show higher rates of resistance to fluconazole. The following table illustrates the *in vitro* potency of anidulafungin against *Candida albicans,* as measured by the $MIC_{90,}$ or the concentration of drug that inhibits the growth of 90% of the fungal strains. The figure demonstrates that to inhibit the growth of *Candida albicans,* less anidulafungin is needed as compared with existing agents caspofungin, amphotericin B and fluconazole.

Candida Activity
MIC_{90}

Species	Anidulafungin	Caspofungin	Fluconazole	Amphotericin B
C albicans n=733	**0.03**	**0.5**	**2**	**0.25**
C glabrata n=458	**0.13**	**1**	**32**	**0.5**
C krusei	**0.13**	**2**	**>64**	**0.5**

n=50

The above table was published in Antimicrobial Agents and Chemotherapy, 2003.

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In vitro data also demonstrated that to inhibit growth of *Aspergillus fumigatus,* less anidulafungin is needed as compared with existing agents voriconazole, itraconazole, caspofungin and amphotericin B (Diagnostic Microbiology and Infectious Disease 2003-45 131-135).

As compared with other antifungal agents, these data illustrate that anidulafungin is more potent *in vitro* than available therapies. Anidulafungin also demonstrated impressive activity in a variety of animal models of *Candida* and *Aspergillus* infection. These included quite severe infections in immunosuppressed animals, such as disseminated infections and pulmonary aspergillosis. Efficacy was shown against different species and strains of *Candida,* including strains resistant to fluconazole. For example, in animal models the number of *Candida* in the liver, spleen, kidneys and lungs were reduced by 99.99% at the anidulafungin dosage of 0.5 mg/kg. In animals infected with *Aspergillus,* 80% of those treated with 2.5 mg/kg/day of anidulafungin survived until the end of the experiment (ten days), whereas all untreated animals died within four days.

Fungicidal. Anidulafungin kills *Candida*. This is an important characteristic of its novel mechanism of action, which affects the integrity of the protective cell wall of fungi. This may be an advantage over the widely-used azole class of antifungal agents, which are fungistatic, meaning that they merely inhibit the growth of *Candida* and do not kill them. For example, when comparing anidulafungin to fluconazole, a fungistatic agent, anidulafungin s killing power is clearly demonstrated: after twelve hours of exposure to anidulafungin, more than 99.5% of the exposed yeast was killed and after 12 hours of exposure to fluconazole, none of the exposed yeast was killed. Patients who are severely immunosuppressed may be more effectively treated with a therapy that is fungicidal rather than fungistatic.

Low potential for developing resistance. In the laboratory it has proven very difficult to develop resistance to anidulafungin.

Tolerability Profile. Anidulafungin has been tested in greater than 20 separate Phase 1, 2 and 3 clinical trials of over 1000 volunteers and patients. In the Phase 3 esophageal candidiasis trial and Phase 3 invasive candidiasis/candidemia trial, anidulafungin demonstrated a safety profile similar to fluconazole.

Dalbavancin A Next-Generation Antibiotic for the Treatment of Serious Gram-Positive Infections

Clinical Experience

Dalbavancin is a novel next-generation lipoglycopeptide antibiotic, a chemically modified derivative of a natural product. We are developing dalbavancin as an alternative to vancomycin for the treatment of serious Gram-positive infections, predominantly in hospitalized patients. Dalbavancin has potent *in vitro* activity against Gram-positive bacteria. In particular, we are targeting infections caused by *Staphylococci*, including methicillin-resistant strains, the principal indication for vancomycin. Serious infections caused by *Staphylococci* include skin and soft tissue infections, bloodstream infections and osteomyelitis. An additional advantage of dalbavancin is its ease of administration, because of its once weekly dosing regimen.

We also initiated a Phase 2 trial in catheter-related bloodstream infections in the first quarter of 2002. In January 2004, we announced the results of this Phase 2 clinical trial for catheter-related bloodstream infections which demonstrated that dalbavancin showed superior activity to vancomycin, a current standard of care for the treatment of Gram-positive catheter-related bloodstream infections (CR-BSI). The Phase 2 CR-BSI trial enrolled 67 patients who were randomized to receive either dalbavancin (one gram on day one, 500mg on day eight) or 14 days of twice daily vancomycin. At the primary endpoint, the follow-up visit in evaluable patients, dalbavancin had an overall success (clinical and microbiological) of 87.0% (20/23) versus vancomycin 50.0% (14/28) in the microbiological ITT population, which was statistically significant. CR-BSIs are one of the most common hospital-acquired infections.

In December 2002 we started two Phase 3 trials with dalbavancin for the treatment of SSTIs. These randomized, double-blind trials each enrolled at least 550 patients who were examined for overall clinical and

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microbiological responses at the conclusion of therapy. In the first trial, patients with cSSTIs received either a one gram intravenous dose of dalbavancin on study day one followed by a 500 mg dose on study day eight or approved doses of linezolid for 14 days. In the second study, patients with uncomplicated skin and soft tissue infections received either a one gram intravenous dose of dalbavancin on study day one, with the option of adding a 500 mg doses on study day eight, or intravenous cefazolin, followed by oral cephalexin. On day eight, the investigator decided the duration of the study medication therapy (seven or 14 days) based on the clinical status of the patient.

In addition, in October 2003 we initiated another Phase 3 clinical trial, which will include up to 150 patients to evaluate the safety and efficacy of dalbavancin, relative to vancomycin, one of the current standards of care for the treatment of SSTIs. Patients received either dalbavancin, one gram intravenous dose on day one plus 500 mg on day eight, or approved daily doses of vancomycin for 14 days.

In August 2004, we announced results from our three Phase 3 SSTI studies.

Phase 3: cSSTI

	Clinically Evaluable			ITT		
	Dalbavancin	Linezolid	(95% CI)	Dalbavancin	Linezolid	(95% CI)[1]
2 week follow-up	88.9%	91.2%	(-7.3,2.9)	76.5%	82.7%	(-12.0, -0.3)

Phase 3: uSSTI

	Clinically Evaluable			ITT		
	Dalbavancin	Cefazolin	(95% CI)	Dalbavancin	Cefazolin	(95% CI)[1]
2 week follow-up	89.1%	89.1%	(-6.8,6.8)	76.0%	75.8%	(-7.7, 8.2)

Phase 3: At Risk for MRSA

	Clinically Evaluable			ITT		
	Dalbavancin	Vancomycin	(95% CI)	Dalbavancin	Vancomycin	(95% CI)[2]
2 week follow-up	89.9%	86.7%	(-13.0,19.4)	86.0%	65.3%	(4.3,37.0)

(1) Prespecified margin of non-inferiority = -12.5%
(2) Prespecified margin of non-inferiority = -20.0%

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Characteristics of Dalbavancin

We believe dalbavancin has the following potential advantages over current therapies:

Greater potency. In the laboratory, dalbavancin demonstrated better activity against a range of Gram-positive bacteria, including all of the staphylococcal species, in particular against Methicillin-resistant Staphylococcus aureus, or MRSA and methicillin-resistant Staphylococcus epidermidis, or MRSE. MRSA has amongst the fewest treatment options of which vancomycin is one of the few options currently available. As shown in the table below, dalbavancin was more potent *in vitro* than other marketed and experimental antibiotics against MSSA and MR-CoNS. The table demonstrates that to inhibit the growth of MRSA and MRSE, less dalbavancin is needed as compared with existing agents vancomycin, teicoplanin, linezolid, and Synercid. Activity is expressed as the MIC_{90}.

	MIC_{90}		
Antimicrobial	**MSSA (n=1815)**	**MRSA (n=1177)**	**MR-CoNS (n=817)**
Dalbavancin	.06	0.06	0.06
Vancomycin	1	2	2
Teicoplanin	1	2	4
Linezolid	2	2	1
Synercid	0.5	1	0.5

Published in Diagnostic Microbiology and Infectious Disease, February 2004

This data illustrates that dalbavancin is more potent than the other antibiotics in vitro. Dalbavancin also demonstrated impressive potency in a number of animal model infections, caused by a variety of Gram-positive bacteria, including those resistant to methicillin. Dalbavancin was efficacious against Staphylococcal endocarditis in animal models, as well as against *Streptococcus pneumoniae* pulmonary infection in normal and immunosuppressed animal models. Pharmacodynamic studies in animal models demonstrated bactericidal activity in the animals coupled with good tissue penetration and distribution of dalbavancin.

Bactericidal. Dalbavancin kills Gram-positive bacteria. This may be an advantage over certain other therapies such as Zyvox, which is bacteriostatic. Patients with serious infections caused by methicillin-resistant staph may be more effectively treated with a therapy that is bactericidal rather than bacteriostatic.

Unique dosing regimen. Phase 3 studies have demonstrated that once weekly dalbavancin is non-inferior in SSTI to at least twice daily linezolid, cephazolin, or vancomycin. Once-weekly dosing may allow some patients to have IV lines discontinued, which translates into fewer opportunities for local infection and blood stream infections. This may also provide pharmacoeconomic benefits, such as shorter hospital stays, less need for follow-up home IV or oral antibiotics and other reduced costs.

Tolerability Profile. Over 1,250 volunteers and patients have received dalbavancin in 13 clinical studies. In the Phase 3 clinical trials for SSSI, dalbavancin had a similar safety profile when compared with cefazolin, linezolid and vancomycin.

Ramoplanin

Ramoplanin is a novel antibiotic with excellent *in vitro* potency against Gram-positive bacteria including VRE. Our licensee Oscient Pharmaceuticals, has conducted a Phase 2 dose response and vancomycin comparator trial to evaluate the safety and efficacy of ramoplanin for the treatment of *Clostridium difficile*-associated diarrhea.

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VIC-Acne

VIC-Acne is a novel topical antibiotic with activity against *Propionibacterium acne* including clindamycin and tetracycline resistant strains. We have completed a Phase 1 clinical trial with this agent as an anti-acne compound which showed it was well tolerated.

VIC-5555

VIC 5555 is the lead product candidate in our lincosamide research program. It is designed as an improvement of clindamycin, an antibiotic often used for anerobic bacterial infections. VIC-5555 has shown improved *in vivo* and *in vitro* activity when compared to clindamycin. We plan to file an IND for VIC-5555 in 2005.

Research Collaborations

Deformylase Inhibitors collaboration with Novartis

We are collaborating with Novartis to develop deformylase inhibitors as antibacterial agents. Deformylase is an essential enzyme present in bacteria but not required for human cells, thus representing a good target for the discovery of inhibitors that can serve as broad spectrum antibacterial agents. Deformylase is a metal-containing enzyme, or metalloenzyme. If this metal is removed or interfered with, the enzyme can no longer function. Since it is possible to design molecules that bind to metals, this makes it especially attractive for the design of mechanism-based drugs. Captopril, the first drug to be rationally designed using this approach, is an inhibitor of a metalloenzyme called Angiotensin Converting Enzyme, or ACE. The design of captopril, which is used to treat hypertension and congestive heart failure, represented a major pharmaceutical breakthrough. Deformylase offers an excellent opportunity for integrating this principle of mechanism-based drug design with our combinatorial chemistry based approach.

Based on our scientists experience in the captopril field, we initiated a highly focused chemistry effort targeting the rational design and synthesis of deformylase inhibitors. We designed a set of pharmacophoric libraries specifically suited for metalloenzyme targets and also developed new synthetic methodologies for the preparation of these libraries. Screening these libraries against deformylase led to the identification of several molecules with excellent enzymatic and whole-cell inhibitory activity. Our proprietary Gene to Screen technology helped identify those leads that inhibited bacterial growth by specifically inhibiting deformylase. Through proper integration of combinatorial chemistry with medicinal chemistry, more specific lead series were further optimized with excellent selectivity, as well as activity against clinically significant multi-drug resistant bacteria. Novartis has filed patent applications on the novel structures that we have synthesized. Many of these compounds have demonstrated good *in vivo* activity in pre-clinical studies when administered orally. The lead compound in this collaboration entered Phase 1 clinical trials by Novartis in the fourth quarter of 2003. In March 2005, we announced that Novartis has suspended progress of this compound in favor of progressing a second deformylase inhibitor.

We entered into our collaboration agreement with Novartis in March 1999. Pursuant to this agreement, we are collaborating to discover and develop novel deformylase inhibitors. In connection with the collaboration, Novartis made an initial equity investment in us of $3.0 million and provides us with funding to support some of our full-time researchers. Under the terms of this agreement, we have established with Novartis a joint research committee and we are responsible for performing the three-year research plan developed by the committee. In return, Novartis has agreed to pay us a fee. We are also entitled to receive payments of up to $13.0 million for our compounds or up to $7.25 million for Novartis

compounds upon Novartis achievement of certain research milestones. In addition, we granted Novartis, and Novartis granted us, reciprocal research licenses. We also granted Novartis an exclusive worldwide commercial license, pursuant to which it may develop, manufacture and sell products resulting from this collaboration. For each product that Novartis develops and launches in specified countries, we are entitled to receive royalties on worldwide sales of the product and additional payments if the product contains one of our compounds and a lesser sum if the product contains a Novartis compound. Novartis

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may offset some of its royalty payments by the amount of previous milestone payments made to us. We have the option to co-promote with Novartis in hospitals in the United States and Canada any product that contains one of our compounds as an active ingredient, but we will not be entitled to royalties from sales of the product in that territory if we exercise our co-promotion option. These licenses and related royalty obligations terminate on a country-by-country basis with respect to a product developed under the collaboration upon the later of 10 years from the date of the first commercial sale of the product in the country or the time at which the product is no longer covered by a pending or issued patent in the country. In addition to the work on deformylase inhibitors, we have been delivering to Novartis under the agreement a series of screening assays based on novel anti-bacterial targets. For each screen that Novartis accepts as validated, we receive a milestone payment. In August 2001 and January 2002, Novartis paid us our fourth and fifth milestone payments, respectively, as a result of our delivery of our fourth and fifth target-based screens, which we expect will be used in Novartis high-throughput screening laboratory to identify new anti-infectives. In March 2002, the collaboration agreement was amended to extend the research term by an additional year, through March 2003, and to provide that Novartis shall make an additional payment to us upon our achievement of a new milestone. In February 2003, the collaboration agreement was amended to extend the research term by an additional two years, through March 31, 2005. Through December 31, 2004, Novartis has made aggregate payments to us under this agreement (excluding equity investments) of $18.2 million. In March 2005, we announced that Novartis has opted to suspend the Phase 1 compound and will advance a second compound. We received a milestone for the designation of this second compound as a late stage preclinical compound.

We do not depend upon continued milestone payments from Novartis to any significant extent because we have funded, and intend to fund, our drug development programs primarily with the proceeds of equity offerings. Although we currently depend upon our collaborations, in-licensing opportunities and in-house research, in the aggregate, for a sustained pipeline of product candidates, we do not depend to any significant extent on any individual collaboration.

Oxazolidinones collaboration with Pfizer

We are collaborating with Pfizer to identify new generations of oxazolidinones. The oxazolidinones are one of the first major new chemical class of antibacterial products to enter the market in over 30 years. Pfizer has received FDA approval, independent of us, for a new drug called Zyvox, the most advanced molecule in this class. Based on historical precedents for antibiotics, it is likely that the development of subsequent generations of oxazolidinones with improved potency and a broader spectrum of activity will create a major market opportunity. Oxazolidinones are active against a broad spectrum of Gram-positive pathogens, including multidrug resistant *Staphylococci, Streptococci* and *Enterococci.* They have a novel mechanism of action involving inhibition of an early step in protein biosynthesis. Oxazolidinones have no cross resistance to other classes of antibiotics.

We began working on oxazolidinones at a time when several large pharmaceutical companies were already actively involved in this area. Our scientists used their expertise in combinatorial chemistry to optimize leads around the core oxazolidinone structure and identified several novel lead structures with good *in vivo* activity when administered orally. Pfizer signed a collaboration agreement with us in March 1999, which we continued when Pharmacia was acquired by Pfizer. We have identified several novel molecules with an enhanced spectrum of activity, including activity against the pathogen *H. influenzae,* improved potency against multidrug resistant bacteria including MRSA, MRSE, VRE and penicillin-resistant *Streptococcus pneumoniae.* Several compounds have also demonstrated good activity in pre-clinical *in vivo* studies when administered orally and are therefore undergoing advanced *in vivo* testing. Advanced *in vivo* testing includes testing the efficacy of the compounds with increased dosages, the absorption of the compound in the blood, the differences between the oral formulation and the intravenous formulation and the toxicity of the compound.

We entered into our collaboration agreement with Pharmacia Corporation, now Pfizer, in March 1999. Pursuant to this agreement, we are collaborating to discover, synthesize and develop second and third generation oxazolidinone product candidates. We supply research, product leads and other specified intellectual property to the collaboration. Pfizer has the right to conduct the development of any product candidates and the manufacture

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and sale of any products resulting from the collaboration. In connection with the collaboration, Pfizer made an equity investment in us of $3.8 million and paid us research support and license fee payments. We have assigned to Pfizer one U.S. patent application and a corresponding Patent Cooperation Treaty patent application relating to this collaboration. Both applications involve the methodology of preparing oxazolidinones, libraries and pharmaceutical compositions. Under the terms of the agreement and in consideration of our research obligations, we are entitled to receive funding from Pfizer to support some of our full-time researchers. If Pfizer s development efforts achieve specified milestones, Pfizer is obligated to pay us additional milestone payments of up to $14 million for each compound. We are entitled to receive royalties on the worldwide sales of any products developed and commercialized from the collaboration. Pfizer is allowed to offset some of its royalty payments by the amount of previous milestone payments made to us. These licenses and royalty agreements will terminate on a country-by-country basis with respect to a product developed under the collaboration upon the later of 10 years from the date of the first commercial sale of the product in the country or the expiration of all product patents in the country. Pursuant to an October 2000 amendment, Pfizer increased its funding for this collaboration by 30%, and in June 2001, we received a milestone payment for the initiation of clinical development of one of the compounds. In July 2002, we and Pfizer amended the agreement to extend the collaboration for an additional three years through March 2005.

Through December 31, 2004, Pfizer has made aggregate payments to us under this collaboration agreement (excluding equity investments) of $20.3 million. We do not depend upon continued milestone payments from Pfizer to any significant extent because we have funded, and intend to fund, our drug development programs primarily with the proceeds of equity offerings. Although we currently depend upon our collaborations, in-licensing opportunities and internal research, in the aggregate, to seek to obtain a pipeline of product candidates, we do not depend to any significant extent on any individual collaboration.

VITACHEM Program

Although natural products have found their widest use as antibiotics, they also represent an important source of structural diversity for other therapeutic uses as well. We are currently involved in exploiting this opportunity through collaborations with other companies. We developed the VITACHEM program to investigate the pharmaceutical and non-pharmaceutical utility of our collection of microbial chemicals in markets outside of the anti-infectives market. To facilitate the efforts of our collaborators, we have established a number of self-contained, but integrated research modules which can be offered to collaborators, including:

- microbial chemical libraries;
- high-throughput screening;
- product fractioning; and
- laboratory-scale fermentation.

Each collaborator can request from VITACHEM the combination of modules best suited to the specific collaboration.

There are two types of collaborations under the VITACHEM program:

fee-for-service collaborations, in which our collaborators provide us with short-term as well as medium/long-term revenues in the form of research fees plus, milestone payments and royalties calculated as a percentage of net sales; and

equal collaborations, based on cost-sharing and reward-sharing.

Currently, we have one equal collaboration with Myriad Genetics Inc. on oncology, cardiovascular and viral targets.

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Consortium Italbiotec (the former Consortium Roberto Lepetit for Biotechnologies)

In February 1998, we established in conjunction with the University of Bologna (now Alma Mater Studiorum University of Bologna) and the University of the Studies of Palermo, the Roberto Lepetit Consortium for Biotechnologies , a non-profit organization aimed at the promotion of the development of biotechnologies through advanced research activities in collaboration with academic institutions with a view to utilizing new technologies and products for industrial purposes.

In November 2002, Newron Pharmaceuticals S.p.A. joined the Consortium, and in February 2003, the University of Calabria also joined as a member. In November 2003, the Consortium changed its name in Consortium Italbiotec . The headquarters of the Consortium is located at our offices in Italy.

Internal Discovery Research

We use a variety of approaches combining the best drug discovery tools available. Thus, we integrate our capabilities in the areas of lead optimization, functional genomics and mechanism-based rational drug design and high-throughput screening of our diversified library of microbial extracts to fill both our proprietary and collaborators product pipelines.

Lead Optimization

Several members of our scientific staff are pioneers in the application of combinatorial chemistry to drug discovery. We have focused our efforts on the practical applications of this powerful technology for the discovery and development of new antibacterial agents. We believe that the best use of combinatorial chemistry is in lead optimization via preparation of hundreds of discrete, well-characterized compounds based on core lead structures. We have analyzed the antibacterial field to arrive at potential lead optimization candidates that are either previously abandoned molecules, or are molecules on which work is still being done. In both cases, we have chosen molecules that have the potential for significant improvements in potency, spectrum of activity or other properties. Our expertise allows us to develop combinatorial methods for modifying structurally complex molecules. Once a suitable molecule for lead optimization is selected, we establish a proprietary position by using combinatorial chemistry to prepare new analogs that fall outside the patent scope of our likely competitors. Following the discovery of novel bioactive lead structures, we integrate our combinatorial and medicinal chemistry efforts to prepare individual molecules that can be navigated efficiently through pre-clinical testing. Once an *in vivo* active lead has been established, we determine whether the molecule best fits our proprietary product or our collaborators product portfolios. The successful execution of this strategy has been demonstrated by our collaborative oxazolidinone project with Pfizer. We are currently working on an internal research program using this approach.

Functional Genomics and Mechanism-Based Rational Drug Design

The complete genetic blueprints, or genomes, of the majority of clinically relevant bacteria are now accessible through the Internet. We take a highly focused and practical approach to using this genomic information by carefully selecting targets that have a mechanism suited to rational drug design. To facilitate efficient integration of mechanism-based drug discovery with combinatorial chemistry, we select mechanism-based families of targets such as metalloenzymes. We search genomes for characteristic genetic signatures and compare different genomes to identify targets that are present in a clinically relevant spectrum of bacteria. We use genetic techniques to establish that any target selected is essential for growth, and confirm this in several relevant bacterial species. Once we have carefully selected the target, we begin a highly focused chemistry

effort using mechanism-based drug design. We then apply our Gene to Screen technology that allows us to increase or decrease the amount of target gene product, which is usually an enzyme, inside a cell by use of a special genetic regulator. Our ability to vary the concentration of a target enzyme inside a cell has proved an important support tool for our chemists, as they can then confirm whether a potent enzyme inhibitor stops the growth of bacteria by inhibiting the same enzyme. Our Gene to Screen technology allows our chemists to select leads that

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have the correct mechanism, without the inhibition of other enzymes that could result in toxicity. This integrated approach has been validated by our metalloenzyme program with Novartis to develop deformylase inhibitors. We are currently working with one additional metalloenzyme target to build on this success in our novel molecules programs.

Diversified Library of Microbial Extracts

The facilities and staff of our research center in Italy are geared to the discovery of novel natural products with clinically useful properties, especially those with antibiotic activity. Our high-throughput screening process consists of three basic steps:

generating a large number of structurally diverse natural product libraries;

screening these extract libraries against specific biological targets to look for useful activity; and

isolating and identifying the structure responsible for any interesting activity found.

The natural products we study are made by microbes found in the soil and other sources. Our scientists have expertise in isolating rare and unusual genetically diverse soil microbes and have now accumulated a unique collection of about 50,000 microbes. Each of these microbes is capable of producing a unique mixture of natural products when grown in liquid media. Depending on the media that they grow in, microbes can produce different mixtures of molecules. Concentrated extracts of these fermented media represent an invaluable source of chemical structural diversity. Thus, a library containing about 170,000 of these extracts has been created. New microbes and extracts are continually being added to this collection.

Other scientists are skilled in identifying relevant biological targets and in creating screening tests that can be used to search this library. Automated and miniaturized test systems are in place to assist in the management of the large number of samples to be handled.

When a positive hit is found with a screen, the next step requires special expertise in isolating and identifying the one molecule in the mixture that is responsible for the activity of interest. Many natural products have complicated chemical structures and our scientists are skilled at rapidly identifying the composition of these molecules. An important part of this process is to determine as early as possible whether the active molecule is a new compound or has already been discovered. This process is referred to as dereplication and we have developed a sophisticated system to rapidly address this problem.

Once a new natural product has been identified, our research center in Italy has pilot plant facilities for scale-up and purification of larger quantities of material. New molecules can be tested in *in vivo* models at the center s vivarium and the efficacy and pharmacokinetics established. As discussed above, chemists at both our research centers are capable of improving the properties of these natural products by selective modification of the molecule; this is referred to as lead optimization.

Our research center in Italy has a long and rich history in the development of important antibiotics having been responsible for the discovery of rifampin, teicoplanin, dalbavancin, ramoplanin and VIC-Acne. Although natural products have found their widest use as antibiotics, it is clear

that they also represent a tremendous source of structural diversity for other therapeutic uses as well. We will exploit these opportunities through collaborations with other companies.

Licensing Agreements

Eli Lilly

In May 1999, we entered into a license agreement with Eli Lilly to obtain an exclusive worldwide license for the development and commercialization of anidulafungin. The license agreement provides for a number of payments from us to Eli Lilly, as follows: (i) an up-front payment for the license; (ii) periodic milestone

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payments bearing on achieving certain goals related to intravenous and oral formulations; (iii) payments during the period 2000 through 2002 for product inventory; and (iv) royalty payments based upon the net sales of the applicable products. We have also granted to Eli Lilly an option to license the exclusive worldwide rights to any oral formulation of anidulafungin, which is exercisable upon successful completion of Phase 2 clinical trials. If Eli Lilly exercises this option, Eli Lilly will pay us an up-front fee and royalties based on net product sales, and will reimburse us for any milestone payments paid plus the value, on a cost-plus basis, of all prior development expenses attributed to the development and commercialization of the oral formulation of anidulafungin. We are not currently working on an oral formulation program.

Oscient Pharmaceuticals (formerly Genome Therapeutics)

In October 2001, we entered into a licensing agreement with Oscient Pharmaceuticals pursuant to which we granted Oscient Pharmaceuticals the right to develop and commercialize ramoplanin, one of our proprietary product candidates, in North America. Under the terms of the agreement, Oscient Pharmaceuticals paid us an initial payment of $2.0 million. Thereafter, Oscient Pharmaceuticals will make further milestone payments to us of up to an additional $8.0 million in a combination of cash and notes convertible into Oscient Pharmaceuticals stock. In addition to purchasing the bulk material from us, Oscient Pharmaceuticals will fund the completion of clinical trials and pay us a royalty on product sales. The combined total of bulk product sales and royalties is expected to be greater than 20% of Oscient Pharmaceuticals net product sales. In return, subject to the terms of the agreement, Oscient Pharmaceuticals has exclusive rights to develop and market oral ramoplanin in the USA and Canada. We retain the rights to market ramoplanin outside these territories.

Sales and Marketing

We intend to market and sell our proprietary products through a direct sales force in the United States and Canada. Because we are targeting the hospital market, we will begin in 2005 to develop a relatively small focused sales force which we believe will be sufficient to provide coverage to sell our hospital products. We plan to employ traditional marketing programs for hospital products which may include continuing medical education, medical science liaisons, literature distribution, trade press advertising and other approaches. Our management has experience in building specialty pharmaceutical sales forces and we are in the process of developing a sales and marketing infrastructure. We have already hired a senior vice-president, sales and a senior vice-president, marketing. We expect to collaborate with other pharmaceutical companies to market our collaboration products in non-hospital markets in the United States and Canada.

Manufacturing

Eli Lilly has supplied us with sufficient anidulafungin echinocandin-B nucleus to market the drug for a couple of years. We produce the active pharmaceutical ingredient for anidulafungin at ChemSym Laboratories, a department of Eagle-Picher Pharmaceutical Services, LLC. The active pharmaceutical ingredient for dalbavancin is produced at the Aventis plant in Brindisi, Italy. The lyophilized sterile vials for both anidulafungin and dalbavancin are produced at Ben Venue Laboratories. In the future, we intend to manufacture products at our own manufacturing plant in Pisticci, Italy, which is currently completing the construction process.

Intellectual Property

The proprietary nature of, and protection for, our products, product candidates, processes and know-how are important to our business. We seek patent protection in the United States 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 that may be granted to us in the future will be commercially useful in protecting our technology.

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Competition

We believe our products will face intense competition from both existing therapies and new generations of antibiotics and antifungals. We expect to compete against existing therapies on the basis of greater potency, improved effectiveness and/or reduced toxicity. Several pharmaceutical and biotechnology companies are actively engaged in research and development related to new generations of antibiotic and antifungal products. We cannot predict the basis upon which we will compete with new products marketed by others. Many of our competitors have substantially greater financial, operational, sales and marketing, and research and development resources than we have. Companies that market or are known to us to be in active development and/or commercialization of antibiotic or antifungal products in our target markets include Bristol-Myers Squibb Co., Schering-Plough Corp., Aventis S.A., Fujisawa Pharmaceutical Co. Limited, Johnson & Johnson Inc., Pfizer Inc., Merck & Co. Inc., Cubist Pharmaceuticals Inc., Enzon, Gilead Sciences Inc., InterMune, Wyeth and Theravance.

Governmental Regulation and Product Approval

Regulation by governmental authorities in the United States and other countries is a significant factor in the manufacture and marketing of pharmaceuticals and in our ongoing research and development activities. All of our products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous pre-clinical testing and clinical trials and other pre-marketing approval requirements by the FDA and regulatory authorities in other countries. In the United States, various federal, and in some cases state statutes and regulations also govern or impact upon the manufacturing, safety, labeling, storage, record-keeping and marketing of such 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, when and if obtained, may be limited in scope which may significantly limit the indicated uses for which a product may be marketed. Further, approved drugs, as well as their manufacturers, are subject to ongoing review, and the discovery of previously unknown problems with such products may result in restrictions on their manufacture, sale or use or in their withdrawal from the market.

Pre-Clinical Stages

The process for new drug approval consists of pre-clinical stages, which occur prior to studies on human volunteers, and clinical trials, which involve testing the compound on human volunteers in clinic settings. Pre-clinical stages include the following:

Drug discovery.

In the initial stages of drug discovery before a compound reaches the laboratory, tens of thousands of potential compounds are randomly screened for activity against an assay assumed to be predictive for particular disease targets. This drug discovery process can take several years. Once a company locates a lead compound, or starting point for drug development, isolation and structural determination may begin. The development process results in numerous chemical modifications to the screening lead in an attempt to improve the drug properties of the lead. After a compound emerges from this process, the next steps are to conduct further preliminary studies on the mechanism of action, further *in vitro* screening against particular disease targets and finally, some *in vivo* screening. If the compound passes these barriers, the toxic effects of the compound are analyzed by performing preliminary exploratory animal toxicology. If the results demonstrate acceptable levels of toxicity, the compound emerges from the basic research mode and moves into the pre-clinical phase.

Pre-clinical testing.

During the pre-clinical testing stage, laboratory and animal studies are conducted to show biological activity of the compound against the targeted disease, and the compound is evaluated for safety. These tests typically take approximately two years to complete, and must be conducted in compliance with the FDA s Good Laboratory Practice regulations.

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Investigational new drug application.

During the pre-clinical testing, an IND is filed with the FDA to begin human testing of the drug. The IND becomes effective if not rejected by the FDA within 30 days. The IND must indicate the results of previous experiments, how, where and by whom the new studies will be conducted, the chemical structure of the compound, the method by which it is believed to work in the human body, any toxic effects of the compound found in the animal studies and how the compound is manufactured. All clinical trials must be conducted in accordance with the FDA s Good Clinical Practice regulations. In addition, an Institutional Review Board at the hospital or clinic where the proposed studies will be conducted, must review and approve the IND. The Institutional Review Board also continues to monitor the study. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. In addition, the FDA may, at any time during the 30-day period, or at any time thereafter, impose a clinical hold on proposed or ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. In some instances, the IND application process can result in substantial delay and expense.

Some limited human clinical testing may be done under a physician s IND in support of an IND application and prior to receiving an IND. A physician s IND is an IND application that allows a single individual to conduct a clinical trial. A physician s IND does not replace the more formal IND process, but can provide a preliminary indication as to whether further clinical trials are warranted, and can, on occasion, facilitate the more formal IND process.

Clinical Trials

Clinical trials are typically conducted in three sequential phases, but the phases may overlap.

Phase 1 clinical trials.

After an IND becomes effective, Phase I human clinical trials can begin. These tests usually involve between 20 and 80 healthy volunteers or patients and typically take one to two years to complete. The tests study a drug s safety profile, and may include the safe dosage range. The Phase I clinical studies also determine how a drug is absorbed, distributed, metabolized and excreted by the body, and the duration of its action.

Phase 2 clinical trials.

In Phase II clinical trials, controlled studies are conducted on an expanded population of patients with the targeted disease. The primary purpose of these tests is to evaluate the effectiveness of the drug on the volunteer patients, as well as to determine if there are any side effects. These studies generally take approximately one year, and may be conducted concurrently with Phase I clinical trials. In addition, Phase I/II clinical trials may be conducted to evaluate not only the efficacy of the drug on the patient population, but also its safety.

Phase 3 clinical trials.

This phase typically lasts one to two years and involves an even larger patient population. During the Phase III clinical trials, physicians monitor the patients to determine efficacy and to observe and report any reactions that may result from long-term use of the drug.

New drug application

After the completion of all three clinical trial phases, if there is substantial evidence that the drug is safe and effective, an NDA is filed with the FDA. The NDA must contain all of the information on the drug gathered to that date, including data from the clinical trials. NDAs are often over 100,000 pages in length.

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The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. In such an event, the NDA must be resubmitted with the additional information and, once again, is subject to review before filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. 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 of an advisory committee. If the FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue either an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA s satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. If the FDA s evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter.

Marketing approval

If the FDA approves the NDA, the drug becomes available for physicians to prescribe. Periodic reports must be submitted to the FDA, including descriptions of any adverse reactions reported.

Phase 4 clinical trials and post marketing studies

Even after the drug is on the market, the FDA may request additional studies (known as Phase 4) to evaluate long-term effects. In addition to studies requested by the FDA after approval, these trials and studies are conducted to explore new indications. The purpose of these trials and studies and related publications is to broaden the application and use of the drug and its acceptance in the medical community.

Orphan drug designation

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years.

Approvals outside of the United States

Steps similar to those in the United States must be undertaken in virtually every other country comprising the market for our products before any such product can be commercialized in those countries. The approval procedure and the time required for approval vary from country to country and may involve additional testing. There can be no assurance that approvals will be granted on a timely basis or at all. In addition, regulatory approval of prices is required in most countries other than the United States. There can be no assurance that the resulting prices would be sufficient to generate an acceptable return to us.

Governmental Support of Medical Research and Training

In order to encourage scientific and medical research and training, both Italy and the European Union, or EU, have instituted targeted investment programs.

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Italian Investment Programs

Italian law provides that companies carrying out certain research and/or training projects may qualify to receive government grants and/or subsidized loans. Italian grants and subsidized loans are awarded by the Ministero Istruzione Università Ricerca, or MIUR, and/or the Ministero Attività Produttive, or MAP.

In order to be awarded grants or subsidies, eligible companies must submit a detailed request to MIUR and/or MAP, as applicable, describing their business and specifying the proposed project. MIUR and/or MAP, as applicable, will then evaluate the request and decide whether to make an award. Each grant and subsidy which is awarded will be paid, depending on the actual progress of the project (a portion of the grants may, however, be disbursed as an advanced payment by MIUR and/or MAP, as applicable). The companies receiving the grants must comply with certain conditions relating to, among other things, the geographical, technical and timeline development of the projects and the characteristics and location of the companies receiving the grants. MIUR and/or MAP, as applicable, are entitled to discontinue or revoke the grants and subsidies under certain circumstances.

Due to the nature of our medical research activities, many of our projects and programs in Italy have qualified for and received grants and subsidized loans from MIUR and/or MAP. Prior to our merger with Biosearch, it received from the Italian authorities government grants and subsidized loans relating to our:

- oncology project (research activities);
- genomics project (training and research activities); and
- antibiotics project (training and research activities).

In addition, in May 2002, our antimicrobial drugs project was approved by MAP, which might result in our receipt of a related grant and a subsidized loan. We have also applied to MIUR for a grant and subsidized loan for a project for identification and implementation of new research technology.

The grant and subsidy agreements entered into between us and the authorized bank, San Paolo IMI S.p.A., provide, in part, that:

- notice of any structural and organizational changes affecting us (including the change of our directors) and/or our business (including the award of further grants or subsidies) must be provided in advance to the authorized bank;
- consent to any merger, de-merger or transformation of us must be received in advance from the authorized bank; and
- any default by us under any of the agreements can cause the termination of all the agreements concerning the payment of grants and subsidies and our obligation to repay some or all of the amounts received by us with interest.

We contributed the assets of former Biosearch into one of our Italian subsidiaries, Vicuron Pharmaceuticals Italy S.r.l. Due to administrative and procedural reasons concerning the authorized bank, however, some grants and subsidies are jointly registered in the names of our company and our Italian subsidiary. Based on the above, in order to seek to avoid the termination of the grants and subsidies and repayment of the amounts received with interest, we contacted the authorized bank in order to start the procedure to obtain its consent to the merger and the subsequent contribution insofar as existing grants and subsidies are concerned. We face the risk that one or both of the transfers might not be approved by the authorized bank and/or by the applicable Italian authorities, in which case we might be required to repay some or all of the grants and subsidies received prior to the completion of the merger and/or contribution, plus accrued interest and applicable damages. In addition, since Vicuron Pharmaceuticals Italy S.r.l. is an Italian company, we expect that it will be eligible to receive new grants and subsidies in the future. However, there can be no assurance that Vicuron Pharmaceuticals Italy S.r.l. will qualify or be approved for any grants or subsidies that may be applicable to it.

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Regional Investment Programs

Biosearch Manufacturing S.r.l., one of our Italian subsidiaries, has been awarded a grant by Regione Basilicata, a local authority in southern Italy, for the construction of a new manufacturing plant. This grant will be paid to our subsidiary in installments in accordance with the completion of various stages of the construction work and can be revoked or reduced if our subsidiary does not comply with its obligations thereunder. In order to maintain eligibility for the entire grant awarded by Regione Basilicata, our subsidiary must also comply with certain requirements relating to, among other things, number of its employees, its turnover levels and its independence of other companies. Following our merger with Biosearch, we anticipate that subject to compliance with the terms and conditions of the grant, a significant portion of the awarded grants will be available to Biosearch Manufacturing S.r.l. post-merger.

European Union Investment Programs

Under EU law, we benefit from EU grant programs for our:

Eurocellwall project;

Megatop project;

Actapharm project; and

Ribosome project.

The agreements relevant to these grants, which are governed by European Union rules, provide that the grants may be awarded only to EU legal entities or entities of an Associated State that has entered into a convention with the EU. The United States has not entered into such a convention.

On June 30, 2003, we contributed the assets formerly of Biosearch to our subsidiary, Vicuron Pharmaceuticals Italy S.r.l. In connection with such contribution, we submitted a request to the EU Commission to transfer the EU grants formerly of Biosearch to our Italian subsidiary. In the name of our Italian subsidiary, we may from time to time in the future, apply to MIUR and the EU Commission for additional grants and subsidies. However, there can be no assurance that our subsidiary will in the future qualify or be approved for any grants or subsidies that may be applicable to it.

General

We were incorporated in Delaware as a wholly-owned subsidiary of Sepracor Inc. in 1995 and we have been operating as an independent company since 1996. In March 2003, we changed our name from Versicor Inc. to Vicuron Pharmaceuticals Inc. Our principal executive offices are located at 455 South Gulph Road, Suite 305, King of Prussia, Pennsylvania 19406. Our telephone number is (610) 205-2300. Our website is

http://www.vicuron.com. The information found on our website and on websites linked to it are not incorporated into or a part of this Annual Report on Form 10-K.

The name Vicuron and our logo are trademarks of Vicuron Pharmaceuticals Inc. Other trademarks and trade names appearing in this Annual Report on Form 10-K are the property of their holders.

Website Access to Our Periodic SEC Reports

We make our periodic SEC reports (Form 10-Q and Form 10-K) and current reports (Form 8-K) available free of charge through our website as soon as reasonably practicable after they are filed electronically with the SEC. We may from time to time provide important disclosures to investors by posting them in the investor relations section of our website, as allowed by SEC rules.

Materials we file with the SEC may be read and copied at the SEC s Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website at www.sec.gov that contains reports, proxy and information statements, and other information regarding our company that we file electronically with the SEC.

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Employees

As of December 31, 2004, we employed 216 persons, 54 of whom hold Ph.D. or M.D. degrees. One hundred and twenty-two employees are engaged in research, 30 in clinical, 32 in manufacturing, 11 in marketing and business development and 21 support administration, finance, management information systems and human resources. We believe that we maintain good relations with our employees.

ITEM 2. PROPERTIES

Our facilities in the United States currently consist of approximately 55,000 square feet of laboratory and office facilities located in Fremont, California, which is leased to us until February 2009, and an aggregate of approximately 27,000 square feet of office facilities in King of Prussia, Pennsylvania, which are leased to us until September 2007.

Vicuron Pharmaceuticals Italy S.r.l., one of our subsidiaries, owns offices and laboratory facilities consisting of approximately 170,000 square feet located in Gerenzano, Italy. We use approximately 70% of the square footage of these buildings and have leased a number of the offices and laboratories we are not currently using to Areta International. Biosearch Manufacturing S.r.l., an indirect subsidiary of ours, owns land consisting of approximately 87,000 square meters in the Pisticci technical area in southern Italy. We also lease 200 square meters in Milan.

We believe that these current facilities are adequate for our needs for the foreseeable future and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

Beginning on June 15, 2004, six shareholder securities class action complaints were filed against the Company and certain of the Company s senior officers in the U. S. District Court for the Eastern District of Pennsylvania. Those actions are styled: *Perry Paragamian vs. Vicuron Pharmaceuticals, Inc., et al.* (Case No. 04cv2627); *John H. Taylor vs. Vicuron Pharmaceuticals, Inc. et al*. (Case No. 04cv2685); *Security Police-Fire Professionals of America vs. Vicuron Pharmaceuticals, Inc. et al.* (Case No. 04cv2708); *Fred Zucker vs. Vicuron Pharmaceuticals, Inc. et al.* (Case No. 04cv2745); *Brian B. Steketee vs. Vicuron Pharmaceuticals, Inc. et al.* (Case No. 04cv3365); and *Brad Staton vs. Vicuron Pharmaceuticals, Inc.* (Case No. 04cv3422), collectively the Federal Class Actions. The Company intends to defend this litigation vigorously.

On August 18, 2004, counsel for all parties involved in the Federal Class Actions stipulated to consolidation of the six actions. Under the stipulation, defendants are not required to respond to the six individual complaints. Rather, defendants will respond to an amended, consolidated class action complaint that will be filed by the court-appointed lead plaintiff and lead plaintiff counsel, or the Consolidated Complaint. The District Court approved the Consolidation Stipulation on August 23, 2004. The Court s order provides that:

the designated lead plaintiff will have 60 days to file the Consolidated Complaint once appointed by the District Court;

defendants will file a responsive pleading within 60 days of service of the Consolidated Complaint; and

in the event defendants responsive pleading is a motion to dismiss, plaintiffs opposition papers will be due 60 days from the filing of the motion, and any reply papers by defendants will be due 30 days thereafter.

Three motions were filed with the District Court pursuant to 15 U.S.C. 78u-4(a)(3)(A)(i)(II) proposing a lead plaintiff and lead plaintiff counsel. On October 7, 2004, the Court entered an order appointing the group of institutional investors (Massachusetts State Guaranteed Annuity Fund, Massachusetts State Carpenters Pension

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Fund, and Greater Pennsylvania Carpenters Pension Fund) as lead plaintiffs, the law firm of Lerach Coughlin Stoia Geller Rudman & Robbins as lead plaintiffs counsel, and the law offices of Marc S. Henzel as liaison counsel.

Based on the Court s order of August 23, 2004, plaintiffs filed the Consolidated Complaint on December 6, 2004. The Consolidated Complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Section 11 of the Securities Act of 1933, arising from our May 24, 2004 press release announcing the issuance of an approvable letter by the FDA indicating that our proposed pharmaceutical, anidulafungin, does not currently support a labeling claim for initial treatment of esophageal candidiasis. The Consolidated Complaint alleges a putative class period from January 6, 2003 through May 24, 2004. The Sections 10(b) and 20(a) claims are based on the allegation that defendants artificially inflated the price of Vicuron s stock during the class period by making allegedly false and misleading statements concerning anidulafungin, the prospects that the FDA would approve the drug for initial treatment of esophageal candidiasis, and the prospects for the drug s marketing success. The Section 11 claim is based on the allegation that our July 2003 Registration Statement and Prospectus for a secondary public stock offering contained a false statement about anidulafungin s expected competitive advantages over existing therapies. The complaints seek compensatory damages, interest, attorneys fees, and injunctive and equitable relief.

Pursuant to the District Court s first scheduling order entered on November 2, 2004, defendants filed a motion to dismiss the Consolidated Complaint on January 20, 2005. Lead plaintiffs filed an opposition on February 22, 2005. The Defendants reply was filed on March 9, 2005. Defendants motion to dismiss stayed all discovery, pending the District Court s resolution of the motion.

On July 2, 2004, a shareholder derivative complaint styled *Jonathan Meyers vs. George F. Horner, III et al.* was filed against certain of the Company s officers and directors in the Court of Common Pleas of the State of Pennsylvania, Montgomery County (Case no. 04-19595). The complaint purports to allege claims of insider selling, breach of fiduciary duty, abuse of control, gross mismanagement, waste of corporate assets, and unjust enrichment. The complaint seeks compensatory damages, disgorgement of profits, imposition of a constructive trust, equitable and injunctive relief, attorneys fees and costs. On August 11, 2004, counsel for the parties entered a stipulation to stay all proceedings in the state court derivative action, pending the District Court s resolution of the motion to dismiss that defendants expect to file in the Federal Class Actions. Under the stipulation to stay, defendants time to respond to the derivative complaint is extended until 60 days after the stay expires. The Court approved the stipulation, and stayed the derivative action, on August 17, 2004.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Our 2004 annual meeting of stockholders was held on October 28, 2004 at the Villanova Conference Center for the purposes of acting upon the following matters:

1. The election of two directors to our board of directors to hold office until our 2007 annual meeting of stockholders or until their successors are duly elected and qualified.

	For	Withhold
Christopher T. Walsh, Ph.D.	30,631,392	3,930,284
Cheryl A. Wenzinger, CPA	34,461,604	100,072

The terms of the following directors continued after the meeting: (i) James H. Cavanaugh, Ph.D.; (ii) George F. Horner III; (iii) Costantino Ambrosio; (iv) David V. Milligan, Ph.D.; and (v) Alan W. Dunton, M.D.

2. To ratify the appointment of PricewaterhouseCoopers LLP as independent auditors for the fiscal year ending December 31, 2004.

For	Against	Abstain
34,400,929	137,687	23,060

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PART II

ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Price Range of Common Stock

Our common stock is listed for trading on both the NASDAQ and the Nuovo Mercato in Italy under the symbol MICU . The following table sets forth for the period from January 1, 2003 through March 11, 2005 the high and low intra-day sales prices, as reported on the NASDAQ composite trading system, for the periods shown:

	Sales Prices	
	High	**Low**
2003		
First Quarter	$ 13.08	$ 10.05
Second Quarter	$ 15.62	$ 10.54
Third Quarter	$ 18.00	$ 11.68
Fourth Quarter	$ 19.46	$ 16.76
2004		
First Quarter	$ 24.54	$ 18.79
Second Quarter	$ 24.30	$ 11.95
Third Quarter	$ 16.99	$ 8.76
Fourth Quarter	$ 18.33	$ 13.25
2005		
First Quarter through March 11, 2005	$ 18.25	$ 14.39

As of March 11, 2005 there were approximately 70 registered holders of our common stock. Because many of such shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

We have never declared or paid a cash dividend on our common stock and do not anticipate paying any cash dividends in the foreseeable future. We currently intend to retain our earnings, if any, for the development of our business. The declaration of any future dividends by us is within the discretion of our board of directors and will be dependent on our earnings, financial condition and capital requirements as well as any other factors deemed relevant by our board of directors.

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ITEM 6. SELECTED FINANCIAL DATA

The selected consolidated financial data set forth below with respect to our statements of operations for the years ended December 31, 2004, 2003, and 2002, and with respect to our balance sheets as of December 31, 2004 and 2003, are derived from our consolidated financial statements that have been audited by PricewaterhouseCoopers LLP, which are included elsewhere in this report, and are qualified by reference to such financial statements. The statements of operations data for the years ended December 31, 2001 and 2000 and the balance sheet data as of December 31, 2002, 2001, and 2000 are derived from our audited financial statements that are not included in this report. Our merger with Biosearch in February 2003 materially affects the comparability of the selected financial data for our years ended December 31, 2004 and 2003 with the selected financial data for our prior years. The selected financial information set forth below should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and related notes appearing elsewhere in this report.

	2004	2003	2002	2001	2000
Statement of Operations Data:					
Revenues					
Collaborative research and development and contract services	$ 7,066	$ 7,929	$ 6,083	$ 6,145	$ 5,338
License fees and milestones	1,306	1,679	258	283	533
Total revenues	8,372	9,608	6,341	6,428	5,871
Operating expenses:					
Research and development	68,538	77,893	48,189	32,612	15,531
General and administrative	22,303	13,531	8,184	9,600	8,891
Acquired in-process research and development		94,532			
Total operating expenses	90,841	185,956	56,373	42,212	24,422
Loss from operations	(82,469)	(176,348)	(50,032)	(35,784)	(18,551)
Other income (expense):					
Interest income	2,552	2,749	1,483	3,313	3,712
Interest expense	(84)	(506)	(247)	(316)	(482)
Other				(60)	18
Net loss before accretion of dividends and income tax benefit	(80,001)	(174,105)	(48,796)	(32,847)	(15,303)
Accretion of dividends on preferred stock					(3,486)
Income tax benefit	(1,479)				
Net loss available to common stockholders	$ (78,522)	$ (174,105)	$ (48,796)	$ (32,847)	$ (18,789)
Net loss per share:					
Basic and diluted	$ (1.40)	$ (3.69)	$ (1.91)	$ (1.42)	$ (1.95)
Weighted average shares	56,025	47,162	25,516	23,090	9,638

	December 31,				
	2004	2003	2002	2001	2000

			(in thousands)		
Balance Sheet Data:					
Cash and cash equivalents and marketable securities	$ 155,271	$ 166,157	$ 62,305	$ 63,768	$ 85,934
Total assets	270,026	258,498	72,736	70,697	91,596
Long term debt, less current portion	10,066	7,493	698	1,004	3,448
Convertible and redeemable preferred stock					
Accumulated deficit	(405,246)	(326,724)	(152,619)	(103,823)	(70,976)
Total stockholders equity	229,591	213,783	48,666	52,894	80,287

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ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion of our consolidated financial condition and results of operations should be read in conjunction with the consolidated financial statements and notes to those statements included elsewhere in this document. This discussion may contain forward-looking statements that involve risks and uncertainties. The words expects, believes, intends, will, anticipates, and similar expressions or the negatives of these words or phrases are intended to identify forward-looking statements. As a result of many factors, such as those set forth under Risk Factors and elsewhere in this document, our actual results may differ materially from those anticipated in such forward-looking statements.

Overview

We are a transatlantic biopharmaceutical company focused on the discovery, development, manufacturing and marketing of pharmaceutical products for the treatment of seriously ill patients. Since our inception in 1995 as a wholly-owned subsidiary of Sepracor Inc., we have devoted substantially all of our efforts to establishing our business and conducting research and development activities related to our proprietary product candidates, including anidulafungin and dalbavancin, as well as collaborative product candidates.

Since 1996, we have been operating as an independent company. In August 2000, we sold 5,290,000 shares of our common stock at $11 per share in an initial public offering and we received total net proceeds of approximately $52.7 million.

In April 2002, we completed a private placement of 2,993,800 shares of our common stock to selected institutional investors at a purchase price of $15.00 per share. We received net proceeds from the private placement of approximately $41.9 million.

In February 2003, we acquired all of the outstanding shares of Biosearch Italia S.p.A., a publicly-listed company in Italy. In connection with that transaction we issued 1.77 shares of our common stock for each outstanding share of Biosearch stock, or approximately 21.4 million shares.

In June 2003, we contributed the former assets, liabilities and business of Biosearch to our wholly-owned subsidiary in Italy, Vicuron Pharmaceuticals Italy S.r.1.

In July 2003, we sold 6,000,000 shares of our common stock at $13.85 per share in a public offering. We received net proceeds of approximately $77.8 million.

In February 2004, we filed a universal shelf registration statement on Form S-3, which will allow us to offer up to $200 million of our common stock, preferred stock, warrants and/or debt securities from time to time in one or more public offerings. In October 2004, we closed our public offering of 5,051,000 shares of our common stock at $14.75. We received net proceeds from the offering and the over-allotment of approximately $71.5 million.

Since we began our operations in 1995, we have not generated any revenues from product sales. In early 2003, we completed a Phase 3 clinical trial with anidulafungin, our lead antifungal product candidate, for the treatment of esophageal candidiasis. Based in part on the results of that trial, in April 2003 we filed a New Drug Application or NDA for anidulafungin for the treatment of esophageal candidiasis, which was accepted for review by the FDA in June 2003. In January 2004, we received notification from the FDA that the agency would complete its review of our anidulafungin NDA in May 2004, which represented a 90-day extension of the original action date. The extension was the result of the FDA s request for additional bioanalytical data. In May 2004, we received an approvable letter from the FDA. Based on the approvable letter and discussions with the FDA, we intend to pursue two paths for approval of anidulafungin, as follows:

amending our existing NDA for the treatment of esophageal candidiasis; and

submitting an additional NDA for the treatment of invasive candidiasis/candidemia.

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In December 2003, we also announced the filing of our marketing authorization application for anidulafungin for the treatment of esophageal candidiasis with the European Agency for the Evaluation of Medicinal Products, which will be reviewed under the European Community centralized licensing procedure, which is the procedure used to determine the scope of marketing authorization for human therapeutic products in all member states of the European Union. A 90 day extension for submitting responses to the EMEA was requested by us and granted by the EMEA. Recently, we requested the withdrawal of the anidulafungin MAA for esophageal candidiasis from the EMEA. We intend to resubmit a new MAA for anidulafungin in invasive candidiasis.

In December 2004, we submitted an NDA for dalbavancin, a novel antibiotic for the treatment of cSSTIs. Dalbavancin is a unique, once weekly IV lipoglycopeptide for the treatment of cSSTIs caused by Gram-positive bacteria, including one of the most difficult-to-treat strains of Staphylococcus MRSA. Dalbavancin is a second-generation lipoglycopeptide antibiotic belonging to the same class as vancomycin, the most widely-used injectable antibiotic for Staphylococcal infections. In February 2005, we received notice from the FDA that our file had been accepted for review and had received priority review.

We also completed a Phase 1 clinical trial of VIC-Acne in 2003. We have several lead compounds in pre-clinical studies.

Our revenues in the near term are expected to consist primarily of collaborative research payments, license fees and milestone payments to be received from our collaborators. Certain of these payments are dependent on achievement of specified milestones. We expect these revenues to decrease in 2005. If the development efforts result in clinical success, regulatory approval and successful commercialization of our products, we will generate revenues from sales of these products and from receipt of royalties on sales of these products.

Our expenses have consisted primarily of costs incurred in research and development of new product candidates, when in-licensing existing product candidates and in connection with our collaboration agreements, and from general and administrative costs associated with our operations. We expect licensing costs to increase as development milestones are achieved, and our research and development expenses to increase as we continue to develop our product candidates. We expect to incur sales and marketing expenses during 2005 as we establish our sales and marketing organization.

Since our inception, we have incurred significant losses. As of December 31, 2004, we had an accumulated deficit of $405.2 million. We anticipate incurring additional losses, which may increase for the foreseeable future, including at least through December 31, 2006.

We anticipate that our quarterly results of operations will fluctuate for the foreseeable future due to several factors, including payments made or received pursuant to licensing or collaboration agreements, progress of our research and development efforts and the timing and outcome of regulatory approvals. The fluctuating nature of these factors makes predictions of our future operations difficult or impossible to ascertain.

Major Research and Development Projects

Our ongoing clinical trials of anidulafungin and dalbavancin are our two most significant research and development projects, generating 25% and 22%, respectively, of our total research and development expenses since our inception.

Anidulafungin

Anidulafungin is our lead antifungal product candidate. We in-licensed anidulafungin from Eli Lilly pursuant to the May 1999 agreement described below. In early 2003, we submitted an NDA for anidulafungin

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with the FDA. In May 2004, we received an approvable letter from the FDA for anidulafungin. Based on the approvable letter and our discussions with the FDA, we intend to pursue two paths for approval of anidulafungin, as follows:

- amending our existing NDA for the potential treatment of esophageal candidiasis; and
- submitting an additional NDA for the potential treatment of invasive candidiasis/candidemia.

We kept open the initial NDA for anidulafungin for the treatment of esophageal candidiasis that we filed in April 2003. We plan to file an amendment to that NDA, which will provide supplemental efficacy and safety data largely at the 100 mg dose, including data from our completed invasive candidiasis/candidemia Phase 3 clinical trial. We intend to file a new NDA for anidulafungin for the treatment of invasive candidiasis/candidemia with integrated efficacy and safety data, including data from our completed Phase 3 clinical trial, the results of which were released in February 2005.

As of December 31, 2004, anidulafungin has also been evaluated in a:

- Phase 3 clinical trial for the treatment of esphageal candidiasis, patient enrollment completed and top line data released;
- Phase 3 clinical trial for the treatment of invasive candidiasis/candidemia, patient enrollment completed and top-line data has been released; and
- Phase 2/3 clinical trial for the treatment of aspergillosis, patient enrollment completed and top line data has already been released.

In May 1999, we obtained from Eli Lilly an exclusive worldwide license for the development and commercialization of anidulafungin. We paid $11.0 million for the license and an additional $3.0 million for product inventory (which we have received). If specified milestones are achieved on the intravenous formulation of anidulafungin in the United States and Canada, we will be obligated to make additional payments of up to $8.0 million to Eli Lilly. We are also obligated to make additional payments of up to $8.0 million to Eli Lilly if specified milestones on the intravenous formulation of anidulafungin are achieved in Europe, and additional payments of up to $8.0 million if specified milestones on the intravenous formulation of anidulafungin are achieved in Japan. We are obligated to make additional payments to Eli Lilly of up to $21.0 million if sales of an intravenous formulation of anidulafungin exceed specified targets in the United States and Canada, Europe and Japan. In addition, we are obligated to make royalty payments in respect of sales of any product resulting from the compound. We also made a $6.0 million milestone payment to Eli Lilly in 2003, which was triggered by our filing of the NDA with the FDA.

We are not currently developing an oral formulation of anidulafungin and do not presently intend to do so in the future. However, under the license agreement with Eli Lilly, we are obligated to make additional payments to Eli Lilly of up to $25.0 million if, and only if, specified milestones are achieved on an oral formulation of anidulafungin in the United States, additional payments of up to $15.0 million if specified milestones are achieved on an oral formulation of anidulafungin in Europe, and additional payments of up to $15.0 million if specified milestones are achieved on an oral formulation of anidulafungin in Japan. In addition, we are obligated to make additional payments to Eli Lilly of up to $21.0 million if, and only if, sales of an oral formulation of anidulafungin exceed specified targets worldwide. Because an oral formulation of anidulafungin is not currently feasible, we believe that it is unlikely that we will be obligated to make any of these payments to Eli Lilly. We have also granted to Eli Lilly an option to license the exclusive worldwide rights to any oral formulation of anidulafungin, which is exercisable upon successful completion of Phase 2 clinical trials. If Eli Lilly exercises this option, Eli Lilly would pay us an up-front fee and royalties based on net product sales, and would reimburse us for any milestone payments paid plus the value, on a cost-plus basis, of all prior development expenses attributed to the development and commercialization of the oral formulation of anidulafungin. However, due to the

speculative nature of the oral formulation of anidulafungin, we believe that it is unlikely that we will be entitled to receive fees or royalties and reimbursement of expenses from Eli Lilly.

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Research and development expense allocated to our anidulafungin project, expressed as a percentage of total research and development expense for the period, was:

- 11% for the year 2004 compared to 22% for the year 2003 and 42% for the year 2002; and
- 25% in the aggregate from our inception through December 31, 2004.

Our development administration overhead costs are included in total research and development expense for each period, but are not allocated among our various projects.

The goal of our anidulafungin project is to obtain marketing approval from the FDA and analogous international agencies; and we will consider the project substantially complete if we obtain those approvals even though subsequent to that time we might incur additional expenses in conducting additional clinical trials and follow-up studies. Material cash inflows relating to our anidulafungin project will not commence until after marketing approvals are obtained, and then only if anidulafungin finds acceptance in the marketplace. To date, we have not received any revenues from product sales of anidulafungin. Because of the many risks and uncertainties relating to the completion of clinical trials, receipt of marketing approvals and acceptance in the marketplace, we cannot predict the total estimated cost to complete, the anticipated completion date or when material cash inflows from our anidulafungin project will commence, if ever.

A failure to obtain marketing approval for anidulafungin would likely have the following results on our operations, financial position and liquidity:

- because our research and development projects are independent, a failure to obtain marketing approval for anidulafungin would not necessarily interrupt our development programs for dalbavancin or our pre-clinical compounds; however, we might reduce our development staff (unless one or more of our other product candidates is then entering in late-stage clinical trials, in which case we might re-assign anidulafungin researchers to those projects);
- we would be relieved of our contingent obligation to make further milestone payments and royalty payments to Eli Lilly;
- we would not earn any sales revenue from anidulafungin, which would increase the likelihood that we would need to obtain additional financing for our other development efforts; and
- our reputation among investors might be harmed, which might make it more difficult for us to obtain equity capital on attractive terms or at all.

Dalbavancin

Dalbavancin is our lead antibiotic product candidate. We filed an NDA for dalbavancin with the FDA in December 2004. In February 2005, we received the acceptance to file notification from the FDA and were granted priority review status by the FDA for the NDA. As of December 31, 2004, dalbavancin has been evaluated in:

three Phase 3 clinical trials for the treatment of skin and soft tissue infections (completed and top-line data released); and

a Phase 2 clinical trial for the treatment of catheter-related blood stream infections (completed and top-line data released and published).

a Phase 2 trial in skin and soft tissue infections (completed and top-line data released and published).

In February 1998, we entered into a license agreement and a collaborative agreement with Biosearch. Under the license agreement, Biosearch granted us an exclusive license to develop and commercialize dalbavancin in the United States and Canada. In exchange for the license and upon the receipt of favorable results in pre-clinical studies, we paid an initial license fee of $2.0 million and issued 250,000 shares of our common stock to Biosearch. In May 2001 and December 2002, we paid Biosearch additional milestone payments for the start of Phase 2 and Phase 3 clinical trials, respectively. As a result of the Biosearch merger, we no longer owe any milestones or royalties on dalbavancin.

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Research and development expense allocated to our dalbavancin project, expressed as a percentage of total research and development expense for the period, was:

- 23% for the year 2004 compared to 30% for the year 2003 and 23% for the year 2002; and
- 22% in the aggregate from our inception through December 31, 2004.

Our development administration overhead costs are included in total research and development expense for each period, but are not allocated among our various projects.

The goal of our dalbavancin project is to obtain marketing approval from the FDA and analogous international agencies; and we will consider the project substantially complete if we obtain those approvals even though subsequent to that time we might incur additional expenses in conducting additional clinical trials and follow-up studies. Before we can obtain such marketing approvals we will need to obtain approval from the FDA. We are unable to estimate the costs to completion for our dalbavancin project due to the risks surrounding the clinical trial process, including the risk that we may repeat, revise or expand the scope of our ongoing clinical trials or conduct additional clinical trials to secure marketing approvals and the additional risks listed under the caption Risk Factors Risks Related to our Business If clinical trials for our product candidates are unsuccessful or delayed, we will be unable to meet our anticipated development and commercialization timelines, which could harm our business and cause our stock price to decline. Material cash inflows relating to our dalbavancin project will not commence until after marketing approvals are obtained, and then only if dalbavancin finds acceptance in the marketplace. Because of the many risks and uncertainties relating to the completion of clinical trials, receipt of marketing approvals and acceptance in the marketplace, we cannot predict the total estimated cost to complete, the anticipated completion date or when material cash inflows from our anidulafungin project will commence, if ever.

A failure to obtain marketing approval for dalbavancin would likely have the following results on our operations, financial position and liquidity:

- because our research and development projects are independent, a failure to obtain marketing approval for dalbavancin would not necessarily interrupt our development programs for anidulafungin or our pre-clinical compounds; however, we might reduce our development staff (unless one or more of our other product candidates is then entering in late-stage clinical trials, in which case we might be able to re-assign dalbavancin researchers to those projects);
- we would not earn any sales revenue from dalbavancin, which would increase the likelihood that we would need to obtain additional financing for our other development efforts; and
- our reputation among investors might be harmed, which might make it more difficult for us to obtain equity capital on attractive terms or at all.

Risks relating to our major research and development projects

We face many risks that could prevent or delay the completion of our anidulafungin and dalbavancin projects, including those listed under the caption Risk Factors Risks Related to Operating in Our Industry.

Development Administration

Research and development expense comprising development administration overhead costs, expressed as a percentage of total research and development expense for the period, was:

11% for the year 2004, compared to 12% for the year 2003 and 12% for the year 2002; and

9% in the aggregate from our inception through December 31, 2004.

We do not allocate our development administration costs among our various projects because our development administration group is managed as a separate cost center and its expenditures are not always project specific.

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Other research and development projects

The remaining 44% of our total research and development expenses from our inception through December 31, 2004 were generated by various pre-clinical studies and drug discovery programs, including our collaborations with Pfizer and Novartis described below.

Oxazolidinones collaboration with Pfizer.

In March 1999, we entered into a collaboration agreement with Pharmacia Corporation, now Pfizer, pursuant to which we are collaborating to discover, synthesize and develop second and third generation oxazolidinone product candidates. In connection with the collaboration, Pfizer made an equity investment in us of $3.8 million and paid us research support and license fee payments. Under the terms of the agreement and in consideration of our research obligations, we are entitled to receive funding from Pfizer to support certain of our full-time researchers. If specified milestones are achieved, Pfizer is obligated to pay us additional payments of up to $14.0 million for each compound, a portion of which may be credited against future royalty payments to which we are entitled on the worldwide sales of any drug developed and commercialized from the collaboration. In October 2000, Pfizer increased its funding for this collaboration by 30%, and in June 2001, we received a milestone payment for the initiation of clinical development of one of the compounds. In July 2002, we amended our arrangement with Pfizer by extending the collaboration for an additional three years through March 2005. Through December 31, 2004, Pfizer has made aggregate payments to us under this collaboration agreement (excluding equity investments) of $20.3 million. In 2004, the Company received $3.7 million in payments, all of which was recognized as revenue.

Research and development expense allocated to our collaboration with Pfizer, expressed as a percentage of total research and development expense for the period, was:

- 6% for the year 2004, compared to 5% for the year 2003 and 7% for the year 2002; and
- 7% in the aggregate from January 1, 1999 through December 31, 2004.

The goal of our collaboration with Pfizer is to discover, synthesize and obtain marketing approval for second and third generation oxazolidinone product candidates. We supply research, product leads and other specified intellectual property to the collaboration. The collaboration also depends upon Pfizer to develop the product candidates, to obtain marketing approval from the FDA and analogous international agencies and to manufacture and sell any products resulting from the collaboration. Material cash inflows in the form of royalties relating to this collaboration will not commence until after marketing approvals are obtained, and then only if the product finds acceptance in the marketplace. One product candidate resulting from the collaboration has entered Phase 1 clinical trials. In order to obtain marketing approval, Pfizer will need to complete Phase 1, 2 and 3 clinical trials with satisfactory results and submit an NDA to the FDA. Pfizer is under no obligation to continue the development of any product candidate resulting from this collaboration. Because of this, and the substantial risks and uncertainties relating to the completion of clinical trials, receipt of marketing approvals and acceptance in the marketplace, we cannot predict the total estimated costs to complete, the anticipated completion date or when material cash inflows from our collaboration with Pfizer will commence, if ever. In May 2003, we announced an agreement to continue this collaboration.

Deformylase inhibitors collaboration with Novartis.

In March 1999, we entered into a collaboration agreement with Novartis Pharma AG pursuant to which we are collaborating to discover and develop novel deformylase inhibitors. In connection with the collaboration, Novartis made an initial equity investment in us of $3.0 million. We have also received a number of milestone payments from Novartis and are entitled to receive additional payments of up to $13.0 million for our compounds or up to $7.25 million for Novartis compounds upon the achievement of specified milestones. Novartis may deduct a portion of these milestone payments from the royalties it will be obligated to pay us on the worldwide sales of any drug developed and commercialized from this collaboration. In February 2003, we amended the original agreement in order to extend the research term through March 31, 2005. In September 2003, we announced achievement of a late-stage pre-clinical milestone for which we received a milestone payment from Novartis, and in December 2003 we

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announced that we received an additional milestone payment from Novartis as a result of entering into Phase 1 work on our research collaboration with Novartis. Through December 31, 2004, Novartis has made aggregate payments to us under this agreement (excluding equity investments) of $18.2 million. In 2004, the Company received $2.6 million, all of which was recognized as revenue. In addition, the Company recognized as revenue in 2004 a $750,000 milestone that it received in 2005. In March 2005, the Company announced that Novartis has opted to suspend the Phase 1 compound and will advance a second compound. The Company received a milestone for the designation of this second compound as a late stage preclinical compound.

Research and development expense allocated to our collaboration with Novartis, expressed as a percentage of total research and development expense for the period, was:

- 4% for the year 2004, compared to 3% for the year 2003 and 5% for the year 2001; and
- 6% in the aggregate from January 1, 1999 through December 31, 2004.

The goal of our collaboration with Novartis is to discover, synthesize and obtain marketing approval for deformylase inhibitor product candidates. We are responsible for supplying research to the collaboration, according to a research plan developed by a joint research committee. Our research obligations currently extend through March 31, 2005. Novartis provides us with funding to support some of our researchers on this project. The collaboration will depend upon Novartis to conduct the development of product candidates and to obtain marketing approval from the FDA and analogous international agencies. Material cash inflows in the form of royalties relating to this collaboration will not commence until after marketing approvals are obtained, and then only if the product finds acceptance in the marketplace. Currently one compound identified by the collaboration is in Phase 1 clinical trials. In order to obtain marketing approval, Novartis will need to initiate and complete Phase 1, 2 and 3 clinical trials with satisfactory results and submit an NDA to the FDA. Novartis is under no obligation to continue the development of any product candidate resulting from this collaboration. Because of this, and the many risks and uncertainties relating to the completion of clinical trials, receipt of marketing approvals and acceptance in the marketplace, we cannot predict the total estimated costs to complete, the anticipated completion date or when material cash inflows from our collaboration with Novartis will commence, if ever.

In addition to the work on deformylase inhibitors, under the collaboration agreement we have been delivering to Novartis a series of screening assays based on novel anti-bacterial targets. For each screen that Novartis accepts as validated, we receive a milestone payment. In August 2001 and January 2002, Novartis paid us our fourth and fifth milestone payment, respectively, as a result of our delivery of our fourth and fifth target-based screens, which we expect will be used in Novartis high-throughput screening laboratory to identify new anti-infectives.

A failure by Pfizer or Novartis to pursue or obtain marketing approval for any product candidate resulting from our collaborations could have the following results on our operations, financial position and liquidity:

- we would not receive any further milestone payments or any royalty revenue from the collaborations; and
- while we do not rely on any particular external development collaboration to produce marketable products (and, ultimately, royalty revenues), the failure of all of our external development collaborations would increase the likelihood that we would need to obtain additional financing for our internal research and development efforts.

Deferred Stock Compensation

We have recorded deferred stock compensation expense in connection with the grant of stock options to employees and consultants. Deferred stock compensation for options granted to employees is the difference between the fair value for financial reporting purposes of our common stock on the date such options were granted and their exercise price. Deferred stock compensation for options granted to consultants has been

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determined in accordance with Statement of Financial Accounting Standards No. 123, Accounting for Stock Based Compensation, as the fair value of the equity instruments issued. Deferred stock compensation for options granted to consultants is periodically remeasured as the underlying options vest in accordance with Emerging Issues Task Force No. 96-18, Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods or Services.

We recorded deferred stock compensation (net of cancellations) of $142,000, $702,000 and $(114,000) for the years ended December 31, 2004, 2003 and 2002, respectively. These amounts were recorded as a component of stockholders equity and are being amortized as charges to operations over the vesting periods of the options. We recorded amortization of deferred stock compensation of $0.4 million, $1.4 million and $2.3 million for the years ended December 31, 2004, 2003 and 2002, respectively.

Results of Operations

Years ended December 31, 2004, 2003 and 2002

Revenues were $8.4 million, $9.6 million and $6.3 million in 2004, 2003 and 2002, respectively. Revenues included $3.7 million, $3.6 million and $3.6 million of collaborative research and development, contract services and licensing fees from Pfizer in 2004, 2003 and 2002, respectively, and $3.4 million, $3.9 million and $2.7 million of collaborative research and development fees and milestone payments from Novartis in 2004, 2003 and 2002, respectively. The decrease in revenues in 2004 is due to the achievement of one Novartis milestone in 2004 as compared to two milestones in 2003. In addition, the Company received fewer grants associated with its European operations. The increase in revenues in 2003 is due to the achievement of additional milestones in the Novartis collaboration and recognition of Biosearch Italia grant revenues.

Research and development expenses were $68.5 million, $77.9 million and $48.2 million in 2004, 2003 and 2002, respectively. Research and development expenses consist of salaries and related costs of research and development personnel, as well as the costs of consultants, parts and supplies and clinical trials associated with research and development projects.

The decrease in research and development expenditures in 2004 as compared to 2003 was due to the completion of several large clinical trials combined with a decrease in development administration costs. This decrease was partially offset by an increase in expenditures related to costs associated with the preparation for the then-expected launch of anidulafungin, operating costs associated with the new manufacturing facility, restructuring charges and operating expenses at our European research facility. The increase in research and development expenditures in 2003 as compared to 2002 was due to increased spending on clinical trials associated with dalbavancin, our merger with Biosearch, as well as a milestone payment to Eli Lilly.

General and administrative expenses were $22.3 million, $13.5 million and $8.2 million in 2004, 2003 and 2002, respectively. General and administrative expenses consist of salaries and related costs for executive and other administrative personnel, as well as the costs of facilities, insurance and legal fees. The majority of this increase in general and administrative expenses for 2004 as compared to 2003 was due to the development of a sales and marketing infrastructure, costs associated with the implementation of measures designed to comply with Sarbanes-Oxley and restructuring charges. The increase in general and administrative expenses for 2003 as compared to 2002 was due to our merger with Biosearch and costs incurred to develop an initial marketing infrastructure.

Interest income was $2.6 million, $2.7 million and $1.5 million in 2004, 2003 and 2002, respectively. Interest income consists of interest income on cash and cash equivalents and marketable securities. The decrease in 2004 was due to a decrease in the amount of interest earning assets. The increase in interest income for 2003 as compared to 2002 is due to additional interest earning assets acquired in our merger with Biosearch combined with the proceeds of our July 2003 stock offering.

Interest expense was $0.1 million, $0.5 million and $0.2 million in 2004, 2003 and 2002, respectively. Interest expense consists of interest on the Company s short term and long term debt. The decrease in 2004 was

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due to the pay off of debt related to the U.S. operations. The increase in interest expense in 2003 was due to the additional debt acquired in our merger with Biosearch. The decrease in interest expense in 2002 was due to the decrease in related debt.

Income taxes.

The statutory and effective tax rates were 35% and 0%, respectively, for the periods ended December 31, 2003 and 2002. The effective tax rate resulted from net operating losses and nonrecognition of any deferred tax asset. In the fourth quarter of 2004, the Company recognized a benefit of $1.5 million related to net operating losses generated by one of its Italian subsidiaries subsequent to the acquisition of Biosearch. This was the result of considering the reversal of temporary differences underlying the deferred tax liabilities associated with Biosearch s opening balance sheet as a source of income in accordance with FAS 109. This benefit, which should have been recorded in 2003, is not material to the results of the fourth quarter or any prior periods. In addition it does not generate any income tax refund (i.e. cash benefit) to the company. At December 31, 2004, the Company had federal, state and foreign tax net operating loss carryforwards, or NOLs of approximately $265.0 million, $135.7 million and $73.0 million, which will expire beginning in the year 2009, 2010 and 2006, respectively. Pursuant to the Internal Revenue Code and changes in our ownership, utilization of the NOLs will be subject to an annual limitation. We had federal and state research and experimentation credit carryforwards of approximately $6.6 million and $5.1 million at December 31, 2004, which will expire beginning in the year 2006.

Liquidity and Capital Resources

We have funded our operations principally with the proceeds of $78.5 million from a series of six preferred stock offerings over the period 1995 through 1999, and net proceeds of $52.7 million from our initial public offering received in August 2000. In addition, in April 2002, we completed a private placement of 2,993,800 shares of our common stock to selected institutional investors at a purchase price of $15.00 per share, from which we received net proceeds of approximately $41.9 million. In July 2003, we sold 6,000,000 shares of our common stock at $13.85 per share in a public offering and received net proceeds of $77.8 million. In addition, in February 2004, we filed a universal shelf registration statement on Form S-3, which allows us to offer up to $200 million of our common stock, preferred stock, warrants and/or debt securities from time to time in one or more public offerings. In October 2004, we closed our public offering of 5,051,000 shares of our common stock at $14.75 and received net proceeds of $71.5 million.

As of December 31, 2004, we have also received approximately $38.4 million in payments for collaborative research, contract services and milestone payments, as well as license fees from our collaborators, including Sepracor.

Further, we had a $6.0 million term loan and $2.0 million equipment note with a commercial bank. The term loan accrues interest at the prime rate plus 0.50% and the equipment note s interest rate is based on the LIBOR rate plus an applicable margin. The terms of the term loan were revised in January 2003 and the balance at that time of $2.8 million became repayable in eight equal quarterly installments beginning on March 31, 2003 with the final payment due on December 31, 2004. The remaining note balance was also payable on December 31, 2004. Also, in January 2003 the term loan was amended to include a three-year equipment note for $1.5 million that we were able to draw down on through December 31, 2003. The note bears interest at the prime rate unless we exercise an option to have the interest on all or any portion of the principal amount based on the LIBOR rate plus an applicable margin. The interest on the note was payable in quarterly installments during the draw down period. The principal of the note is payable in equal installments beginning on March 31, 2004 with the final payment due on December 31, 2004. As of December 31, 2004 and 2003, there was an outstanding loan balance of $0 and $2.1 million, respectively.

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In addition, in the period from March 2003 through December 2004, Biosearch Manufacturing S.r.l. received proceeds of 7.5 million euros from a loan facility entered into by Biosearch Manufacturing S.r.l. with Basilicata Region of Italy for the construction of Biosearch Manufacturing S.r.l. s manufacturing plant in Pisticci. Under the loan agreement, Biosearch Manufacturing S.r.l. has a total loan facility of 7.5 million euro repayable in 10 years. The term loan bears interest at 6 months LIBOR rate plus a 1.65% spread less a 4% interest rate which is charged to the Basilicata Region. The loan matures in 2012. The interest rate was 3.89% at December 31, 2004. As of December 31, 2004 and 2003, the outstanding loan balance was $10.1 million and $6.4 million, respectively.

Years ended December 31, 2004, 2003 and 2002

Cash used in operations was $84.4 million, $72.1 million and $42.0 million in 2004, 2003 and 2002, respectively. The net loss for 2004 includes a non-cash charge of $5.8 million for depreciation and amortization. This was more than offset by a decrease in accounts payable and accrued liabilities related to the completion of several large clinical trials. The net loss of $174.1 million for 2003 includes a non-cash charges for the write off of acquired in-process research and development of $94.5 million and the amortization of non-cash stock compensation and depreciation of $6.3 million. The net loss of $48.8 million for 2002 was offset by non-cash charges for the amortization of non-cash stock compensation and depreciation of $3.5 million and an increase in accounts payable and accrued liabilities associated with clinical trial expenditures offset by an increase in prepaid expenses and other current assets which primarily relates to prepaid acquisition costs incurred during the merger with Biosearch.

Investing activities provided $4.2 million and $69.2 million of cash and used $2.6 million of cash during 2004, 2003 and 2002, respectively. The decrease in cash provided in 2004 was due to the realignment of the investment portfolios in 2003 subsequent to the Biosearch merger. Capital expenditures were $13.8 million, $11.7 million and $0.9 million in 2004, 2003 and 2002, respectively. Higher capital expenditure in 2004 and 2003 related to the construction of our manufacturing facility in Italy.

Financing activities provided $84.2 million, $82.6 million and $41.6 million of cash in 2004, 2003 and 2002, respectively. In 2004, our principal source of cash resulted from net proceeds of $71.5 received from the sale of 5,051,000 shares of stock in a public offering combined with $11.6 million received from stock option exercises. In addition, the Company received $3.1 million in loan proceeds related to the construction of its manufacturing facility. This increase was partially offset by $2.5 million in loan repayments primarily related to the Company s term loan. In 2003, our principal source of cash resulted from the net proceeds of $77.8 million received from the sale of 6,000,000 shares of stock in a public offering. In 2002, our principal source of cash resulted from net proceeds of $41.9 million received from the private placement of 2,993,800 shares of common stock to certain institutional investors in April 2002.

We expect to have negative cash flow from operations for the foreseeable future. We expect to incur increasing research and development, and general and administrative expenses, including expenses relating to clinical development, additions to personnel, production and commercialization efforts and the integration of our operations with those of Biosearch. Our future capital requirements will depend on a number of factors, including our success in developing markets for our products, payments received or made under collaboration agreements, the timing and outcome of regulatory approvals, the need to acquire licenses to new products or compounds, the status of competitive products and the availability of other financing. We believe our existing cash and cash equivalents and marketable securities, in addition to the cash and cash equivalents, trading securities and available-for-sale securities acquired in the merger, will be sufficient to fund our operating expenses, debt repayments and capital requirements for at least 18 months.

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Financial Condition

Assets

At December 31, 2004 our total assets were approximately $270.0 million compared to approximately $258.5 million at December 31, 2003. The reason for this increase is a result of the increase in the value of the euro during 2004 which was offset by the Company s use of cash and cash equivalents to fund operations, offset by the issuance of common stock.

Liabilities

At December 31, 2004 our total liabilities were approximately $40.4 million compared to approximately $44.7 million at December 31, 2003. The reason for this decrease was primarily due to the completion of several large clinical trials.

Contractual Obligations and Commitments.

	Payments due by period				
Contractual Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Long-Term Debt Obligations	$ 11,291	$ 1,225	$ 2,638	$ 2,911	$ 4,517
Operating Lease Obligations	8,012	2,054	3,796	2,162	
Purchase Obligations	2,546	2,546			
Total	$ 21,849	$ 5,825	$ 6,434	$ 5,073	$ 4,517

The interest expense on the loan to Biosearch Manufacturing S.r.l. bears interest at the six-month LIBOR rate plus a 1.65% spread, less a 4% interest rate which is charged to the Basilicata Region of Italy. The interest rate was 3.89% at December 31, 2004.

Stockholders Equity

Stockholders equity at December 31, 2004 was approximately $229.6 million compared to approximately $213.8 million at December 31, 2003. The reason for this increase is attributed to the issuance of 5,051,000 shares of common stock in a public offering combined with stock option exercises and an increase in accumulated other comprehensive income. These increases were partially offset by the current year loss.

Off-Balance Sheet Arrangements

Since inception, we have not maintained any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. Further, we have not guaranteed any obligations of unconsolidated entities nor do we have any commitment or intent to provide additional funding to any such entities.

Recent Accounting Pronouncements

In November 2004, the FASB issued Statement of Financial Accounting Standards No. 151, Inventory Costs an amendment of ARB 43, chapter 4 (FAS 151). FAS 151 clarifies the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage) in the determination of inventory carrying costs. The statement requires such costs be recognized as a current-period expense. FAS 151 also requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities. This statement is effective for fiscal years beginning after July 15, 2005. We do not expect the adoption of this standard to have a material impact on our financial condition or results of operations.

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In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123R (revised 2004), Share-Based Payment (FAS 123R). In summary, FAS 123R requires companies to expense the fair value of employee stock options and similar awards as of the date the Company grants the awards to employees. The expense would be recognized over the vesting period for each option and adjusted for actual forfeitures that occur before vesting. The effective date for this standard is interim and annual periods beginning after June 15, 2005, and applies to all outstanding and unvested share-based payment awards at a company s adoption date. We are currently assessing each of the three transition methods offered by FAS 123R and believe adoption of FAS 123R will have a material impact on our consolidated financial statements, regardless of the method selected.

Application of Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. We base our estimates on historical experience and other various assumptions that we believe to be reasonable under the circumstances. Actual results may differ from these estimates.

Our critical accounting policies are as follows:

Revenue Recognition

We recognize revenues as they are earned. Revenue from license fees and contract services are recognized over the initial license or contract service term as the related work is performed, which generally is on a straight-line basis. Collaborative research and development payments are recognized as the related work is performed.

Nonrefundable milestone payments received are recognized when they are earned, which is when the specific events which coincide with the achievement of substantive elements in the related collaboration agreements are achieved. Milestone payments received that are creditable against future royalty payments are deferred and recognized as revenue when the royalties are earned or when the payment is no longer creditable against future payments.

Valuation Allowance

We have established a valuation allowance to reduce our deferred tax asset to an amount that is more likely than not to be realized. We account for income taxes under the provisions of Statement of Financial Accounting Standards No. 109 Accounting for Income Taxes . Under this method, deferred tax assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income.

In-Process Research and Development

In the first quarter of 2003, we recorded a non-cash charge to operations of $94.5 million for acquired in-process research and development resulting from our merger with Biosearch. This amount represents the estimated fair value relating to incomplete research and development projects, which, at the time of the merger, had no alternative future use and for which technological feasibility had not been established.

Intangible Assets

The identifiable intangible assets resulted from the merger, after allocation of negative goodwill. These intangibles represent patents and core technology, a library of microbial extracts and a bioinformatics software platform. These identifiable intangible assets have estimated useful lives of between two and thirteen years.

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RISK FACTORS

In addition to the other information included or incorporated by reference into this Annual Report on Form 10-K, you should carefully consider the following factors in evaluating our company or an investment in any of our securities. Our actual future results and trends might differ materially from our historical results or trends to date, or those anticipated in our forward-looking statements, depending on a variety of factors, including, the factors set forth in this section. Additional risks not presently known to us or that we currently deem immaterial might also harm our business.

Risks Related to Our Business

Our ability to become profitable is heavily dependent upon our obtaining FDA approval of anidulafungin and dalbavancin, our two lead product candidates, and marketing them successfully.

In order to become profitable, we anticipate that we will need to obtain FDA marketing approval for anidulafungin and dalbavancin and then commercialize them successfully. In April 2003, we filed an NDA with the FDA seeking approval to market anidulafungin for the treatment of esophageal candidiasis, which was accepted for review by the FDA in June 2003. In May 2004, we received an approvable letter from the FDA indicating that the NDA submission for anidulafungin did not currently support a labeling claim for the initial treatment of esophageal candidiasis. Based on the approvable letter and discussions with the FDA, we intend to pursue two paths for approval of anidulafungin, as follows:

- amending our existing NDA for the potential treatment of esophageal candidiasis; and
- submitting an additional NDA for the potential treatment of invasive candidiasis/candidemia.

In addition, we recently completed Phase 3 clinical trials with dalbavancin for the treatment of both complicated and uncomplicated skin and soft tissue infections and we completed a Phase 2 clinical trial of dalbavancin for catheter-related bloodstream infections. We filed an NDA for Dalbavancin for complicated skin and soft tissue infections on December 21, 2004.

Factors that could negatively affect or delay our receipt of FDA approval of one or both of these drugs include:

- a refusal by the FDA to approve our NDAs for these drugs or a request for additional information or data.
- delays in completing clinical trials for anidulafungin and dalbavancin; and
- negative or inconclusive results of our ongoing clinical trials of anidulafungin and dalbavancin.

Our success is also dependent upon successful commercialization of these two product candidates. Successful commercialization requires acceptance of anidulafungin and dalbavancin by hospital-based physicians, patients and other medical decision makers.

Our success will further depend upon our ability to protect our intellectual property and products. We rely on a combination of patent, trade secret and regulatory protections to protect us from competitors with similar technologies. With regard to anidulafungin, we rely on patents covering the compound, methods of production and methods of use to protect this product candidate from generic competition. With regard to dalbavancin, we rely primarily on regulatory provisions, such as the data exclusivity provisions under the Hatch-Waxman Act, as well as international patents and know-how to protect this product candidate from generic competition. However, in each case there can be no assurances that we will obtain protection for any specified duration.

If we are unable to develop and successfully commercialize our product candidates, we might not generate significant revenues or become profitable.

To date, we have not commercialized any products or recognized any revenue from product sales and none of our product candidates are approved for sale. Successful commercialization of a new drug product requires

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significant investment in research and development, pre-clinical testing and clinical trials, regulatory approval, and sales and marketing activities. Most of our product candidates are in early stages of development. The FDA reviewed our NDA for anidulafungin and found that it did not currently support a labeling claim for the initial treatment of esophageal candidiasis. Anidulafungin and three of our other product candidates are in clinical trials. Our efforts to commercialize our product candidates are subject to a variety of risks inherent in the development of biopharmaceutical products based on new technologies. These risks include the following among others:

- Pre-clinical testing and clinical trials are protracted, expensive and uncertain processes. It might take us and our collaborators 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;

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

- Any or all of our NDAs might be denied by the FDA and analogous foreign regulators.

- Our product candidates, even if found to be safe and effective, might be difficult to develop into commercially viable drugs or to manufacture on a large scale or might be uneconomical to market commercially.

- Third-party proprietary rights might preclude us from marketing our drugs.

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

- Even if our product candidates are successfully developed and effectively marketed, the size of their potential market might change such that our sales revenue is less than initially contemplated. In any such case, we might never generate sufficient or sustainable revenues to enable us to become profitable.

We expect to incur losses for the foreseeable future and might never achieve profitability.

We have incurred net losses since our inception in 1995. As of December 31, 2004, our accumulated deficit was $405.2 million, including the $94.5 million write-off of acquired in-process research and development resulting from our merger with Biosearch.

Our accumulated deficit results from our net losses of $1.1 million in 1995, $4.8 million in 1996, $6.7 million in 1997 (including $0.4 million in accretion of dividends on preferred stock), $15.1 million in 1998 (including $2.5 million in accretion of dividends on preferred stock), $67.4 million in 1999 (including deemed dividends of $35.1 million and $3.1 million in accretion of dividends on preferred stock), $18.8 million in 2000 (including $3.5 million in accretion of dividends on preferred stock), $32.8 million in 2001, $48.8 million in 2002, $174.1 million in 2003 (including a $94.5 million write-off of acquired in-process research and development resulting from our merger with Biosearch), and $78.5 million in 2004.

On February 28, 2003 we merged with Biosearch, which also has incurred net losses since its inception in 1996. Biosearch s net losses were $23.6 million for 2000, $9.8 million for 2001 and $9.0 million for 2002 and $5.4 million from January 1, 2003 through the merger date of February 28, 2003. At February 28, 2003, Biosearch had an accumulated deficit of $54.8 million.

These losses reflect amortization of negative goodwill, less losses on trading securities in the net amount of (4%) of Biosearch s aggregate operating expenses from January 1, 2000 through February 28, 2003.

We expect to incur substantial losses for the foreseeable future as a result of our research and development costs, including costs associated with conducting pre-clinical testing, clinical trials and sales and marketing, and charges related to purchases of technology and other assets. We expect that our operating losses will fluctuate significantly from quarter to quarter as a result of the timing of receipt of regulatory approval of anidulafungin and our other product candidates, the success of our commercialization efforts following regulatory approval,

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increases or decreases in our research and development efforts, the execution or termination of collaborative arrangements, the initiation, success or failure of clinical trials, or other factors. Our prospects of achieving profitability will depend on numerous factors, including success in:

- receiving regulatory approvals for our product candidates;
- developing and testing new product candidates;
- licensing rights to our product candidates to third parties;
- qualifying for and receiving grants and subsidies;
- manufacturing products;
- marketing products; and
- competing with products from other companies.

Many of these factors will depend on circumstances beyond our control. We cannot assure you that we will become profitable.

If we do not compete successfully in the development and commercialization of products and keep pace with rapid technological change, we will be unable to capture and sustain a meaningful market position.

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies for treatment. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies, specialized biotechnology companies and universities, and other research institutions. Specifically:

- if anidulafungin receives FDA and international marketing approval, it will face competition from commercially available drugs such as amaphotericin B, fluconazole, itraconazole, and from caspofungin, which was the first to receive FDA approval of a new class of antifungal agents called echinocandins (which includes anidulafungin). One of our competitors initially obtained approval only for the narrow indication of aspergillosis salvage therapy, but has recently expanded its scope to include other serious fungal infections;
- if dalbavancin receives FDA and international marketing approval, it will face competition from commercially available drugs such as vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin and daptomycin; and
- if ramoplanin receives FDA and international marketing approval, it will face competition from commercially available drugs such as metronidazole and oral vancomycin.

Our future products, if any, might also compete with new products currently under development or developed by others in the future.

Many of our potential competitors, either alone or together with their collaborators, have substantially greater financial resources and larger research and development regulatory and marketing teams than we do. In addition, many of these competitors, either alone or together with their collaborators, have significantly greater experience than we do in developing, manufacturing and marketing products and working with regulators. As a result, these competitors products might come to market sooner or might prove to be more effective, to be less expensive, to have fewer side effects or to be easier to administer than ours. In any such case, sales of our eventual products would likely suffer and we might never recoup the significant investments we are making to develop these product candidates.

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If clinical trials for our product candidates are unsuccessful or delayed, we will be unable to meet our anticipated development and commercialization timelines, which could harm our business and cause our stock price to decline.

Before obtaining regulatory approvals for the commercial sale of any products we might develop, we must demonstrate through pre-clinical testing and clinical trials that our product candidates are safe and effective for use in humans. Conducting pre-clinical testing and clinical trials is a protracted, time-consuming and expensive process. Completion of clinical trials might take several years or more. Our commencement and rate of completion of clinical trials might be delayed by many factors, including:

slower than expected rate of hospital and patient recruitment;

inability to manufacture sufficient quantities of the study drug for use in clinical trials;

unforeseen safety issues;

lack of efficiency during the clinical trials;

inability to adequately follow patients after treatment;

governmental or regulatory delays; and/or

a decision to expand clinical trials or add studies to increase the statistical significance of the results.

In addition, the results from pre-clinical testing and early clinical trials are often not predictive of results obtained in later clinical trials. For example, clinical trials may not demonstrate attributes of a product candidate that we observed in pre-clinical testing, such as potency. In addition, in general, a number of new drugs have shown promising results in early clinical trials, but subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals. Data obtained from pre-clinical and clinical activities are susceptible to varying interpretations, which might delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections might be encountered as a result of many factors, including perceived defects in the design of clinical trials and changes in regulatory policy during the period of product development.

The FDA reviewed an NDA for one of our product candidates, anidulafungin, and found that it did not currently support a labeling claim for the initial treatment of esophageal candidiasis. We completed a Phase 3 clinical trial for anidulafungin for invasive candidiasis/candidemia. We expect to use the results of this Phase 3 clinical trial in a new NDA that we plan to file for anidulafungin for the treatment of invasive candidiasis and to partially support an amended NDA for anidulafungin for the treatment of esophageal candidiasis. We also filed an NDA for dalbavancin on December 21, 2004. In addition, we have two other product candidates in clinical trials; ramoplanin, which has completed Phase 2; and VIC-Acne, which has completed Phase 1. We also had anidulafungin in Phase 2/3 for an additional indication and dalbavancin and ramoplanin in Phase 2, each for an additional indication; all of which have concluded and released top-line data. Patient follow-up for these clinical trials has been limited and more trials may be required before we will expect to apply for or obtain regulatory approvals.

Clinical trials conducted by us or by third parties on our behalf might not demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for anidulafungin, dalbavancin, ramoplanin or VIC-Acne or any other potential product candidates. Such a failure might delay development of our other product candidates and hinder our ability to conduct related pre-clinical testing and clinical trials. It might also cause regulatory authorities to prohibit us from undertaking any additional clinical trials for our other product candidates. In addition, the final label of any product candidate that receives regulatory approval will be the subject of discussions with the FDA and the product label may be more restrictive than the labeling initially sought by us. Our other product candidates are in pre-clinical development, and we have not submitted investigational new drug applications, or INDs, to commence clinical trials involving these compounds. Our pre-clinical development efforts might not be successfully completed and we might not file further INDs. Any delays in, or termination of, our clinical trials would harm our development and commercialization timelines, which could cause our stock price to decline. Any of these events could also impede our ability to obtain additional financing.

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If our third-party clinical trial managers do not perform, clinical trials for our product candidates might be delayed or unsuccessful.

As of December 31, 2004, we had 30 full-time development employees. We expect to continue to rely on third parties, including our collaborators, clinical research organizations and outside consultants, to assist us in managing and monitoring clinical trials. If these third parties fail to perform satisfactorily under the terms of our agreements with them, clinical trials for our product candidates might be delayed or unsuccessful. Furthermore, the FDA and/or other regulatory agencies of the EU, might inspect some of our clinical investigational sites, our collaborators records and our facilities and files to determine if the clinical trials were conducted according to good clinical practices. If the FDA determines that our clinical trials were not in compliance with applicable requirements, we might be required to repeat the clinical trials.

If our third-party manufacturers do not produce our product candidates on a timely basis, clinical trials and commercialization of our product candidates could be delayed.

We currently do not have manufacturing facilities capable of manufacturing our products in quantities necessary for large-scale trials or marketing. Eli Lilly has supplied us with sufficient anidulafungin echinocandin-B nucleus to market the drug for a few years. We produce anidulafungin (active pharmaceutical ingredient) API at ChemSym Laboratories, a department of Eagle-Picher Pharmaceutical Services, LLC. Dalbavancin API is produced at the Aventis plant in Brindisi, Italy. The lyophilized sterile vials for both anidulafungin and dalbavancin are produced at Ben Venue Laboratories. We do not, however, have any long term agreements with any of these third parties. In the future, we intend to manufacture products at our own manufacturing plant in Pisticci, Italy, wherein the construction process is being completed.

To the extent that our manufacturing capabilities are insufficient to produce all of the necessary active ingredients for our current and future product candidates, we anticipate that we might need to rely on third parties to manufacture some or all of these active ingredients. However, there are a limited number of facilities in which our product candidates can be produced, and third-party manufacturers have limited experience in manufacturing anidulafungin, dalbavancin, ramoplanin, VIC-Acne and VIC-5555, in quantities sufficient for conducting clinical trials or for commercialization. Difficulties are often encountered in manufacturing new products, including problems involving production yields, quality control and assurance, shortage of qualified personnel, compliance with FDA and other regulations, production costs, and development of advanced manufacturing techniques and process controls. Any contract manufacturer might not perform as agreed or might not remain in the contract manufacturing business for the time we require to successfully develop, produce and market our product candidates. If any of our contract manufacturers fails to perform satisfactorily under its agreements with us, such as by failing to deliver the required quantities of our product candidates for clinical use on a timely basis and at commercially reasonable prices, and if we do not find a replacement manufacturer or develop our own manufacturing capabilities, clinical trials involving our product candidates, or commercialization of our products, could be delayed.

If we do not establish successful marketing and sales capabilities or do not enter into successful marketing arrangements with third parties, we will not be able to commercialize our future products and will not become profitable.

If we successfully develop and obtain regulatory approval for the product candidates we are currently developing, we intend to sell a portion of our future products, including anidulafungin and dalbavancin, through our own sales force. At present, however, we have no sales infrastructure and we lack any experience in direct marketing, sales and distribution. Our future profitability will depend in part on our ability to develop a direct sales and marketing force to sell our future products, if any, to our target market. We might not be able to attract and retain qualified salespeople or be able to build an efficient and effective sales and marketing force. To the extent that we enter into marketing and sales arrangements with other companies, our revenues will depend on the efforts of others. These efforts might not be successful. If we are unable to enter into third-party arrangements, then we must substantially expand our marketing and sales force in order to achieve commercial success for certain products, and to compete with other companies that have experienced and well-funded marketing and sales operations.

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If we cannot enter into new in-licensing arrangements, our product portfolio and potential profitability could be harmed.

An important component of our business strategy is to in-license drug compounds discovered by other pharmaceutical and biotechnology companies or academic research laboratories, in order to develop them ourselves. Currently we in-license anidulafungin from Eli Lilly. Anidulafungin is our lead antifungal product candidate and one of our four product candidates in clinical development. Under our license arrangement with Eli Lilly, we acquired exclusive worldwide rights to anidulafungin. This license arrangement will terminate on a country-by-country basis upon the later of the expiration of all product patents in the country or 10 years from the date of the first commercial sale of anidulafungin in the country. If we do not comply with the terms of this license agreement, we could lose our rights to anidulafungin. Competition for new promising compounds can be intense. If we are not able to identify future in-licensing opportunities and enter into future licensing arrangements on acceptable terms, our future product portfolio and potential profitability could be harmed.

If we do not establish and maintain collaborations or if our collaborators do not perform, we will be unable to develop our joint product candidates.

We have entered into two collaboration arrangements with third parties to develop product candidates, one of which expires by its terms on March 31, 2005. Additional collaborations might be necessary in order for us to fund our research and development activities and third-party manufacturing arrangements, to seek and obtain regulatory approvals and to successfully commercialize our existing and future product candidates. If we do not maintain our existing collaborative arrangements or do not enter into additional collaborative arrangements, the number of product candidates from which we could receive future revenues would decline. In addition, our dependence on collaborative arrangements with third parties subjects us to a number of risks, including the following:

The collaborative arrangements might not be on terms favorable to us. Agreements with collaborators typically allow the collaborators significant discretion in electing whether to pursue any of the planned activities. We cannot control the amount and timing of resources our collaborators devote to the product candidates or their prioritization of the product candidates, and our collaborators might choose to pursue alternative products. In addition, agreements with collaborators frequently contain prohibitions on, and may in the future prohibit us from, conducting certain types of research or other activities in the field that is the subject of the collaboration. In such event, these prohibitions may limit the areas of research and development that we may pursue, either alone or in cooperation with other third parties.

Our collaborators might also not perform their obligations as expected. Business combinations or significant changes in a collaborator s business strategy might adversely affect a collaborator s willingness or ability to complete its obligations to us.

Moreover, we could become involved in disputes with our collaborators which could lead to delays in, or the termination of, our development programs with them, as well as time-consuming and expensive litigation or arbitration.

Even if we fulfill our obligations under any collaborative agreement, our collaborators can generally terminate the agreements under specified circumstances.

If any collaborator were to terminate or breach their collaborative agreement with us, or otherwise fail to complete its obligations in a timely manner, our chances of successfully commercializing products could be harmed.

If our future products are not accepted by the market, we are not likely to generate significant revenues or become profitable.

Even if we obtain regulatory approval to market products in the future, we might not gain market acceptance among physicians, patients, healthcare payors and the medical community. The degree of market acceptance of any pharmaceutical product that we might develop will depend on a number of factors, including:

- demonstrations of clinical efficacy and safety;

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cost-effectiveness;

potential advantages over alternative therapies, including fewer side effects or easier administration;

reimbursement policies of government and third-party payors; and

the effectiveness of our marketing and distribution capabilities.

Physicians will not recommend therapies using any of our future products until clinical data or other factors demonstrate their safety and efficacy as compared to other drugs or treatments. Even if the clinical efficacy and safety of therapies using any of our future products is established, physicians might elect not to recommend the therapies for a number of other reasons, including the possibility that the mode of administration of our future product might not be effective for their patients indications and locations. For example, many antibiotic or antifungal products are typically administered by infusion or injection, which requires substantial cost and inconvenience to patients and might not be practical in non-hospital settings.

Physicians, patients, third-party payors and the medical community might not accept and utilize any product candidates that we or our collaborators develop. If none of our future products achieve significant market acceptance, we are not likely to generate significant revenues or become profitable.

If we are unable to attract and retain skilled employees and consultants, we will be unable to develop and commercialize our product candidates.

We are highly dependent on our skilled management and scientific staff. In order to pursue our product development, marketing and commercialization plans, we might need to hire additional personnel with experience in clinical testing, government regulation, manufacturing, marketing and finance. We might not be able to attract and retain personnel on acceptable terms given the intense competition for such personnel among high technology enterprises, including biotechnology, pharmaceutical and healthcare companies, universities and non-profit research institutions. Most of our management and scientific staff do not have employment contracts. If we lose a significant number of these persons, or are unable to attract and retain qualified personnel, our business, financial condition and results of operations might be harmed. We do not maintain key person life insurance on any of our personnel.

In addition, we rely on consultants and members of our scientific and clinical advisory boards to assist us in formulating research and development strategies. All of these consultants and the members of our scientific and clinical advisory boards are employed by others, and they might have commitments to, or advisory or consulting agreements with, others that might limit their availability to us. If we lose the services of these advisors, our achievement of our development objectives might be impeded, and our business, financial condition and results of operations might be harmed. Finally, except for work performed specifically for and at our direction, the inventions or processes discovered by our scientific and clinical advisory board members and other consultants will not become our intellectual property, but will be the intellectual property of the individuals or their institutions. If we desire access to these inventions, we will be required to obtain appropriate licenses from the owners. We face the risk that we might not be able to obtain such licenses on favorable terms or at all.

Our revenues are subject to significant fluctuations, which makes it difficult to draw meaningful comparisons from period-to-period changes in our operating results.

We expect that substantially all of our revenues for the foreseeable future will result from payments under collaborative arrangements, with some Italian and EU grant and subsidy revenue. To date, collaborative payments have taken the form of up-front payments, reimbursement for research and development expenses and milestone payments. Milestone payments to us under collaborative arrangements are subject to significant fluctuation in both timing and amount. As a result, comparisons of our revenues and results of operations between periods might not produce meaningful indications of our progress toward commercializing one or more product candidates. Moreover, the historical revenues of Vicuron and Biosearch on a stand-alone basis might not be indicative of our future performance or of our ability to continue to achieve additional milestones and to receive additional milestone payments from our collaborators.

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We might seek additional funding, which could dilute our stockholders interest in our company or impose burdensome financial restrictions, and if we do not obtain necessary funding, we might be forced to delay or curtail the development of our product candidates.

We expect to incur significant research and development, general and administrative and sales and marketing expenses over the next several years. Based on our current plans and assumptions, we estimate that our cash and liquid assets at December 31, 2004 will be sufficient to fund our operating losses for the next 18 months. However, if our plans change and/or our assumptions are inaccurate, we might need to seek and obtain capital sooner than anticipated. Some of our more significant plans and assumptions relate to:

- receipt of regulatory approval for anidulafungin and commencement of a marketing campaign for anidulafungin;
- payments received or made under possible future collaborative agreements;
- continued progress in the research and development of our future products;
- costs associated with protecting our patent and other intellectual property rights;
- costs associated with developing marketing and sales capabilities; and
- the rate of market acceptance of any future products.

Other than our Italian loan facility for the construction of our manufacturing plant, we have no committed sources of additional capital. To the extent our capital resources are insufficient to meet our future capital requirements, we will have to raise additional funds, perhaps on unfavorable terms, to continue the development of our product candidates. We might also seek additional funding much earlier than we would otherwise need in order to take advantage of attractive opportunities in the capital markets.

We might seek to raise funds from a traditional lender or through public or private debt or equity offerings. To the extent we raise additional capital through the sale of equity or convertible debt securities, the securities could be sold at a discount to prevailing market price and the issuance of those securities could result in dilution to our stockholders. Moreover, the incurrence of debt financing could result in a substantial portion of our operating cash flow being dedicated to the payment of principal and interest on such indebtedness, and we might be subject to restrictive covenants as a result of such debt financing. This could render us more vulnerable to competitive pressures and economic downturns and could impose restrictions on our operations. If adequate funds are not available from any of those sources, our business might be harmed. We might be required to delay, reduce the scope of, or eliminate one or more of our research and development programs or otherwise significantly curtail operations. In addition, we might be required to obtain funds by entering into arrangements with collaborators on unattractive terms or relinquish rights to certain technologies or drug candidates that we would not otherwise relinquish in order to continue independent operations.

If we enter into any strategic transactions, we will incur a variety of costs and might never realize the anticipated benefits.

If appropriate opportunities become available, we might attempt to acquire additional products, product candidates or businesses, or enter into joint ventures or reciprocal licensing arrangements, that we believe are a strategic fit with or potentially advantageous to, our business. We are not currently a party to any such strategic agreements. If we pursue any transaction or arrangement of that sort, the process of negotiating the transaction and integrating an acquired product, product candidate or business or entering into the joint venture or reciprocal licensing arrangement might result in operating difficulties and expenditures and might require significant management attention that would otherwise be available for ongoing development of our business, whether or not any such transaction is ever consummated. Moreover, we might never realize the anticipated benefits of any transaction or arrangement. Future acquisitions or other such transactions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or impairment expenses related to goodwill and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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If our use of hazardous materials results in contamination or injury, we could suffer significant financial loss.

Our operations include the controlled use of hazardous materials, primarily small quantities of toxic biological materials and chemical compounds which we store, collect, combine, analyze and, at times, produce in connection with our research and manufacturing activities. We cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident or environmental discharge, we might incur remediation expense and be held liable for any resulting damages. We do not currently maintain separate insurance to cover contamination or injuries relating to hazardous materials, and such liabilities might not be covered by our general liability insurance coverage.

We might be required to repay some or all of the Italian and/or EU research grants and loan subsidies previously received by Biosearch and we might not qualify or be approved for new grants and subsidies.

Biosearch historically funded a portion of its operations through research grants and loan subsidies awarded by Italian and EU authorities. Under applicable law, any transfer of those grants and subsidies (including transfer by merger) requires written approval. In connection with the merger, and the subsequent contribution of Biosearch s assets to Vicuron Pharmaceuticals Italy S.r.l., our wholly-owned Italian subsidiary, we applied for permission to transfer Biosearch s grants and subsidies to our Italian branch and subsidiary. Although the merger and the contribution have been completed, the Italian and EU authorities have not as yet reached an official decision on whether to approve our transfer requests. If the transfers are approved, we intend to apply for further permission to contribute the grants and subsidies to Vicuron Pharmaceuticals Italy S.r.l., our wholly-owned subsidiary in Italy. We face the risk that one or both of the transfers might not be approved, in which case we might be required to repay some or all of the grants and subsidies received by Biosearch prior to the merger, in the aggregate amount of up to approximately $1.8 million as of December 31, 2004, plus accrued interest and applicable damages, and we may forfeit grants and subsidies awarded to Biosearch but not yet disbursed as of December 31, 2004 by the authorized bank in the amount of up to approximately $1.5 million (based on exchange rates then prevailing). Regardless of whether or not we are required to repay those grants, we anticipate that our Italian subsidiary will be eligible to apply for new research grants and subsidies from both the Italian and EU authorities. However, grants and subsidies are awarded at the discretion of those authorities and we face the risk that our Italian subsidiary might not qualify or be approved for any additional grants or subsidies in the future.

Complying with two national regulatory structures might result in administrative challenges.

Our operations must comply with applicable laws of and rules of the United States (including Delaware corporate law and the rules and regulations of the SEC and the NASDAQ National Market), the EU legal system and the Republic of Italy (including the rules and regulations of the Commissione Nazionale per le Società e la Borsa, or CONSOB, and Borsa Italiana, which collectively regulate companies listed on Italy s public markets such as the Nuovo Mercato). Conducting our operations in a manner designed to comply with all applicable laws and rules will require us to allocate additional time and resources to regulatory compliance matters. For example:

- issuing each material announcement in both English and Italian might cause administrative challenges;
- submitting filings and applications with regulatory and governmental authorities in the U.S., Italy and the EU, and approving translations of each significant document into the other language, if necessary, is time-consuming and expensive;
- under Italian employment law, our relations with our employees in Italy are governed by collective bargaining agreements negotiated at the national level (and over which we have no control), which reduce the methods customarily available in the United States to motivate and/or make changes to our Italian workforce;

under EU data protection regulations, we are unable to send without restriction private personal data, including many employment records and some clinical trial data, from our Italian offices to our U.S. offices; and

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tariffs, customs, duties, import restrictions, tax effects and other trade barriers might delay or increase the cost of relocating personnel and, if marketing approvals are obtained, commercial quantities of our products between nations.

We are subject to risks resulting from fluctuations in the exchange rate of the dollar relative to the euro, which could cause costs to be greater than we expect and introduce additional volatility in our reported quarterly results.

As a result of our 2003 merger with Biosearch, we are exposed to risks associated with foreign currency transactions insofar as we might desire to use dollars to make contract payments denominated in euros or vice versa. As the net positions of our unhedged foreign currency transactions fluctuates, our earnings might be negatively affected. In addition, we are exposed to risks associated with the translation of euro-denominated financial results and balances and cash flows into U.S. dollars. Although our reporting currency remains the U.S. dollar, a portion of our consolidated revenues and costs now arise in euros, which we restate in dollars for purposes of financial reporting. In addition, the reported carrying value of our euro-denominated assets and liabilities will be affected by fluctuations in the value of the U.S. dollar as compared to the euro. Accordingly, changes in the value of the U.S. dollar relative to the euro might have an adverse effect on our reported results of operations and financial condition, and fluctuations in exchange rates might introduce additional volatility in our reported results and accounts from period to period.

We are in the process of determining whether to reduce the number of our employees in Italy, and if we decide to do so, we could incur substantial costs.

In order to reduce the number of our employees in Italy, we would need to obtain the approval of the Italian labor unions. Because of the applicable rules and collective bargaining agreements, this process could be protracted and we could incur substantial costs, which have not been fully ascertained, if we seek to implement any such reduction. The Italian labor unions may reject any request we make to reduce the number of our employees in Italy, and our labor force may decide to strike. Even if we obtain the approval of the Italian labor unions, such approval could require us to make severance payments to our former employees in Italy. Further, our former employees in Italy may assert claims relating to the termination of their employment or their receipt or purchase of our securities in connection with such employment. These claims, regardless of their merits, could cause us to incur substantial costs in defending ourselves and could divert the attention of our management away from our operations, which could harm our business. Further, if any such claims were to result in a judgment against us, we could be required to pay damages, which could harm our business.

Risks Related to Operating in Our Industry

If we experience delays in obtaining regulatory approvals, or are unable to obtain them at all, for one or more of our product candidates, commercialization of those products will be delayed.

Our efforts to develop and market our product candidates will be subject to extensive and rigorous domestic regulation. FDA rules govern, among other matters, the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products in the United States. Any products that we market abroad will also be subject to extensive regulation by foreign governments. In order to obtain permission to sell our product candidates, we must provide the FDA and foreign regulatory authorities with clinical data demonstrating that our proposed drugs are safe in humans and effective at treating an indicated condition. None of our product candidates has been approved for sale in the United States or any foreign market, and we cannot predict whether regulatory clearance will be obtained for any product that we are developing or intend to develop. The regulatory review and approval process takes many years, is dependent upon the type, complexity and novelty of the product candidate, requires the expenditure of substantial resources, involves post-marketing surveillance, and might involve ongoing requirements for post-marketing studies. Delays in

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obtaining regulatory approvals such as the delays we experienced as a result of receiving the approvable letter for anidulafungin might:

- impede the commercialization of any drugs that we or our collaborators develop;
- require us or our collaborators to comply with costly additional procedures;
- diminish any competitive advantage that we or our collaborators might attain from early market introduction of a new product; and
- delay or eliminate our receipt of revenues or royalties.

Any required approvals, once granted, might be withdrawn. Further, if we do not comply with applicable FDA and foreign regulatory requirements at any stage during the regulatory process, we might be subject to sanctions, including:

- imposed delays in clinical trials or commercialization;
- refusal by the FDA and foreign regulators to review pending market approval applications or supplements to approval applications;
- product recalls or seizures;
- suspension of production;
- withdrawals of previously issued marketing approvals; and
- fines, civil penalties and criminal prosecutions.

We choose to develop some proprietary product candidates ourselves and to out-license other product candidates to third parties for collaborative development. The licensing or collaboration agreement will generally specify which party is responsible for directing the clinical trial process and seeking regulatory approvals. Regardless of whether the process is directed by us or by our collaborators, in each case we face the risk that our clinical trials might be unsuccessful, and that the FDA will not grant us marketing approval. We might also encounter delays or rejections based upon future changes in government regulation, legislation or FDA policy during the period of product development, clinical trials and FDA regulatory review. If we do not obtain required governmental approvals, we will be precluded from marketing the candidate for which approval was sought. If regulatory clearance for marketing a future product is granted, this clearance will be limited to those disease states and conditions for which the product is demonstrated through clinical trials to be safe and effective.

Outside the United States, the ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. This foreign regulatory approval process typically includes all of the risks associated with FDA clearance described above and might include additional risks.

If our manufacturing subsidiary or our contract manufacturers fail to comply with applicable Good Manufacturing Practice requirements, we could be subject to fines or other sanctions, or be precluded from marketing any future products.

Manufacturing facilities are required to comply with the FDA s Good Manufacturing Practice regulations. Even facilities outside the United States, such as the manufacturing plant we are constructing in Italy, must comply with these regulations if the manufactured products will be sold in the United States. Good Manufacturing Practice regulations include requirements relating to quality control and quality assurance as well as to maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. These facilities must be approved before we can use them in commercial manufacturing of our products. Comparable Good Manufacturing Practice regulations also apply in the EU, Italy and other foreign countries. Our contract manufacturers and our manufacturing subsidiary might not be able to comply with the applicable Good Manufacturing Practice requirements and other FDA or other EU, Italian or foreign regulatory agencies regulatory requirements.

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If our intellectual property rights do not adequately protect our product candidates or future products, others could compete against us more directly, which would harm our business.

Our success depends in part on our ability to protect our intellectual property from unauthorized use by third parties, which we will be able to do only to the extent that our intellectual property is covered by valid and enforceable patents or is effectively maintained as a trade secret. We have rights relating to a number of patents and patent applications in the United States and abroad.

The patent position of biopharmaceutical companies involves complex legal and factual questions and, therefore, we cannot predict with certainty whether they will be enforceable. We have in the past and might in the future receive office actions or other notices from U.S. or foreign patent authorities seeking to limit or otherwise qualify some patent claims. Patents, if issued, might be challenged, invalidated, circumvented or expired. Thus, any patents that we own or license from third parties might not provide any protection against competitors or expire at an inopportune time. Our pending patent applications, those we might file in the future, or those we might license from third parties, might not result in patents being issued. Also, we periodically review our U.S. and foreign patent filings to determine whether their maintenance is commercially justified. As a result, we may determine from time to time to abandon certain patent applications or allow certain patents to lapse. Moreover, patent rights might not provide us with adequate proprietary protection or competitive advantages against competitors with similar technologies. The laws of many foreign countries do not protect intellectual property rights to the same extent as do the laws of the United States.

In addition to patents, we rely on trade secrets and proprietary know-how. We seek protection, in part, through confidentiality and proprietary information agreements. These agreements might not provide meaningful protection or adequate remedies for our technology in the event of unauthorized use or disclosure of confidential and proprietary information. Failure to protect our intellectual property rights could seriously impair our competitive position and harm our business.

If third parties claim we are infringing their intellectual property rights, we could suffer significant litigation or licensing expenses or be prevented from marketing our future products.

Our success depends in part on our ability to operate without infringing upon the intellectual property rights of others. Research has been conducted for many years in the areas in which we focus our research and development efforts. This has resulted in a substantial number of issued patents and an even larger number of still-pending patent applications. U.S. patent applications, which are not foreign filed, can be maintained in secrecy until issuance. U.S. patent applications which are also intended for foreign filing usually publish 18 months after the earliest priority date or within six months of the U.S. filing date, whichever is later. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made. Our commercial success will depend significantly on an ability to operate without infringing the patents and other intellectual property rights of third parties. However, our technologies might infringe the patents or violate other intellectual property rights of third parties without our knowledge. In the event an infringement claim is brought against us, we might be required to pay legal and other expenses to defend such a claim and, if our defense is unsuccessful, we might be prevented from pursuing product development and commercialization and might be subject to damage awards.

Our success also depends in part on our ability to prevent others from infringing our intellectual property rights. The biotechnology and pharmaceutical industries have been characterized by extensive litigation regarding patents and other intellectual property rights. The defense and prosecution of intellectual property legal actions, U.S. Patent and Trademark Office interference proceedings and related legal and administrative proceedings in the United States and internationally involve complex legal and factual questions. As a result, such proceedings are costly and time-consuming to pursue and their outcome is uncertain. Litigation might be necessary to:

enforce patents that we own or license;

protect trade secrets or know-how that we own or license; or

determine the enforceability, scope and validity of the intellectual property rights of others.

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If we become involved in any litigation, interference or other administrative proceedings, we will incur substantial expense and the efforts of our technical and management personnel will be significantly diverted. An adverse determination might subject us to loss of proprietary position or to significant liabilities, or require us to seek licenses that might not be available from third parties. We might be restricted or prevented from manufacturing and selling products, if any, in the event of an adverse determination in a judicial or administrative proceeding or if we fail to obtain necessary licenses. Costs associated with these arrangements might be substantial and might include ongoing royalties. Furthermore, we might not be able to obtain the necessary licenses on satisfactory terms, if at all.

If the government or other third-party payors fail to provide adequate coverage and reimbursement rates for our future products, if any, our revenues and prospects for profitability will be harmed.

In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health administration authorities, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price, and examining the cost effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payors satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development. Domestic and foreign governments continue to propose and pass legislation designed to reduce the cost of healthcare. For example, in some foreign markets, the government controls prescription pharmaceuticals pricing and profitability. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental control. In addition, increasing emphasis on managed care in the United States will continue to put pressure on pharmaceutical product pricing. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenues and profitability. Accordingly, legislation and regulations affecting the pricing of pharmaceuticals might change before our proposed products are approved for marketing. Adoption of such legislation could further limit reimbursement for pharmaceuticals.

If a successful product l