INTRABIOTICS PHARMACEUTICALS INC /DE
Form 424B4
May 05, 2004

Table of Contents

**Filed pursuant to**
**Rule 424(b)(4)**
**File No. 333-114451**

# 3,000,000 Shares
## Common Stock

This is a public offering of common stock of IntraBiotics Pharmaceuticals, Inc. We are offering 3,000,000 shares of our common stock. Our common stock is traded on the Nasdaq National Market under the symbol IBPI. On May 4, 2004, the last reported sale price of our common stock on the Nasdaq National Market was $14.30 per share.

**Investing in our common stock involves risk. See Risk Factors beginning on page 7 of this prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

| | Per Share | Total |
|---|---|---|
| Public offering price | $13.00 | $39,000,000 |
| Underwriting discounts and commissions | $0.78 | $2,340,000 |
| Proceeds, before expenses, to IntraBiotics | $12.22 | $36,660,000 |

We have granted the underwriters the right to purchase up to 450,000 additional shares of common stock to cover over-allotments.

**Deutsche Bank Securities** **Piper Jaffray**

**Lazard**

The date of this prospectus is May 5, 2004.

Table of Contents

## PROSPECTUS SUMMARY

*This summary highlights some of the information found in greater detail elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus, including Risk Factors and our financial statements and accompanying notes, before making an investment decision.*

### Our Company

We are developing novel antimicrobial drugs designed to overcome many of the shortcomings of currently prescribed anti-infectives. These shortcomings result from the wide range of microbes responsible for serious infections and the fact that many microbes have become resistant to current therapies. We have selected our product candidate, iseganan, for development because it kills a broad spectrum of microbes and has a low propensity to engender resistance. Iseganan is currently in clinical development for two indications: the prevention of ventilator-associated pneumonia, or VAP, and the treatment of lung infections associated with cystic fibrosis, or CF. Additionally, we are evaluating the use of iseganan for other types of infection where we believe that its properties may render it more effective than current therapies.

VAP is the most common infection contracted by patients in the intensive care unit. Worldwide, more than one million patients annually are at risk of developing VAP. VAP represents a significant unmet medical need, as there are no drugs approved for its prevention. VAP is caused by aspiration of infectious microbes into the lungs of ventilated patients. Prophylaxis with combinations of conventional antimicrobial drugs has been shown to reduce the incidence of VAP, but is not generally used due to concerns over antimicrobial resistance. Iseganan has been granted Fast Track designation by the FDA for this indication and has been accepted for inclusion into the FDA s CMA Pilot 2 Program. In addition, we have established a Special Protocol Assessment, or SPA, in collaboration with the FDA, detailing an agreed-upon pivotal trial design for prevention of VAP that, if successful, will support registration of iseganan for this indication. The SPA requires us to conduct two identical pivotal trials, the first of which is currently enrolling patients. We expect results from this first trial by the end of 2004.

CF is a lethal disease in which patients develop chronic, progressive infections in their lungs, beginning in infancy. In the United States, approximately 30,000 people suffer from CF. Patients are treated with inhaled antibiotics, but efficacy is limited by antimicrobial resistance, narrow antimicrobial spectrum, or both. Most patients die of progressive lung infection and the median survival of CF patients is 33 years of age. Iseganan kills the majority of pathogens that cause lung infection in CF, including multi-drug resistant pathogens. Based on our completed Phase I studies, we believe we have sufficient safety data to submit to the FDA in support of a Phase II study, which we plan to initiate in the second half of 2004.

We have chosen to pursue indications for which clinical proof-of-principle exists, but where resistance diminishes the therapeutic value of existing drugs. We believe that targeting indications where antimicrobial drugs have already demonstrated effectiveness may reduce our development risk. Additionally, in contrast to the conventional practice of delivering antibiotics systemically to treat infection, we have focused on conditions where we can deliver iseganan directly to the site or source of disease. We believe that this strategy may optimize efficacy by maximizing drug concentrations where the infection occurs, and reduce potential toxicity by limiting systemic drug exposure. We retain worldwide commercial rights to iseganan for all indications. Our key U.S. patents, which cover the composition of iseganan, expire in 2015.

### Background

Two interrelated problems are thwarting efforts to improve the prevention and treatment of infectious disease. First, patients are vulnerable to infection caused by a wide range of

Table of Contents

microbes. Second, many microbes encountered by patients today are not susceptible to current therapies. The result of these problems is that infectious diseases are increasingly difficult to treat and are adding substantial costs to the health care system.

Since the discovery of penicillin more than 50 years ago, many types of antimicrobial drugs have been developed to fight microbial infections. Until recently, these antimicrobial drugs have been highly successful in controlling the morbidity associated with serious infections. In recent years, however, many microbes have developed resistance to currently marketed antibiotics. Once microbes become resistant, infections can become difficult or impossible to treat.

The antibiotic resistance problem is worsening, in part, because of the use of multiple antibiotics to treat individual cases of infection. In order to combat infection, doctors typically prescribe combinations of antibiotics for two reasons. First, many infections can be caused by a broad range of microbial pathogens, while most current antibiotics individually have a narrow spectrum of activity. Second, because the results of diagnostic tests that determine the pathogen(s) causing an infection are often not available in a timely fashion, physicians are frequently forced to prescribe multiple antibiotics to cover the range of possible microbes. As pathogens have evolved to evade the activity of the commonly-prescribed antibiotics, multi-drug resistant strains have proliferated.

**Key Features and Benefits of Iseganan**

We are developing a novel class of drugs designed to kill a broad range of microbes without engendering resistance. These drugs are derived from a class of antimicrobial peptides known as protegrins that have evolved in mammals and are a natural part of the body s mechanism to kill microbes and fight infection. In contrast, conventional antimicrobial drugs, developed from plants, molds and other non-mammals, are naturally narrower in spectrum and engender resistance. Iseganan is a synthetic protegrin analog that we have optimized to enhance its microbe-killing activity. We believe that four key features of iseganan will translate into important clinical benefits.

*Broad Spectrum.* Iseganan kills a diverse range of pathogens, including the two major classes of bacteria as well as yeast-like fungi, which are often not naturally susceptible to antibiotics. Treating these three classes of pathogens typically requires two or three antimicrobial drugs. Iseganan is also active against the vast majority of drug-resistant pathogens. We are unaware of any other agent on the market or in clinical development that possesses this breadth of antimicrobial activity.

*Low Propensity to Engender Resistance.* Iseganan destroys the cell membranes of microbes, thus damaging their structural integrity. Based on tests conducted in the laboratory, iseganan works 100 to 1,000 times faster than conventional antibiotics. Because the cell membrane is a fundamental structure and cannot readily change, and because iseganan destroys membranes so quickly, there is little chance for a microbe to survive iseganan s killing activity and develop resistance. In laboratory experiments designed to engender resistance, organisms have remained susceptible to iseganan s killing effects while developing significant resistance to conventional antibiotics. This has been confirmed in both drug-susceptible, as well as multi-drug resistant, strains of pathogens.

*Low Propensity to Engender Cross-Resistance.* Cross-resistance, which arises when an organism develops resistance to a second antibiotic upon exposure to a first, unrelated antibiotic, is particularly problematic because it can severely limit the number of viable therapeutic options a physician has to treat a patient. Organisms treated with iseganan have been shown to remain susceptible to the killing effects of other drugs. As a result, we believe that use of iseganan will preserve therapeutic options.

Table of Contents

*Safe and Well-Tolerated.* Based on our experience to date, iseganan appears to be safe and well-tolerated at therapeutically relevant doses when administered to the oral cavity, the planned route of administration for the prevention of VAP. In addition, we believe that we have sufficient safety data from our completed Phase I studies to support a Phase II study for inhaled iseganan in CF patients.

**Iseganan for Ventilator-Associated Pneumonia**

We completed a 42-patient, Phase I/ II clinical trial in patients on artificial life support. In this trial, local oral administration of iseganan was safe and resulted in several hundred-fold reductions in levels of microbes in the mouth. Our SPA calls for two identical pivotal trials that will each enroll approximately 900 patients. The primary efficacy end point in each of the two trials will be the occurrence of VAP. The analysis of the primary end point in each trial will be the proportion of patients developing VAP among survivors. In addition, the data from the two trials will be combined and analyzed for VAP-free survival. This pooled analysis will be the primary analysis used by the FDA for product registration. The first pivotal trial began enrolling patients in September 2003 and has enrolled more than 450 patients to date.

Given that VAP arises through the aspiration of microbes from the mouth into the lungs, decontaminating the mouth using antimicrobial drugs to prevent VAP is an approach that has received significant medical and scientific interest. Since 1984, there have been more than 30 randomized clinical trials using conventional antimicrobial drugs topically applied in the oral cavity. Most of these trials have independently been statistically significant, and, in the aggregate, they have demonstrated reductions in the incidence of VAP of approximately 50%.

Despite these positive results, oral decontamination using conventional antimicrobial drugs generally has not been adopted as a prevention strategy for VAP due to concerns over causing resistance and cross-resistance. We believe that iseganan, due to the features and benefits discussed above, could become an attractive therapeutic option for the prevention of VAP.

**Iseganan for Cystic Fibrosis**

We have completed four Phase I studies in a total of 41 healthy human volunteers and 81 adult CF patients. We believe that the safety data support a Phase II study. Preclinical studies suggest that the inhaled dose administered in our multi-dose Phase I study is in a therapeutically relevant range. Based on this, we have designed a Phase II study in collaboration with the Cystic Fibrosis Foundation to evaluate the antimicrobial efficacy of inhaled iseganan in patients with CF.

A principal treatment for CF today is an inhaled antibiotic, tobramycin solution for inhalation, known as TOBI®. This drug had annual sales of approximately $170 million worldwide in 2003. Because of resistance to TOBI, it must be administered intermittently, in a schedule that calls for one-month breaks following each month of therapy. During the six months of the year in which patients do not use TOBI, microbes re-accumulate in the patients lungs, and gradually their condition deteriorates. We believe that iseganan may represent an attractive treatment option for CF. In particular, because of its low propensity to engender resistance, iseganan may be suitable for continuous, uninterrupted therapy.

**Iseganan for Other Indications**

We believe that iseganan s pharmacologic properties may make it an attractive therapeutic option for a variety of other indications, including ear infections, acne, folliculitis or other skin infections, and vaginitis. These conditions each are characterized by infections that are caused by a diverse range of microbes not normally susceptible to a single antimicrobial drug, are caused by multi-drug resistant pathogens in which therapeutic options may already be limited and occur in parts of the body that can be directly accessed by iseganan. We are evaluating

Table of Contents

microbiological efficacy, formulation requirements and market opportunities to enable selection of our next clinical development program.

**Our Management Team**

We have assembled a senior management team with prior experience in developing, registering and partnering novel pharmaceutical products. The members of this team have more than 50 years of combined experience in the biotechnology and pharmaceutical industries, and have been collectively responsible for the successful development and registration of seven new pharmaceutical products. We are also advised by leaders in the fields of pulmonary and critical care medicine, infectious disease and biostatistics. We believe that our collective experience will facilitate the successful development and commercialization of iseganan for multiple indications.

**Risks Related to Our Business**

We are at an early stage in the development of our company with a limited operating history and have had no revenues derived from operations. We are subject to numerous risks and obstacles, and we have highlighted the most important of them in Risk Factors, beginning on page 7. In particular, we have experienced significant operating losses since our inception, and we expect to continue to incur substantial additional operating losses. If we are unable to develop, receive approval for, or successfully commercialize our lead product candidate, iseganan, we may never be profitable and may have to cease operations.

**Corporate Information**

We were founded and incorporated in Delaware on January 19, 1994. Our principal offices are located at 2483 East Bayshore Road, Suite 100, Palo Alto, CA 94303, and our telephone number is (650)526-6800. Our website address is www.intrabiotics.com. The information found on our website is not part of this prospectus.

Unless the context requires otherwise, in this prospectus the terms IntraBiotics, we, us and our refer to IntraBiotics Pharmaceuticals, Inc. IntraBiotics and the IntraBiotics logo are trademarks of IntraBiotics Pharmaceuticals, Inc. This prospectus also includes trademarks, trade names and service marks of other companies. Use by us of other parties trademarks, trade names or service marks is not intended to and does not imply a relationship with, or endorsement or sponsorship of us by, these other parties and those names or marks are the property of their respective holders.

Table of Contents

**The Offering**

| | |
|---|---|
| Common stock offered by IntraBiotics | 3,000,000 shares |
| Common stock to be outstanding after this offering | 10,074,258 shares |
| Use of proceeds | For conducting clinical trials, research and development and general corporate purposes. See Use of Proceeds for more information regarding our planned use of the proceeds from this offering. |
| Nasdaq National Market symbol | IBPI |

The number of shares of common stock to be outstanding after this offering is based on the number of shares outstanding as of March 31, 2004 and assumes the conversion of all of the outstanding shares of our Series A preferred stock into 1,709,875 shares of common stock. This number excludes:

- 948,987 shares issuable upon exercise of outstanding options at a weighted average exercise price of approximately $7.41 per share;
- 1,262,235 shares issuable upon the exercise of outstanding warrants at a weighted average exercise price of approximately $5.48 per share; and
- 1,252,987 shares available for future grant under our stock plans.

*Unless otherwise indicated, all information in this prospectus assumes no exercise of the underwriters over-allotment option.*

Table of Contents

**Summary Financial Data**

The following table sets forth summary financial data for our company. You should read this information together with the financial statements and the notes to those statements appearing elsewhere in this prospectus and the information under Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations. Please see the financial statements and the notes to the statements appearing elsewhere in this prospectus for the determination of the number of shares used in computing the basic and diluted net loss per share.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2001 | 2002 | 2003 |
| | (In thousands, except per share data) | | |
| **Statement of Operations Data:** | | | |
| Operating expenses: | | | |
| Research and development | $ 38,034 | $ 23,053 | $ 7,727 |
| General and administrative | 9,202 | 8,617 | 5,782 |
| Restructuring and other charges | 21,956 | 6,118 | |
| Arbitration settlement | | (3,600) | |
| Impairment of acquired workforce | | 1,365 | |
| Total operating expenses | 69,192 | 35,553 | 13,509 |
| Operating loss | (69,192) | (35,553) | (13,509) |
| Interest income | 2,843 | 703 | 166 |
| Interest expense | (1,110) | (459) | |
| Other income, net | 93 | 856 | 31 |
| Net loss | (67,366) | (34,453) | (13,312) |
| Non-cash deemed dividend related to beneficial conversion feature of Series A preferred stock | | | (1,436) |
| Non-cash dividends on Series A preferred stock | | | (182) |
| Net loss applicable to common stockholders | $(67,366) | $(34,453) | $(14,930) |
| Basic and diluted net loss per share applicable to common stockholders | $ (27.47) | $ (11.25) | $ (4.01) |
| Shares used to compute basic and diluted net loss per share applicable to common stockholders | 2,453 | 3,064 | 3,720 |

The following table is a summary of our balance sheet as of December 31, 2003. The as adjusted column reflects our receipt of the estimated net proceeds from the sale of the shares of common stock offered in this offering at the public offering price of $13.00 per share after deducting the underwriting discount and estimated offering expenses payable by us. See Use of Proceeds and Capitalization.

| | As of December 31, 2003 | |
|---|---|---|
| | Actual | As Adjusted |
| | (In thousands) | |
| **Balance Sheet Data:** | | |

| | | |
|---|---|---|
| Cash, cash equivalents and short-term investments | $ 26,394 | $ 62,504 |
| Working capital | 25,424 | 61,534 |
| Total assets | 27,326 | 63,436 |
| Long-term obligations, less current portion | | |
| Accumulated deficit | (215,199) | (215,199) |
| Total stockholders equity | 25,628 | 61,738 |

Table of Contents

## RISK FACTORS

*An investment in our common stock is risky. You should carefully consider the following risks, as well as the other information contained in this prospectus. If any of the following risks actually occurs, it could harm our business. In that case, the trading price of our common stock could decline, and you might lose all or a part of your investment. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us or that we currently see as immaterial, may also harm our business. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements. Our future financial condition, results of operations and disclosures could be materially affected by the risks and uncertainties discussed below, or otherwise, and historic trends should not be used to anticipate results or trends in future periods.*

### Risks Related to Our Business

**If either of our two pivotal clinical trials of iseganan for the prevention of ventilator-associated pneumonia, or VAP, or any future clinical trials of iseganan for other indications are unsuccessful, we may have to cease operations.**

We currently have only one product candidate in late stage clinical trials. We previously completed three Phase III clinical trials of iseganan for the prevention of ulcerative oral mucositis, a complication that develops in certain cancer patients receiving chemotherapy or radiation therapy that results in painful ulcer-like sores in the mouth and throat. All three of these clinical trials failed to meet their primary end points, and we are no longer pursuing iseganan for the prevention of ulcerative oral mucositis. We are currently pursuing iseganan for the prevention of VAP. Enrollment in the first of two pivotal trials commenced in September 2003, and we expect to announce results of this first trial by the end of 2004. The failure of either of these two pivotal trials in meeting their primary end points, or of any other future clinical trials of iseganan for alternative indications, will negatively impact our future operating results and may force us to cease operations. In addition, even if the trials meet their primary end points, iseganan may not be approved, if, for instance, there are significantly more deaths in the treatment group than in the placebo group.

**If we fail to complete any clinical trial, or fail to obtain U.S. Food and Drug Administration, or FDA, approval for any product candidate that we develop, acquire or license, we may never achieve profitability and may have to cease operations.**

We do not have a drug approved for sale in the United States or any foreign market. We do not know whether we will be successful in developing iseganan for the prevention of VAP or other indications, or in developing, acquiring or licensing any other products and successfully obtaining FDA or foreign approvals for them. We must successfully complete clinical trials and demonstrate manufacturing capability before we can file with the FDA for approval to sell any product in the United States or with foreign regulatory authorities in order to sell in other countries. The FDA could require us to repeat or perform additional clinical trials as a result of its regulatory review. There is no guarantee that foreign regulatory authorities will approve our products on the same data required by the FDA, and, as a result, we may be required to perform additional clinical trials before being approved to sell in foreign markets. Delays in obtaining or failure to obtain regulatory approvals may:

- delay or prevent the successful commercialization of our drug candidate;
- diminish any competitive advantage we may have; and
- defer or decrease our receipt of revenues or royalties.

Table of Contents

The regulatory review and approval process is lengthy, expensive and uncertain. Extensive preclinical and clinical data and supporting information must be submitted to the FDA for each indication to establish safety and effectiveness in order to secure FDA approval. A number of new drugs for certain indications, iseganan for the prevention of oral mucositis included, have shown promising results in early clinical trials, but subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals. A number of companies have also suffered significant setbacks in advanced clinical trials, including issues related to the design or conduct of those trials. We have had to re-perform a Phase III clinical trial in the past, following a drug dispensing error by a contract vendor. We have limited experience in obtaining drug approvals. We cannot be certain when, if ever, we will receive these regulatory approvals. If we are unable to demonstrate the safety and efficacy of any drug candidate, we will be unable to obtain the required regulatory approvals, and we will be unable to commercialize a drug candidate and generate product revenue.

In addition to initial regulatory approval, any drug will be subject to extensive and rigorous ongoing domestic and foreign government regulation. Any approvals, once obtained, may be withdrawn if compliance with regulatory requirements is not maintained or safety problems are identified. Failure to comply with these requirements may subject us to stringent penalties.

**Difficulties and risks associated with conducting our clinical trials could cause delays in, or prevent us from, receiving approval or successfully commercializing our product, which would materially harm our business.**

Planned clinical trials may not begin on time or may need to be restructured after they have begun. Clinical trials can be delayed for a variety of reasons, including:

- competition in recruiting clinical investigators;
- negotiating acceptable clinical trial agreement terms with prospective trial sites;
- obtaining institutional review board approval to conduct a clinical trial at a prospective site;
- recruiting patients to participate in a clinical trial;
- management of data related to our clinical programs;
- the need to repeat clinical trials as a result of inconclusive results or poorly executed testing;
- the placement of a clinical hold on a study;
- the failure of third parties conducting and overseeing the operations of clinical trials to perform their contractual or regulatory obligations in a timely fashion;
- exposure of clinical trial patients to unexpected and unacceptable health risks or noncompliance with regulatory requirements, which may result in suspension of the trial; and
- inability to obtain prompt regulatory review and agreement on key design features of clinical studies.

In addition, there are a number of difficulties and risks associated with clinical trials. These difficulties and risks may result in the failure to receive regulatory approval to sell our product candidates or the inability to commercialize any of our product candidates. The possibility exists that:

- we may discover that a product candidate does not exhibit the expected therapeutic results in humans, causes harmful side effects or has other unexpected characteristics that delay or preclude regulatory approval or limit commercial use if approved;

Table of Contents

the results from early clinical trials may not be predictive of results that will be obtained in expanded, advanced clinical trials;

patients may drop out of our clinical trials;

our clinical trials may not yield a sufficient number of infected patients in the placebo group to provide statistically significant results;

the clinical procedures outlined in our clinical trial protocols may not be properly followed, which could produce inconclusive results or prematurely end such clinical trial;

our clinical trials may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials; and

the cost of our clinical trials may be greater than we currently anticipate.

**We expect to continue to incur operating losses for the foreseeable future and may never achieve profitability.**

We have never generated revenues from product sales and have incurred significant net losses in each year since inception. We incurred net losses of $67.4 million in 2001, $34.5 million in 2002 and $13.3 million in 2003. As of December 31, 2003, our accumulated deficit was approximately $215.2 million. We expect to continue to incur substantial additional losses for the foreseeable future, and we may never become profitable. To date, we have financed our operations primarily through the private sale of equity securities, funds received from a terminated collaboration agreement, the proceeds of equipment financing arrangements, and our initial public offering of common stock in March 2000. We are currently conducting a pivotal trial of iseganan for the prevention of VAP. We are also developing iseganan for cystic fibrosis, or CF, and may develop iseganan for other indications in the future or acquire or license other products.

We will receive revenues from product sales or royalties only if we complete clinical trials with respect to one or more products, receive regulatory approvals and successfully commercialize such products. We do not know whether we will be successful in developing iseganan for our currently planned prevention of VAP indication or other indications, or in acquiring or licensing other products.

**We must raise capital to continue our operations, and, if we fail to obtain the capital necessary to fund our operations, we will be unable to develop our drug candidates and may have to cease operations.**

We will need to raise additional funds to continue our operations, complete the FDA approval process of iseganan for the prevention of VAP if our trials are successful, commence commercialization if FDA approval is received, and pursue other indications. We do not know whether additional financing will be available when needed or on acceptable terms, if at all. If we are unable to raise additional financing when necessary, we may have to delay our product development efforts or any product acquisitions or be forced to cease operations. Our future liquidity and capital requirements will also depend on many other factors, including:

the timing, cost and progress of our prevention of VAP trials and any other clinical trials we may conduct;

the timing of, and the costs involved in, obtaining regulatory approvals for any product in the United States and other countries;

decisions with respect to strategic alternatives;

the success of our development and commercialization of our product candidates;

Table of Contents

the scope and results of our clinical trials;

advancement of other product candidates into clinical development;

potential acquisition or in-licensing of other products or technologies;

the costs of manufacturing activities;

the costs of commercialization activities, including product marketing, sales and distribution;

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims and other intellectual property-related costs, including any possible litigation costs;

the effect of competing technological and market developments; and

our ability to establish and maintain collaborative and other strategic arrangements.

Adequate financing may not be available on terms acceptable to us, if at all. We may continue to seek additional capital through public or private equity offerings, debt financings or collaborative arrangements and licensing agreements.

**If the contract research organizations assisting in our clinical trials fail to appropriately manage our clinical trials, the trials could be delayed or could fail, and our results of operations and financial condition would suffer.**

We rely on contract research organizations to assist us in managing and monitoring our clinical trials. We have entered into agreements with Amarex, LLC, Orion Clinical Services, Ltd, Advanced Clinical Trials, Inc. and Icon Laboratories, Inc., among others, to provide clinical research services. The investigators and contract research organizations are not our employees, and we cannot control, other than by contract, the amount of resources, including time, that they devote to our product candidates. However, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols that have been approved by regulatory agencies for such trials. We have previously experienced a drug dispensing error by one of our contract research organizations, which adversely affected the results of one of our clinical trials for iseganan in oral mucositis.

The FDA requires us to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting clinical trials to assure that data and reported results are credible and accurate and that the rights and confidentiality of trial participants are protected. The FDA may inspect some of our clinical investigational sites, our contract research organizations records and our facility and files to determine if clinical trials are conducted according to good clinical practices. If the FDA determines that a trial is not in compliance with good clinical practices, we may be required to repeat the clinical trial. If our contract research organizations fail to perform in accordance with our agreements with them, we may not complete our clinical programs on time or at all.

In connection with our reliance on our independent clinical investigators and contract research organizations, our clinical trials may be extended, delayed, suspended or terminated for a variety of reasons, including:

the failure of investigators and contract research organizations to comply with good clinical practice or to meet their contractual duties;

the failure of our independent investigators to devote sufficient resources to the development of our product candidates or to perform their responsibilities with sufficient expertise and care;

our need to replace these third parties for any reason, including for performance reasons or if these third parties go out of business; or

Table of Contents

problems in the quality or accuracy of the data they obtain due to the failure to collect, compile or analyze data appropriately, adhere to clinical protocols or regulatory requirements or for other reasons.

Extensions, delays, suspensions or terminations of our clinical trials as a result of the performance of our independent clinical investigators and contract research organizations will delay, and make more costly, regulatory approval for any product candidates that we may develop. Any change in a contract research organization during an ongoing clinical trial could seriously delay that trial and potentially compromise the results of the trial.

**We will be dependent on third-party contract manufacturers for the future production of iseganan and for producing information required to register iseganan with the FDA, if our trials are successful.**

We have relied on a single contract manufacturer to manufacture the iseganan bulk drug substance for our pivotal clinical trials. We currently maintain a sufficient inventory of iseganan to complete planned clinical trials. However, if no alternate sources of supply are developed, we will depend on this manufacturer to produce iseganan for FDA registration and to produce iseganan for future commercial use if our pivotal trials are successful. In 2003, we received a manufactured lot from this contract manufacturer that we have not yet been satisfied was manufactured in accordance with a validation plan or that related documentation is adequate. Although this lot is not expected to be required for our pivotal clinical trials, it is expected to be used to validate the manufacturing process. If the manufacturer is unable to validate the manufacturing process, produce iseganan and the required information for FDA registration, or produce iseganan for future commercial use on a timely basis and in accordance with set specifications, or we experience similar issues to those experienced on this order, we may not have sufficient quantities of iseganan and sufficient information to meet registration requirements or sufficient quantities of iseganan for future commercial use. We do not currently have any supply agreement with this or any other contract manufacturer to provide iseganan bulk drug substance.

We also rely on a single third-party supplier to produce iseganan formulated drug product for use in our clinical trials. We do not currently have any supply agreement with this third-party supplier. If this supplier is unable or fails to produce the required quantities of iseganan formulated drug product for clinical use or commercial sale on a timely basis, at commercially reasonable prices, and with sufficient purity, we will not have sufficient quantities to complete all of our planned clinical trials, or to meet commercial demand.

**The Fast Track designation for development of iseganan may not actually lead to a faster development or regulatory review or approval process and our Special Protocol Assessment approved by the FDA is subject to change.**

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. Marketing applications filed by sponsors of products in Fast Track development may qualify for expedited review under policies or procedures offered by the FDA, but the Fast Track designation does not assure such qualification. We have been granted Fast Track designation from the FDA for iseganan for the prevention of VAP. Iseganan s Fast Track designation may be withdrawn by the FDA if the FDA believes that it is no longer supported by data from our clinical development program. In addition, iseganan s Fast Track designation does not guarantee that we will be able to take advantage of the expedited review procedures and does not increase the likelihood that the FDA will ultimately approve iseganan.

Table of Contents

In September 2003, we formalized an agreed-upon pivotal clinical trial design for iseganan for the prevention of VAP with the FDA through a Special Protocol Assessment, or SPA. The SPA requires us to conduct a second identical pivotal trial. The SPA is subject to change based upon data produced from our pivotal trials, data produced from clinical trials conducted by third parties and other events outside of our control. The SPA does not guarantee that the requirements for approval of our product will not change and does not necessarily increase the likelihood that the FDA will ultimately approve our product for the prevention of VAP.

**Development and commercialization of competitive products or new technologies could reduce or prevent sales of any future products that we develop, acquire or license, which could materially harm our business.**

We may be unable to compete successfully if other companies develop and commercialize competitive products that are less expensive, more effective, have fewer side effects or are easier to administer than drug candidates that we develop, acquire or license. If we are unable to compete successfully with any future drug candidate, physicians may not prescribe and patients may not buy our drug.

We are aware of a clinical trial in Europe testing the utility of chlorhexidine, an antiseptic approved for gingivitis, also known as Peridex, for use in the prevention of VAP. We are also aware of one medical device product on the market and other medical device products in development for the prevention of VAP. In addition, it is possible that antimicrobial or antiseptic products already approved by the FDA for other indications may be used off-label by physicians for the prevention of VAP. Pharmaceutical companies, biotechnology companies and medical device companies may also develop products in the future that compete with iseganan for the prevention of VAP.

There are two approved pharmaceutical products used for the treatment of CF. TOBI is sold by Chiron Corporation and generated approximately $170 million in sales in 2003. Colistin is sold by several manufacturers, in greater volume in Europe than in the United States. We are aware of two products that are in clinical development for the treatment of CF. Aztreonam is a product already approved for intravenous use in other bacterial infections and is in Phase II testing for the treatment of CF by Corus Pharma, Inc. Doripenem is an experimental agent in Phase I studies sponsored by Peninsula Pharmaceuticals, Inc. Both of these products are active against pseudomonas aeruginosa, the major pathogen in CF.

Many of these companies have substantially greater experience, financial resources and larger research and development staffs than we do. In addition, many of these companies, either alone or together with their collaborative partners, have significantly greater experience than we do in developing products, obtaining regulatory approvals, manufacturing and marketing. We also compete with these organizations and other companies for in-licensing opportunities for future drug candidates, and for attracting scientific and management personnel.

**We currently have no sales and marketing organization and, therefore, must develop a sales and marketing organization or enter into distribution arrangements and marketing alliances, which could require us to give up rights to our product candidates.**

Developing the sales force to market and sell products is a difficult, expensive and time-consuming process. We have no experience developing a sales organization and may be unsuccessful if we attempt to do so. If we are unable to develop an internal sales and marketing operation, we may not be able to increase market awareness and sell our product. We may also rely on third-party distributors to distribute our products or enter into marketing alliances to sell our products. We may not be successful in entering into distribution arrangements and marketing alliances with third parties. Our failure to successfully develop a sales organization or

Table of Contents

to enter into these arrangements on favorable terms could delay or impair our ability to commercialize our product candidates and could increase our costs of commercialization. Dependence on distribution arrangements and marketing alliances to commercialize our product candidates will subject us to a number of risks, including:

- we may be required to relinquish important rights to our products or product candidates;
- we may not be able to control the amount and timing of resources that our distributors or collaborators may devote to the commercialization of our product candidates;
- our distributors or collaborators may experience financial difficulties; and
- business combinations or significant changes in a collaborator s business strategy may also adversely affect a collaborator s willingness or ability to complete its obligations under any arrangement.

**If physicians, patients, health care payors and the medical community do not accept our products, we may be unable to generate significant revenues, if any, and we may have to cease operations.**

Any drug candidate that we develop, acquire or license may not gain market acceptance among physicians, patients, health care payors and the medical community. If any drug candidate fails to achieve market acceptance, we may be unable to successfully market and sell the product, which would limit our ability to generate revenue. The degree of market acceptance of any drug candidate depends on a number of factors, including:

- the belief of the medical community that VAP is a health issue that needs to be addressed;
- demonstration of clinical efficacy and safety;
- cost-effectiveness, in particular with iseganan s anticipated application for the prevention of VAP;
- convenience and ease of administration;
- potential advantage over alternative treatment methods;
- sales, marketing and distribution support; and
- the inability to administer our product in hospitals due to such third parties internal policies and procedures that may deter the use and application of our product to their patients due to concerns of resistance or otherwise.

Physicians will not prescribe our products until such time as clinical data or other factors demonstrate the safety and efficacy of our drugs as compared to other treatments. In practice, competitors may be more effective in marketing their drugs. Even if the clinical safety and efficacy of our product is established, physicians may elect not to prescribe its use. For example, physicians may be reluctant to use our product widely because of concern about developing microbial strains that are resistant to our drugs, or because of the cost of our drug.

**The failure to recruit and retain our chief executive officer and other employees may delay our ability to execute our business plan and our results of operations could suffer.**

We are highly dependent on our management and technical staff. Competition for personnel is intense. If we lose the services of any of our senior management or technical staff, we may be unable to successfully complete our planned clinical trials. In particular, the loss of the services of Henry J. Fuchs, our President and Chief Executive Officer, could significantly impede our research and development efforts, our relations with potential collaborators and completion of our planned clinical trials. We do not maintain key person life insurance and do not have an

Table of Contents

employment agreement with Dr. Fuchs or our other members of our management and technical staff. In October 2002, we completed a restructuring that included a reduction in force of approximately 70% of our workforce. As of April 12, 2004, we had 12 full-time employees. In order to pursue any future product development, marketing and commercialization, we will need to hire additional qualified scientific personnel to perform research and development and personnel with expertise in clinical testing, government regulation, manufacturing, marketing and finance. We may not be able to attract and retain personnel on acceptable terms given the competition for such personnel among biotechnology, pharmaceutical and other companies.

We rely on consultants to assist us in formulating our research and clinical development strategy. These consultants may have commitments to, or relationships with, other entities that may limit their availability to us. The loss of the services of these personnel may delay our research and development efforts.

**The departure of Henry J. Fuchs, our President and Chief Executive Officer, could require us to refund money to holders of our Series A preferred stock.**

If we fail to use our reasonable best efforts to retain the services of Henry J. Fuchs, our President and Chief Executive Officer, until the earlier to occur of the unblinding and public announcement of the results of our first pivotal clinical trial for VAP or May 1, 2005, then we must pay to each holder of our Series A preferred stock a one-time payment equal to 15.0% of the applicable holder s aggregate Series A preferred stock purchase price. Based on the number of shares of Series A preferred stock outstanding as of March 31, 2004, our potential exposure for this provision is $487,500. This penalty will not apply if Dr. Fuchs departure is the result of his death, disability or family emergency or if we retain services of an executive officer to replace Dr. Fuchs within 60 days of Dr. Fuchs departure, for reasons other than his death, disability or family emergency, and such replacement is approved by the Board, including the member(s) of our Board designated by Tang Capital Partners.

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

We are a small company with 12 employees as of April 12, 2004. To continue our clinical trials and commercialize our product candidates, we will need to expand our employee base for managerial, operational, financial and other resources. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

manage our development efforts effectively;

manage our clinical trials effectively;

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

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

hire and train additional qualified personnel.

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

Table of Contents

**If we are unable to adequately protect our intellectual property, we may be unable to sell our products or to compete effectively.**

We rely on a combination of patents, trade secrets and contractual provisions to protect our intellectual property. If we fail to adequately protect our intellectual property, other companies or individuals may prevent us from selling our products or may develop competing products based on our technology. Our success depends in part on our ability to:

obtain patents;

protect trade secrets;

operate without infringing upon the proprietary rights of others; and

prevent others from infringing on our proprietary rights.

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets.

We expect to protect our proprietary position by filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. For example, we own two issued U.S. patents and one pending patent application in the United States and several foreign jurisdictions that contain claims covering iseganan. However, the patent position of biopharmaceutical companies involves complex legal and factual questions. We cannot predict the enforceability or scope of any issued patents or those that may issue in the future. Patents, if issued, may be challenged, invalidated or circumvented. In addition, some of our patents have only been filed in a limited number of jurisdictions which may limit our ability to protect our rights in other jurisdictions. We currently do not have any issued patents in Europe or Japan covering iseganan, and we do not know whether any of our pending patent applications will result in the issuance of patents in these jurisdictions. Consequently, if any patents that we own or license from third parties do not provide sufficient protection, our competitive position would be weakened. Furthermore, others may independently develop similar technologies or duplicate any technology that we have developed.

In addition to patents, we rely on trade secrets and proprietary know-how. Our contract manufacturers perform the manufacturing processes covered by these trade secrets. Accordingly, our contract manufacturers and we must maintain confidentiality. We have confidentiality and proprietary information agreements with our contract manufacturers and with our employees. These agreements may not provide meaningful protection or adequate remedies for our technology in the event of unauthorized use or disclosure of confidential and proprietary information.

**We may be subject to intellectual property litigation that could be costly and time-consuming and would affect our results of operations and financial condition.**

The biotechnology and pharmaceutical industries have been characterized by extensive litigation regarding patents and other intellectual property rights. Although we are not currently a party to any lawsuits, third parties may assert infringement or other intellectual property claims against us. We may have to pay substantial damages, including treble damages for past infringement, if it is ultimately determined that our products infringe a third party s proprietary rights. The defense and prosecution of intellectual property suits, U.S. Patent and Trademark Office interference proceedings and related legal and administrative proceedings in the United States and internationally are costly and time-consuming to pursue and their outcome is uncertain. If we become involved in any of these proceedings, we will incur substantial expense, and the efforts of our technical and management personnel will be significantly diverted. An

Table of Contents

adverse determination may result in the invalidation of our patents, subject us to significant liabilities or require us to seek licenses that may not be available from third parties on satisfactory terms, or at all. Our stock price could decline because of litigation or interference proceedings initiated or threatened against us.

**Because there is a risk of product liability associated with our products, we face potential difficulties in obtaining insurance.**

Our business exposes us to potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceutical products, and we may not be able to avoid significant product liability exposure. While we have insurance covering product use in our clinical trials, it is possible that we will not be able to maintain such insurance on acceptable terms or that any insurance obtained will provide adequate coverage against potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or limit the commercialization of any products we develop. A successful product liability claim in excess of our insurance coverage could exceed our net worth.

Currently, we are not aware of any anticipated product liability claims with respect to our product candidates. In the future, an individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

inability to conduct our clinical trials;

withdrawal of clinical trial participants;

costs of related litigation;

substantial monetary awards to patients;

loss of revenues;

product recalls;

injury to our reputation;

decreased demand for our product candidates; and

the inability to commercialize our product candidates.

**Directors, executive officers, principal stockholders and affiliated entities beneficially own approximately 52% of our capital stock and may be able to exert control over our activities, and the results of our operations and financial condition may suffer.**

As of March 31, 2004, our directors, executive officers, principal stockholders and affiliated entities beneficially own, in the aggregate, approximately 52% of our outstanding common stock and Series A preferred stock on an as-converted basis. These stockholders, if acting together, will be able to control the outcome of any matter requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions.

**The holders of our Series A preferred stock have voting and other rights that they could exercise against your best interests.**

The holders of our Series A preferred stock have rights to designate two members of our Board and to vote as a separate class on certain significant corporate transactions. The holders of Series A preferred stock are entitled to receive cumulative annual dividends of 8% of the

**Table of Contents**

original purchase price of $10,000 per share, payable in common stock. In addition, upon our liquidation or dissolution (including a merger or acquisition), the holders of our Series A preferred stock are entitled to receive a liquidation preference in an amount equal to the greater of (i) $10,000 per share of Series A preferred stock, or approximately $3.25 million based on the 325 shares of Series A preferred stock currently outstanding, plus any declared but unpaid dividends or (ii) the amount that would have been paid had each such share of Series A preferred stock been converted to common stock. The holders of Series A preferred stock also have the right of first refusal to purchase their pro rata portion of any equity securities we propose to offer to any person. Such right of first refusal is subject to certain customary exclusions, including for shares issued pursuant to any options or other stock awards granted to employees, directors or consultants of IntraBiotics, equipment leasing arrangements, debt financings, strategic financings and public offerings that have been approved by the Board. The holders of Series A preferred stock may exercise these rights to the detriment of our common stockholders.

The holders of our Series A preferred stock also have the right at any time to request that we register for resale the shares of our common stock that they acquire upon conversion of their Series A preferred stock or upon exercise of their warrants to purchase our common stock, subject to certain limitations. A registration statement has been filed with the Securities and Exchange Commission and is currently effective for the resale of the shares of common stock issuable upon conversion of our Series A preferred stock and upon the exercise of those warrants. In addition, the holders of our Series A preferred stock may convert their Series A preferred stock into common stock and sell those shares of the common stock acquired upon such conversion in the public market in reliance upon Rule 144, subject in some cases to volume and other limitations. Future sales in the public market of such common stock, or the perception that such sales might occur, could adversely affect the prevailing market price of our common stock and could make it more difficult for us to raise funds through a public offering or private placement of our equity securities.

**Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us more difficult.**

Provisions of our certificate of incorporation and bylaws could make it more difficult for a third party to acquire us, even if doing so would be beneficial to our stockholders. These provisions:

provide for a classified board of directors of which approximately one-third of the directors will be elected each year;

allow the authorized number of directors to be changed only by resolution of the Board;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;

establish advance notice requirements for nominations to the Board or for proposals that can be acted on at stockholder meetings;

require the approval from the holders of Series A preferred stock, prior to May 1, 2005, for any merger into or consolidation with any other corporation (other than a wholly-owned subsidiary corporation or for the purposes of changing our domicile) or the completion of any transaction or series of related transactions in which fifty percent or more of our voting power is transferred or the sale, lease or other disposition of all or substantially all of our assets;

Table of Contents

authorize our Board to issue blank check preferred stock to increase the amount of outstanding shares; and

limit who may call stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit large stockholders from consummating a merger with, or acquisition of us. These provisions may prevent a merger or acquisition that would be attractive to stockholders and could limit the price that investors would be willing to pay in the future for our common stock.

**The change in our stock price over time may significantly impact our results of operations through certain stock compensation charges that depend upon our closing stock price at the end of each quarter.**

Market prices for securities of biotechnology companies are general highly volatile and our stock may be subject to such volatility. Our non-cash variable stock compensation expense in relation to 308,835 stock options that were cancelled and re-granted in a one-for-one exchange and 12,500 options that were re-granted in connection with the cancellation of 54,166 unexercised stock options in February 2003 is dependent upon the price of our common stock at each quarter end. In 2003, we recorded non-cash stock compensation expense of approximately $1.0 million in relation to these options. Non-cash stock compensation expense will be incurred through the five-year term of the options, unless previously forfeited or exercised. Future changes in our stock price may therefore have a significant impact on our future results of operations as a result of this dependency.

**Our stock price has been, and will be volatile, and the value of your investment may decline.**

During the three-month period ended March 31, 2004, our closing stock prices ranged from a low of $13.46 to a high of $18.00, and in 2003 ranged from a low of $1.71 to a high of $16.95. The following factors, in addition to the other risk factors described in this section, may have a significant impact on the market price of our common stock:

announcements regarding strategic alternatives, including a merger or sale of the company or acquisition or license of products or product candidates;

publicity regarding actual or perceived adverse events in our clinical trial or relating to products under development by us or our competitors;

the regulatory status of our product candidates;

failure of any of our product candidates, if approved, to achieve commercial success;

our ability to manufacture any products to commercial standards;

announcements of technological innovations or new commercial products by our competitors or us;

developments concerning proprietary rights;

regulatory developments in the United States or foreign countries;

litigation;

significant short-selling in our common stock;

economic and other external factors; and

period-to-period fluctuations in our financial results and changes in analysts recommendations.

Table of Contents

## Risks Related to this Offering

**We have substantial discretion as to how to use the proceeds from this offering.**

Our management has broad discretion as to how to spend the proceeds from this offering and may spend these proceeds in ways with which our stockholders may not agree. We cannot predict that investment of the proceeds will yield a favorable or any return. See Use of Proceeds.

**Future sales of shares could affect our stock price.**

If our stockholders sell substantial amounts of our common stock, including shares issued upon the exercise of outstanding options and warrants, in the public market following this offering, the market price of our common stock could fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. Upon completion of this offering, we will have outstanding 10,074,258 shares of common stock, based upon 7,074,258 shares outstanding as of March 31, 2004, assuming no exercise of the underwriters over-allotment option, no exercise of outstanding options or warrants after March 31, 2004, and assuming the conversion of 325 shares of Series A preferred stock, which are convertible into 1,709,875 shares of our common stock. All of the holders of Series A preferred stock may sell shares of the common stock acquired upon such conversion in the public market in reliance upon Rule 144, subject in some cases to volume and other limitations, or under a currently effective registration statement without such restrictions upon conversion of the shares of Series A preferred stock into common stock. The 3,000,000 shares sold in this offering will be freely tradable. Of the 7,074,258 shares of outstanding common stock and common stock issuable upon conversion of the Series A preferred stock held by existing stockholders, 3,194,815 will be eligible for sale in the public market 90 days after the date of this prospectus upon the expiration of lock-up agreements, subject in some cases to restrictions imposed on our affiliates under Rule 144. See Shares Eligible for Future Sale for further information concerning potential sales of our shares after this offering.

**Purchasers in this offering will incur immediate and substantial dilution.**

We expect that the public offering price of our common stock will be substantially higher than the book value per share of the outstanding common stock. As a result, based on our capitalization as of December 31, 2003, you will incur immediate and substantial dilution of $5.56 per share in the net tangible book value per share of common stock from the assumed public offering price. In the past, we issued options and warrants to acquire common stock at prices significantly below the public offering price. The exercise of options and warrants currently outstanding could cause additional, substantial dilution to you. See Dilution for more detailed information regarding the potential dilution you may incur.

Table of Contents

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some statements contained in this prospectus are forward-looking with respect to our operations, economic performance and financial condition. Statements that are forward-looking in nature should be read with caution because they involve risks and uncertainties, including, for example, in specific and general discussions about:

our strategy;

sufficiency of our cash resources;

revenues from collaborations;

product development;

the development of the markets and demand for our products;

our product development plans and anticipated activities designed to pursue these plans, including corporate partnering arrangements;

our research and development and other expenses;

our ability to scale-up manufacturing capabilities and facilities;

the protection afforded to us by intellectual property law;

future levels of operating expenses associated with our business;

our operational and legal risks;

our future revenues and results of operations;

our future exposure to market risks;

our future capital needs and our ability to fund those needs; and

our plans, objectives, expectations and intentions and any other statements that are not historical facts.

Various terms and expressions similar to them are intended to identify these cautionary statements. These terms include: anticipates, believes, continues, could, estimates, expects, intends, may, might, plans, seeks, should, future, would, envision, results may differ materially from those expressed or implied in those statements. Unless required by law, we undertake no obligation to publicly update or revise any forward-looking statements to reflect new information or future events or otherwise. Factors that could cause these differences include, but are not limited to, those discussed under Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations.

## ABOUT THIS PROSPECTUS

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information that is different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

Table of Contents

## USE OF PROCEEDS

Our net proceeds from the sale of the 3,000,000 shares of common stock we are offering will be approximately $36.1 million, or $41.6 million if the underwriters over-allotment option is exercised in full, based on the public offering price of $13.00 per share, after deducting the underwriting discount and commissions and the estimated offering expenses payable by us.

We currently expect to use the net proceeds of this offering for conducting clinical trials, research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although no portion of the net proceeds has been allocated for any specific acquisition or for acquisitions generally. Pending these uses, the net proceeds will be invested in short-term, investment grade, interest-bearing instruments.

## DIVIDEND POLICY

We have never paid dividends on our common stock. We currently intend to retain any future earnings to support the development of our business. The holders of our Series A preferred stock are entitled to receive cumulative dividends at the rate of 8% per annum of the original purchase price of $10,000 per share of Series A preferred stock, prior to and in preference to any declaration or payment of a dividend to the holders of common stock. The dividends are payable quarterly in shares of common stock, and the number of shares payable are determined based on the average closing sale price of the common stock on the Nasdaq National Market or other market on which our common stock is traded for each of the five trading days immediately preceding the applicable dividend payment date. Until accrued and unpaid dividends on the Series A preferred stock are paid and set apart, no dividends or other distributions in respect of any other shares of our capital stock shall be declared. Therefore, we do not currently anticipate paying any cash dividends in the foreseeable future.

Table of Contents

## PRICE RANGE OF COMMON STOCK

Our common stock began trading on The Nasdaq National Market on March 28, 2000, under the symbol IBPI. Prior to that time, there had been no public market for our common stock. We effected a 1:12 reverse stock split on April 10, 2003. All amounts herein have been retroactively adjusted to reflect this stock split. The table below sets forth the high and low sales prices for our common stock for the periods indicated, as reported by the Nasdaq National Market:

| | Price range of common stock | |
|---|---|---|
| | **High** | **Low** |
| **Fiscal 2002** | | |
| First Quarter | $55.32 | $27.84 |
| Second Quarter | 59.52 | 11.04 |
| Third Quarter | 28.20 | 3.96 |
| Fourth Quarter | 7.68 | 3.00 |
| **Fiscal 2003** | | |
| First Quarter | $ 4.08 | $ 1.56 |
| Second Quarter | 6.48 | 1.54 |
| Third Quarter | 15.60 | 3.08 |
| Fourth Quarter | 17.50 | 10.50 |
| **Fiscal 2004** | | |
| First Quarter | $19.25 | $13.25 |
| Second Quarter (through May 4, 2004) | 18.00 | 11.88 |

As of March 31, 2004, there were 129 holders of record of our common stock. Because many of these shares are held by brokers and other institutions on behalf of our stockholders, we are unable to estimate the total number of stockholders represented by these record holders. On May 4, 2004, the closing sale price for our common stock was $14.30.

Table of Contents

## CAPITALIZATION

The following table sets forth our capitalization as of December 31, 2003:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 3,000,000 shares of our common stock at the public offering price of $13.00 per share in this offering, after deducting the underwriting discounts and commissions and our estimated offering expenses.

You should read this table with Management s Discussion and Analysis of Financial Condition and Results of Operations and our Financial Statements and Notes to the Financial Statements appearing elsewhere in this prospectus.

| | As of December 31, 2003 | |
|---|---|---|
| | Actual | As Adjusted |
| | (Dollars in thousands) | |
| Stockholders equity: | | |
| Convertible preferred stock, $0.001 par value: 5,000,000 shares authorized, actual and as adjusted; 325 shares issued and outstanding, actual and as adjusted | $ 1,771 | $ 1,771 |
| Common stock, $0.001 par value: 70,000,000 shares authorized, actual and as adjusted; 5,298,206 shares issued and outstanding, actual, and 8,298,206 shares issued and outstanding, as adjusted | 5 | 8 |
| Additional paid-in capital | 239,237 | 275,344 |
| Deferred stock compensation | (188) | (188) |
| Accumulated other comprehensive income | 2 | 2 |
| Accumulated deficit | (215,199) | (215,199) |
| Total stockholders equity | 25,628 | 61,738 |
| Total capitalization | $ 25,628 | $ 61,738 |

The number of shares of common stock outstanding excludes the following as of December 31, 2003:

- 822,981 shares issuable upon exercise of outstanding options at a weighted average exercise price of approximately $3.73 per share;
- 1,272,235 shares issuable upon the exercise of outstanding warrants at a weighted average exercise price of approximately $5.53 per share;
- 240,032 shares available for future grant under our stock plans; and
- 1,709,875 shares to be issued upon conversion of all of the outstanding shares of our Series A preferred stock.

Table of Contents

## DILUTION

Our net tangible book value at December 31, 2003 was approximately $25.6 million, or $4.84 per share. Net tangible book value per share represents total net tangible assets less liabilities, divided by common shares outstanding.

After giving effect to our sale of shares of common stock in this offering at the public offering price of $13.00 per share, and after deducting the estimated underwriting discount and offering expenses payable by us, our pro forma net tangible book value as of December 31, 2003 would have been $61.7 million, or $7.44 per share. This represents an immediate increase in pro forma net tangible book value of $2.60 per share to existing stockholders and an immediate dilution of $5.56 per share to new investors purchasing shares of common stock in this offering. Dilution in pro forma net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of our common stock in this offering and the pro forma net tangible book value per share of our common stock immediately following this offering. The following table illustrates this per share dilution:

| | | |
|---|---|---|
| Price to public | | $13.00 |
| Net tangible book value per share at December 31, 2003 | $4.84 | |
| Increase per share attributable to new investors | 2.60 | |
| Pro forma net tangible book value per share after the offering | | 7.44 |
| Dilution per share to new investors | | $ 5.56 |

The number of shares of common stock used in the calculations above excludes the following as of December 31, 2003:

822,981 shares issuable upon exercise of outstanding options at a weighted average exercise price of approximately $3.73 per share;

1,272,235 shares issuable upon the exercise of outstanding warrants at a weighted average exercise price of approximately $5.53 per share;

240,032 shares available for future grant under our stock plans; and

1,709,875 shares to be issued upon conversion of all of the outstanding shares of our Series A preferred stock.

Table of Contents

## SELECTED FINANCIAL DATA

The selected financial data set forth below is derived from our financial statements. The statement of operations data for the years ended December 31, 1999 and 2000 and the balance sheet data as of December 31, 1999, 2000 and 2001 are derived from our audited financial statements not included in this prospectus. The statement of operations data for the years ended December 31, 2001, 2002 and 2003, and the balance sheet data as of December 31, 2002 and 2003 are derived from audited financial statements included in this prospectus. See Note 2 of Notes to Financial Statements for a detailed explanation of the determination of the shares used to compute basic and diluted net loss per share applicable to common stockholders. Our historical results are not necessarily indicative of results to be expected for future periods. You should read the following selected financial data along with our Financial Statements and related Notes and Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this prospectus.

| | Year Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 1999 | 2000 | 2001 | 2002 | 2003 |
| | (In thousands, except per share data) | | | | |
| **Statement of Operations Data:** | | | | | |
| Contract revenues | $ 7,863 | $ | $ | $ | $ |
| Operating expenses: | | | | | |
| Research and development | 26,102 | 39,152 | 38,034 | 23,053 | 7,727 |
| General and administrative | 6,082 | 11,560 | 9,202 | 8,617 | 5,782 |
| Restructuring and other charges | | | 21,956 | 6,118 | |
| Arbitration settlement | | | | (3,600) | |
| Impairment of acquired workforce | | | | 1,365 | |
| Total operating expenses | 32,184 | 50,172 | 69,192 | 35,553 | 13,509 |
| Operating loss | (24,321) | (50,712) | (69,192) | (35,553) | (13,509) |
| Interest income | 1,372 | 5,699 | 2,843 | 703 | 166 |
| Interest expense | (166) | (563) | (1,110) | (459) | |
| Other income, net | | | 93 | 856 | 31 |
| Net loss | (23,115) | (45,576) | (67,366) | (34,453) | (13,312) |
| Non-cash deemed dividend related to beneficial conversion feature of Series A preferred stock | | | | | (1,436) |
| Non-cash dividends on Series A preferred stock | | | | | (182) |
| Net loss applicable to common stockholders | $(23,115) | $(45,576) | $(67,366) | $(34,453) | $(14,930) |
| Basic and diluted net loss per share applicable to common stockholders | $(259.48) | $ (24.29) | $ (27.47) | $ (11.25) | $ (4.01) |
| Shares used to compute basic and diluted net loss per share applicable to common stockholders | 89 | 1,876 | 2,453 | 3,064 | 3,720 |

| | As of December 31, |
|---|---|

| | 1999 | 2000 | 2001 | 2002 | 2003 |
|---|---|---|---|---|---|
| | | | (In thousands) | | |
| **Balance Sheet Data:** | | | | | |
| Cash, cash equivalents, restricted cash and short-term investments | $ 31,429 | $ 86,065 | $ 35,470 | $ 13,315 | $ 26,644 |
| Working capital | 25,743 | 86,142 | 29,629 | 15,191 | 25,424 |
| Total assets | 35,958 | 108,288 | 42,465 | 16,226 | 27,326 |
| Long-term obligations, less current portion | 1,725 | 8,309 | 5,000 | | |
| Accumulated deficit | (52,874) | (98,450) | (165,816) | (200,269) | (215,199) |
| Total stockholders equity | 27,914 | 89,955 | 26,212 | 15,480 | 25,628 |

Table of Contents

## MANAGEMENT S DISCUSSION AND ANALYSIS

## OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and related notes appearing elsewhere in this prospectus. This discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. The 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 set forth under Risk Factors. All forward-looking statements included in this document are based on information available to us on the date of this document and we assume no obligation to update any forward-looking statements contained in this prospectus.*

**Overview**

We are developing novel antimicrobial drugs derived from protegrins, a class of mammalian peptides that is part of the body s natural defense against invading microbes, including bacteria, fungi and viruses. Our product candidate, iseganan, is a synthetic protegrin analog that has been selected for its broad spectrum microbe-killing activity and its low propensity to engender resistance. Iseganan is currently in clinical development for two indications: the prevention of ventilator-associated pneumonia, or VAP, and the treatment of lung infections associated with cystic fibrosis, or CF. Additionally, we are evaluating the use of iseganan in other types of infection where we believe that its properties may render it more effective than current therapies.

Our research and development expenses are expected to at least double in 2004 as compared to 2003, primarily as a result of the costs associated with our first pivotal trial for the prevention of VAP. If this trial is successful, a second pivotal trial will be required to support registration of iseganan.

A trial s completion date and completion costs are difficult to predict, and delays may be caused by many factors, including: slower than expected rate of patient enrollment; inability to adequately obtain data about patients after their treatment in our clinical trials; additional regulatory requests; inability to manufacture sufficient quantities of materials for clinical trials or validation; the failure by contract research organizations to appropriately manage clinical trials; or unforeseen safety issues. As a result, our research and development expenses may fluctuate significantly, and past trends are not indicative of future spending.

Our cash, cash equivalents, restricted cash and short-term investments totaled $26.6 million as of December 31, 2003, including the proceeds of two private placements during 2003. In May 2003, we completed a preferred stock placement resulting in net cash proceeds of $3.2 million, and in October 2003 we completed a common stock placement resulting in net cash proceeds of $18.5 million. The primary purpose of the financings was to provide additional funding for the two pivotal trials of iseganan for the prevention of VAP, as well as for other general corporate purposes and working capital.

We will need to raise additional funds to continue our operations, complete the FDA approval process of iseganan for the prevention of VAP if our trials are successful, commence commercialization if FDA approval is received, and pursue other indications. We cannot be certain that the results of either of the two pivotal trials for the prevention of VAP or trials for other indications will be successful, and product revenues may only be generated if we receive the required regulatory approvals and can successfully commercialize a product.

As of December 31, 2003, we had received and accepted over eight kilograms of finished iseganan drug substance, which was booked to research and development expense in 2002 in accordance with our standard accounting practices. The quantity is sufficient to complete our planned clinical trials, but further quantities will be required to validate the manufacturing process, and for commercial use if we successfully obtain FDA approval for any indication.

Table of Contents

In 2003, we wrote off $2.4 million of prepaid iseganan drug substance to research and development expense, relating to an order of seven kilograms of drug substance that was expected to be delivered in 2003, but that we have not yet been satisfied was manufactured in accordance with a validation plan or with adequate documentation. We are currently discussing this matter with our contract manufacturer, and the write-off was recorded due to significant uncertainty over the timing and outcome of these discussions.

In 2003, we recorded non-cash stock compensation expense of approximately $1.0 million for 308,835 unexercised stock options that were cancelled and re-granted in a one-for-one exchange and 12,500 options that were re-granted in connection with the cancellation of 54,166 unexercised stock options in February 2003. The re-granted options have an exercise price equal to the closing price of our common stock on the Nasdaq National Market on February 5, 2003, or $2.76 per share. The options generally vest over a four-year period and will expire in February 2008 if not previously exercised. Variable accounting is being applied to the re-granted options throughout their term. The related compensation expense depends on both the cumulative vesting of outstanding options and the price of our common stock at each quarter end, and therefore may have a significant impact on our future results of operations.

On April 3, 2003, our stockholders authorized a 1-for-12 reverse stock split of all outstanding shares of our common stock, which was effected on April 10, 2003. All share and per share amounts have been retroactively adjusted to reflect the stock split for all periods presented.

We intend that the following discussion of our financial condition and results of operations will provide information to assist in the understanding of our financial statements, the changes in certain key items in those financial statements from year to year, and the primary factors that accounted for those changes, as well as how certain accounting principles, policies and estimates affect our financial statements.

**Critical Accounting Policies and Estimates**

Our discussion and analysis of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses, and related disclosures. On an ongoing basis, we evaluate these estimates, including those related to clinical trial accruals and stock-based compensation. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could therefore differ materially from those estimates under different assumptions or conditions.

An accounting policy is deemed to be critical if it requires an accounting estimate to be made based on assumptions about matters that are highly uncertain at the time the estimate is made, and if different estimates that reasonably could have been used, or changes in the accounting estimates that are reasonably likely to occur periodically, could materially impact the financial statements. Management believes the following critical accounting policies reflect its more significant estimates and assumptions used in the preparation of the financial statements.

*Clinical Trial Accruals*

Our accrued costs for clinical trial activities are based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations, or CROs, investigators, drug processors, laboratories, consultants, or other clinical trial service providers that perform the activities. Related contracts vary significantly in

**Table of Contents**

length, and may be for a fixed amount, a variable amount based on actual costs incurred, capped at a certain limit, or for a combination of these elements. Activity levels are monitored through close communication with the service provider, including detailed invoice and task completion review, analysis of expenses against budgeted amounts, and pre-approval of any changes in scope of the services to be performed. Each CRO provides an estimate of costs incurred but not invoiced at the end of each period for each individual trial. The estimates are reviewed and discussed with the CRO as necessary, and included in research and development expenses for the related period. For investigator study grants, which are paid quarterly on a per-patient basis to the institutions performing the clinical study, we accrue an estimated amount based on patient enrollment in each quarter. All estimates may differ significantly from the actual amount subsequently invoiced. No adjustments for material changes in estimates have been recognized in any period presented.

*Stock-Based Compensation*

In February 2003, the Board approved a cancellation and re-grant of 308,835 unexercised stock options held by our existing employees and directors in a one-for-one exchange and 12,500 options that were re-granted in connection with the cancellation of 54,166 unexercised stock options held by one of our directors. The options generally vest over a four-year period and will expire in February 2008 if not previously exercised. Variable accounting is being applied to the newly-granted options throughout their term. The related compensation expense depends on both the cumulative vesting of outstanding options and the price of our common stock at each quarter end, and therefore may have a significant impact on our future results of operations. No adjustments for material changes in estimates have been recognized in any period presented.

As permitted by Statement of Financial Accounting Standards No. 123 ( SFAS 123 ), *Accounting for Stock-Based Compensation,* as amended by Statement of Financial Standards No. 148, *Accounting for Stock-Based Compensation Transition and Disclosure,* we elected to follow APB 25 and related interpretations in accounting for stock-based employee compensation. Under APB 25, if the exercise price of an employee or director stock option is set equal or in excess of the fair market value of the underlying stock on the date of grant, no compensation expense is recognized. In February 2003, certain employee and director stock options for which the exercise prices had originally been set at less than the fair market value of the underlying stock on the grant date, were cancelled and re-granted in a one-for-one exchange. We recorded deferred compensation for the difference between the original exercise price and the fair market value of the underlying stock on the grant date as a component of stockholders equity, and the total was being amortized on a straight-line basis over the vesting period of the original awards, ranging from four to six years. The related re-granted options all vest over a four-year period, and the remaining unamortized deferred compensation as of the re-grant date is now being amortized over the new four-year vesting schedule, commencing at the date of re-grant. The amount of deferred stock compensation expense to be recorded in future periods could decrease if options, for which accrued but unvested compensation has been recognized, are forfeited prior to vesting. No adjustments for material changes in estimates have been recognized in any period presented.

Options or stock awards issued to non-employees are recorded at their fair value as determined in accordance with SFAS 123 and the FASB s Emerging Issues Task Force issue No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services,* and are recognized over the related service period and are periodically re-measured as the underlying options vest. The fair values are estimated using the Black-Scholes option pricing model, and are periodically re-measured as the underlying options vest. The option pricing model is dependent on a number of inputs, which may change over time. Other option pricing models may produce fair values that are

Table of Contents

substantially different from the Black-Scholes model. No adjustments for material changes in estimates have been recognized in any period presented.

**Comparison of Years Ended December 31, 2003, 2002 and 2001**

*Revenues*

IntraBiotics had no product sales or contract revenues for the years ended December 31, 2003, 2002 and 2001. We do not anticipate any product revenues until we obtain FDA approval for, and commence commercialization of, any product candidate.

*Expenses*

*Research and Development*

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| Research and development | $7,727 | (66.5)% | $23,053 | (39.4)% | $38,034 |

Research and development expenses primarily include clinical trial expenses, research and development payroll expense, drug substance expense, allocated facilities costs and non-cash stock compensation charges. Research and development expenses decreased in 2003 by $15.3 million from 2002, primarily due to a $9.3 million reduction in clinical trial expenses and a $3.2 million reduction in research and development payroll expense, allocated facilities costs and non-cash stock compensation charges as a result of restructuring activities in 2002 following termination of our oral mucositis program. The clinical trial expenses of $4.3 million in 2003 relate to the first pivotal trial of iseganan for the prevention of VAP, which commenced in September 2003. In 2002 and 2001, clinical trial expenses of $13.6 million and $20.0 million, respectively, primarily related to studies of iseganan for oral mucositis, an indication that we are no longer pursuing. Research and development expenses decreased in 2002 by $15.0 million from 2001, primarily due to reductions of $5.0 million in research and development payroll expense, $6.7 million in outside services related to clinical trials and $2.1 million in license fees.

In 2003, research and development expenses include a write-off of $2.4 million for prepaid iseganan drug substance, relating to an order of seven kilograms of iseganan bulk drug substance that was expected to be delivered in 2003. We have not yet been satisfied that the lot was manufactured in accordance with a validation plan or that related documentation is adequate, and we are currently discussing this with our contract manufacturer. Due to significant uncertainty over the timing and outcome of these discussions, the entire $2.4 million prepaid amount was written off in September 2003. In 2002, research and development expenses included a $4.8 million charge related to the delivery of iseganan bulk drug substance as a result of terminating a supply agreement with the same contract manufacturer as part of our restructuring. Non-cash stock compensation charges were $60,000, $656,000 and $1.5 million for the years ended December 31, 2003, 2002 and 2001, respectively. The decreases between each period are primarily due to the cancellation of options for terminated employees and consultants.

We expect research and development expenses to at least double in 2004 compared to 2003 as patients continue to be enrolled in the first pivotal trial of iseganan for the prevention of VAP, which is currently our primary focus.

Drug development in the United States is a process that includes several steps defined by the FDA. The process begins with the filing of an investigational new drug, or IND, application that, if successful, allows clinical study of the potential new drug. Clinical development typically involves three phases of study: Phase I, II and III. Pivotal trials are trials that are suitable for submission to the FDA for regulatory approval, and generally comprise Phase III trials. The most significant costs associated with clinical development are for Phase III trials, as they tend to be

Table of Contents

the longest and largest studies conducted during the drug development process. After completion of clinical trials, a new drug application, or NDA, may be filed with the FDA. In responding to an NDA, the FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not provide an adequate basis for approval. The lengthy process of seeking regulatory approvals, and the subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could have a material adverse effect on our results of operations.

*General and Administrative*

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| General and administrative | $5,782 | (32.9)% | $8,617 | (6.4)% | $9,202 |

General and administrative expenses in 2003 decreased by $2.8 million from 2002, primarily due to reduced headcount and facility-related costs as a result of a restructuring in October 2002. The decrease in 2002 of $585,000 from 2001 was primarily attributed to the reduction in headcount as a result of a restructuring implemented in May 2001, partially offset by the acquisition of Apothogen, Inc., or Apothogen, in April 2002, which increased general and administrative headcount, and a $344,000 charge in conjunction with the termination of two property leases in the fourth quarter of 2002. We expect total general and administrative expenses to be similar in 2004 compared to 2003, although a number of factors may significantly impact the total expense in 2004, including the impact of changes in our stock price on non-cash stock compensation charges.

General and administrative costs primarily include administrative payroll expense, outside contractors, legal and accounting fees, insurance, non-cash stock compensation charges, facilities, travel and other general administrative expenses. Non-cash stock compensation charges were $1.3 million, $1.7 million and $1.4 million for the years ended December 31, 2003, 2002 and 2001, respectively.

*Restructuring and Other Charges*

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| Restructuring and other charges | $ | (100.0)% | $6,118 | (72.1)% | $21,956 |

There were no restructurings during 2003. In 2002, restructuring expenses were primarily comprised of $5.2 million as a result of a facilities lease termination agreement and $848,000 of severance costs as a result of our restructuring in October 2002 due to the termination of our oral mucositis program. The restructuring reduced our headcount to 11 as of December 31, 2002 from 37 as of December 31, 2001. The $5.2 million lease termination expense included cash payments, the issuance of common stock and the write-off of a deferred rent balance. Of the $848,000 severance costs, $784,000 was paid in 2002 and the remaining $64,000 was paid in January 2003.

Restructuring charges of $22.0 million were recorded in 2001 resulting from a restructuring plan implemented in May 2001 in order to conserve capital and focus resources on the development of iseganan. The restructuring charges included asset write down charges of $11.8 million, costs related to work force reduction of $2.9 million, termination costs for collaboration agreements of $4.1 million and facilities consolidation costs of $3.2 million.

The workforce reduction was comprised of 90 employees, who were all terminated in 2001, representing a 71% reduction in force. The estimated cost of terminating the collaboration agreements was increased by $483,000 in the fourth quarter of 2001 and $166,000 in 2002.

Table of Contents

The facilities consolidation costs related to the vacating of three facilities in Mountain View, California, totaling 142,000 square feet. One of the vacated facilities was subleased during 2001, the second was terminated in October 2001 and the third in January 2003. In 2001, an adjustment was made to increase restructuring charges associated with facilities consolidation by $1.9 million for additional costs related to the third vacated facility. In November 2002, we reached agreements with the landlords of this building and the facility, which we had subleased, to terminate the leases. The additional expense recorded during 2002 was $5.2 million and included cash payments, the issuance of common stock and the write-off of a deferred rent balance.

Additionally, as part of the May 2001 restructuring plan, we wrote down to estimated fair value $11.8 million of leasehold improvements, laboratory equipment, computers and other assets that were no longer being used. In the fourth quarter of 2001 we received proceeds from the disposition of certain leasehold improvements and other assets previously written down in excess of the amounts originally estimated. As a result, we recognized a gain of $2.2 million that offset restructuring and other charges in the statement of operations for 2001.

*Arbitration Settlement*

During the year ended December 31, 2002, we received $3.6 million from a contract vendor as a result of an arbitration settlement relating to a drug dispensing error in a Phase III trial of iseganan for oral mucositis. We had no comparable item in 2003 or 2001.

*Interest Income and Expense*

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| Interest income | $166 | (76.4)% | $ 703 | (75.3)% | $ 2,843 |
| Interest expense | $ | (100.0)% | $(459) | (58.7)% | $(1,110) |

Interest income decreased in both 2003 and 2002, primarily resulting from decreases in average interest earning investment balances and lower interest rates in each year.

Interest expense decreased to zero in 2003 due to the repayment of our line of credit and bank loan in October 2002. The decrease in 2002 from 2001 was primarily attributed to a reduction in the average balance of our line of credit and a reduction in applicable interest rates.

*Other Income, net*

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| Other income, net | $ 31 | (96.4)% | $856 | 820.4% | $ 93 |

Other income, net in 2002 includes $975,000 from the sale of two preclinical anti-infective programs to Micrologix Biotech Inc., or Micrologix, a Canadian company, in May 2002, for $400,000 in cash and 750,000 shares of Series A preferred stock of Micrologix. The shares are redeemable at $1 per share or convertible into common stock at the election of Micrologix upon the occurrence of certain time and achievement milestones as follows:

shares converted into common stock with a value of $400,000 upon the four month anniversary of the effective date of the agreement;

shares will convert into common stock with a value of $100,000 upon commencement of certain toxicology studies; and

shares will convert into common stock with a value of $250,000 upon filing for marketing approval for certain drugs in certain countries.

Table of Contents

Other income of $775,000 was recognized in the second quarter of 2002 upon receipt of the $400,000 in cash and the 750,000 shares, and other income of $200,000 was recognized in the third quarter of 2002 upon redemption of 400,000 of the shares at $1 per share, which was triggered by the first milestone set forth above. No other income was recorded in either 2003 or 2001 as a result of this transaction.

**Income Taxes**

Since inception, we have incurred operating losses and accordingly have not recorded a provision for income taxes for any of the periods presented. As of December 31, 2003, we had net operating loss carryforwards for federal and state income tax purposes of approximately $192.0 million and $44.0 million, respectively. We also had federal and state research and development tax credits each of approximately $3.3 million. If not utilized, the net operating losses and credits will expire in the years 2004 through 2023. Utilization of net operating losses and credits may be subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended. The annual limitation may result in the expiration of our net operating losses and credit carryforwards before they can be used. Please read Note 11 of the Notes to the Financial Statements included in this prospectus for further information.

**Liquidity and Capital Resources**

| | 2003 | Change | 2002 | Change | 2001 |
|---|---|---|---|---|---|
| | | | (Dollars in thousands) | | |
| Cash, cash equivalents, restricted cash and short-term investments | $26,644 | 100.1% | $13,315 | (62.5)% | $35,470 |

At December 31, 2003, we had cash and cash equivalents of $14.3 million, representing an increase of $4.1 million from December 31, 2002. Short-term investments were $12.1 million in 2003 as compared to $2.9 million in 2002, and restricted cash remained at $250,000. We had no debt outstanding as of December 31, 2003. We invest excess funds in short-term money market funds and securities pursuant to our investment policy guidelines. The following is an analysis of changes in our cash and cash equivalents in each respective year.

| | 2003 | 2002 | 2001 |
|---|---|---|---|
| | | (In thousands) | |
| Net cash used in operating activities | $ (8,823) | $(26,347) | $(53,602) |
| Net cash provided by (used in) investing activities | (9,211) | (1,552) | 44,693 |
| Net cash provided by (used in) financing activities | 22,150 | 10,087 | (2,092) |
| Net increase (decrease) in cash and cash equivalents | $ 4,116 | $(17,812) | $(11,001) |

The net cash used in operating activities decreased in 2003 from 2002, primarily due to a reduction in the net loss from $34.5 million to $13.3 million, which primarily resulted from lower clinical trial expenses between the respective years and restructuring actions taken in 2002. The decrease from 2001 to 2002 was primarily due to a reduction in net loss from $67.4 million to $34.5 million, which primarily resulted from $22.0 million of restructuring expenses in 2001, and related reductions in operating cash outflows as a result of lower clinical trial activity and internal operating costs in 2002.

The net cash used in investing activities in 2003 relates to the purchase of $12.1 million of short-term investments, partially offset by the maturity of short-term investments of $2.9 million. In 2002, the cash used primarily relates to the purchase of $2.9 million of short-term investments, partially offset by the proceeds from the sale of two pre-clinical programs to Micrologix for $800,000. The change from 2001 to 2002 was primarily due to the maturities of short-term investments totaling $51.8 million in 2001.

Table of Contents

The cash provided by financing activities in 2003 primarily related to two private placement transactions. In May 2003, we sold 350 shares of a newly created Series A convertible preferred stock and issued warrants to purchase 920,699 shares of common stock, resulting in net cash proceeds of $3.2 million, and in October 2003, we sold 1,774,000 shares of newly issued common stock and issued warrants to purchase 354,800 shares of common stock, resulting in net cash proceeds of $18.5 million. Cash provided by financing activities in 2002 was primarily due to net proceeds of approximately $14.0 million and $5.0 million from two private placements of common stock, partially offset by $9.4 million in payments on financing obligations to a bank. The cash used in financing activities in 2001 was primarily due to payments on financing obligations of $13.8 million, partially offset by proceeds from financing obligations of $11.2 million.

**Contractual Obligations**

The impact that our contractual obligations as of December 31, 2003 are expected to have on our liquidity and cash flow in future periods is as follows:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less Than 1 Year | Between 1-3 Years | Between 3-5 Years | More Than 5 Years |
| | | | (In thousands) | | |
| Drug substance(1) | $450 | $300 | $100 | $ 50 | $ 0 |
| Operating leases(2) | 43 | 43 | | | |
| Total contractual commitments | $493 | $343 | $100 | $ 50 | $ 0 |

(1) Drug substance commitments are to the same contract manufacturer to which we prepaid $2.4 million for an order of seven kilograms of iseganan bulk drug substance. In 2004, the commitment represents the potential payment of $250,000 upon acceptance of this order, when and if this occurs, and $50,000 in fees for storage of iseganan. The remaining $150,000 represents storage fees for iseganan through 2007.

(2) Operating leases relate to the lease for our facility in Palo Alto, California, which was due to expire on June 30, 2004. Under the terms of the original lease we had committed to pay $43,000 in 2004. In March 2004 we agreed to extend the existing lease through June 30, 2005 for an additional rent commitment of $96,768. We also added an additional facility in the same building for an additional rent commitment of approximately $119,000 from April 1, 2004 to June 30, 2005. The new lease for both premises includes an option to extend until December 31, 2005 at the then market rents for the building.

There were no purchase obligations as of December 31, 2003 that included material penalties for cancellation and were enforceable and legally binding.

**Off-Balance Sheet Arrangements**

We do not have any off-balance sheet arrangements (as that term is defined in relevant SEC rules) that are reasonably likely to have a current or future material effect on our financial condition, results of operations, liquidity, capital expenditures or capital resources.

**Indemnifications**

In the ordinary course of business, we enter into contractual arrangements under which we may agree to indemnify the third party to such arrangement from any losses incurred relating to the services they perform on behalf of IntraBiotics or for losses arising from certain events as defined within the particular contract, which may include, for example, litigation or claims relating to past performance. Such indemnification obligations may not be subject to maximum loss clauses. Historically, payments made related to these indemnifications have been immaterial. In addition, we have entered into indemnity agreements with each of our directors and executive officers. Such indemnity agreements contain provisions which are in some respects broader than the specific indemnification provisions contained in Delaware law. We

Table of Contents

also maintain an insurance policy for our directors and executive officers insuring against certain liabilities arising in their capacities as such.

**Future Capital Requirements**

We expect to continue to incur substantial operating losses and will not receive any product revenues until a product candidate has been approved by the FDA and successfully commercialized. We currently anticipate our cash, cash equivalents and investments to be sufficient to fund operations for at least the next 12 months. We expect, however, that we will need to raise significant additional funds to continue our operations, complete the FDA approval process of iseganan for VAP if our trials are successful, commence commercialization if FDA approval is received, and pursue other indications.

This forecast is a forward-looking statement that involves risks and uncertainties, and actual results could vary. Our future capital requirements will depend on many factors, including:

the timing, delay, cost, extent and results of clinical trials;

future opportunities for raising capital;

payments to third parties for manufacturing scale up and validation;

the costs and timing of regulatory approvals;

the costs of establishing sales, marketing and distribution capabilities; and

the progress of our development activities.

Until we can generate sufficient cash from our operations, which we do not expect for the foreseeable future, we expect to finance future cash needs through private and public financings, including equity financings. We may also generate cash through collaboration or licensing arrangements, although no such transactions are currently under negotiation. We cannot be certain, however, that additional funding will be available when needed or on favorable terms. If additional funding is not available, we may need to delay or curtail our development and clinical trial activities to a significant extent, or we may be forced to cease operations.

Table of Contents

**Quarterly Results of Operations**

The following table presents a summary of our unaudited quarterly operating results for each quarter of the last two years. We derived this information from unaudited interim financial statements that, in the opinion of management, have been prepared on a basis consistent with the financial statements contained elsewhere in this prospectus and include all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of such information when read in conjunction with our audited financial statements and related notes. The operating results for any quarter are not necessarily indicative of results for any future period.

| | Three Months Ended | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | March 31, 2002 | June 30, 2002 | Sept. 30, 2002 | Dec. 31, 2002 | March 31, 2003 | June 30, 2003 | Sept. 30, 2003 | Dec. 31, 2003 |
| | (In thousands, except per share amounts) | | | | | | | |
| Operating expenses: | | | | | | | | |
| Research and development | $ 7,041 | $ 6,411 | $ 3,955 | $ 5,646 | $ 268 | $ 1,352 | $ 3,641 | $ 2,466 |
| General and administrative | 1,460 | 2,447 | 2,388 | 2,322 | 1,665 | 1,043 | 1,125 | 1,949 |
| Restructuring and other charges | 91 | | 5,140 | 887 | | | | |
| Arbitration settlement | (3,600) | | | | | | | |
| Impairment of acquired workforce | | | | 1,365 | | | | |
| Total operating expenses | 4,992 | 8,858 | 11,483 | 10,220 | 1,933 | 2,395 | 4,766 | 4,415 |
| Operating loss | (4,992) | (8,858) | (11,483) | (10,220) | (1,933) | (2,395) | (4,766) | (4,415) |
| Interest income | 265 | 215 | 143 | 80 | 26 | 45 | 28 | 67 |
| Interest expense | (153) | (113) | (131) | (62) | | | | |
| Other income, net | | 784 | 200 | (128) | | | | 31 |
| Net loss | (4,880) | (7,972) | (11,271) | (10,330) | (1,907) | (2,350) | (4,738) | (4,317) |
| Non-cash deemed dividend related to beneficial conversion feature of Series A preferred stock | | | | | | (1,418) | | (18) |
| Non-cash dividends on Series A preferred stock | | | | | | (47) | (70) | (65) |
| Net loss applicable to common stockholders | $(4,880) | $(7,972) | $(11,271) | $(10,330) | $(1,907) | $(3,815) | $(4,808) | $(4,400) |
| Basic and diluted net loss per share applicable to common stockholders | $ (1.73) | $ (2.58) | $ (3.59) | $ (3.23) | $ (0.58) | $ (1.17) | $ (1.46) | $ (0.87) |
| Shares used to compute basic and diluted net loss per share applicable to common stockholders | 2,815 | 3,095 | 3,143 | 3,200 | 3,269 | 3,270 | 3,283 | 5,056 |

**Quantitative and Qualitative Disclosure About Market Risk**

The primary objective of our investment activities is to preserve our capital until it is required to fund operations while at the same time maximizing the income we receive from our investments without significantly increasing risk. As of December 31, 2003, we owned financial instruments that are sensitive to market risk as part of our investment portfolio. To minimize this risk, in accordance with our investment policy guidelines, we place investments with high credit quality issuers and limit the amount of credit exposure to any one issuer. The average duration of our investment portfolio in 2003 and 2002 was less than one year. Due to the short-term nature of these investments, a 50 basis point

movement in market interest rates would not have a material impact on the fair value of our portfolio as of December 31, 2003

Table of Contents

and 2002. We have no investments denominated in foreign country currencies and therefore our investments are not subject to foreign currency exchange risk.

The following table summarizes the average interest rate and fair market value of the short-term investments held by us as of December 31, 2003 and 2002:

| Short-term investments | Total Cost | Fair Market Value | Average Interest Rate |
|---|---|---|---|
| | | (Dollars in thousands) | |
| December 31, 2003 | $12,106 | $12,108 | 1.36% |
| December 31, 2002 | $ 2,895 | $ 2,895 | 1.83% |

**Recent Accounting Pronouncements**

See Note 2 of the financial statements for a full description of recent accounting pronouncements including the respective effects on our financial condition, results of operations and disclosure.

Table of Contents

## BUSINESS

### Overview

We are developing novel antimicrobial drugs designed to overcome many of the shortcomings of currently prescribed anti-infectives. These shortcomings result from the wide range of microbes responsible for serious infections and the fact that many microbes have become resistant to current therapies. We have selected our product candidate, iseganan, for development because it kills a broad spectrum of microbes and has a low propensity to engender resistance. Iseganan is currently in clinical development for two indications: the prevention of ventilator-associated pneumonia, or VAP, and the treatment of lung infections associated with cystic fibrosis, or CF. Additionally, we are evaluating the use of iseganan in other types of infection where we believe that its properties may render it more useful than current therapies.

We believe that the prevention of VAP represents a significant unmet medical need and an attractive market opportunity. VAP is the most common infection contracted by patients in the intensive care unit, or ICU. Worldwide, over one million patients annually are at risk of developing VAP. Because these patients are critically ill, developing pneumonia can have particularly serious consequences.

There are no currently approved therapies for the prevention of VAP. While antibiotics, a class of antimicrobial drugs that kill bacteria, have been demonstrated to be effective in preventing VAP, concerns about antibiotic resistance have precluded their use as the standard of care for prevention. As a result, physicians wait until pneumonia is diagnosed before prescribing an antibiotic. We believe that iseganan may be effective as a prophylactic agent in this market as a result of its broad spectrum, microbe-killing activity and low propensity to engender resistance.

We have retained worldwide commercial rights to iseganan and the intellectual property around it. Iseganan has been granted Fast Track designation with the FDA for the prevention of VAP. Iseganan has also been accepted for inclusion into the FDA s CMA Pilot 2 Program, providing for enhanced access to guidance and feedback from FDA staff. In addition, we have established a Special Protocol Assessment, or SPA, with the FDA, detailing an agreed-upon pivotal clinical trial design for the prevention of VAP. The SPA requires us to conduct two identical pivotal clinical trials, the first of which is currently enrolling patients. We expect results from the first VAP trial by the end of 2004.

### Background

Two interrelated problems are thwarting efforts to improve the prevention and treatment of infectious disease. First, patients are vulnerable to infection caused by a wide range of microbes. Second, many microbes encountered by patients today are not susceptible to current therapy. The result of these problems is that infectious diseases are increasingly difficult to treat and are adding substantial costs to the health care system.

Since the discovery of penicillin more than 50 years ago, many types of antimicrobial drugs have been developed to fight microbial infections. Until recently, antimicrobial drugs have been highly successful in controlling the morbidity associated with serious infections. In recent years, however, many microbes have developed resistance to currently marketed antibiotics. Once microbes become resistant, infections can become difficult or impossible to treat. According to the FDA, approximately 70% of microbes that cause infections in hospitals are resistant to at least one of the drugs most commonly used to treat infections. The Centers for Disease Control and Prevention has stated that antibiotic resistance is among the organization s top concerns. The increasing prevalence of drug-resistant microbes has led to increased morbidity, prolonged hospitalizations and increased health care costs.

Table of Contents

The antibiotic resistance problem is worsening, in part because of the use of multiple antibiotics to treat individual cases of infection. In order to combat infection, doctors typically prescribe combinations of antibiotics for two reasons. First, many infections can be caused by a broad range of microbial pathogens. Second, because the results of diagnostic tests that determine the pathogen(s) causing an infection are often not available in a timely fashion, physicians are frequently forced to prescribe multiple antibiotics to cover the range of possible microbes. As pathogens have evolved to evade the activity of the commonly-prescribed antibiotics, multi-drug resistant strains have proliferated.

The serious health risk posed by microbial infection, the variability of microbes that cause infection and the proliferation of microbes resistant to current drugs have created a significant medical need in hospitals worldwide. To address this problem, an ideal antimicrobial drug would:

have a broad spectrum of killing activity;

not engender microbial resistance or cross-resistance; and

be safe and easy to administer.

Such a drug would not only serve as an effective treatment option for drug-resistant microbes, but could also be useful in prophylaxis, thereby preventing infections in the first place, preserving treatment options and reducing costs to the health care system.

**Our Solution**

We are developing a novel class of drugs designed to kill a broad range of microbes without engendering resistance. These drugs are derived from antimicrobial peptides that have evolved in mammals and are a natural part of the body s mechanism to kill microbes and fight infection. In contrast, conventional antimicrobial drugs, developed from plants, molds and other non-mammals, are naturally more narrow in spectrum and engender resistance. We believe that our mammalian-derived peptides will improve outcomes in a broad range of serious infections.

We have chosen to develop a class of peptides called protegrins from the more than 200 antimicrobial peptides found in nature. These antimicrobial peptides, which are found on moist surfaces, such as those in the mouth and lungs as well as in white blood cells, represent the principal infection-fighting mechanism of the mammalian immune system. Iseganan is an analog of a naturally-occurring protegrin that we have optimized to enhance its killing activity.

**Our Strategy**

There are two elements of our development strategy that we believe will enable us to develop safe and effective antimicrobial solutions.

*Target indications for which clinical proof-of-principle exists, but where resistance diminishes therapeutic effect.* In the case of VAP, there have been numerous large clinical studies that have shown that oral administration of antimicrobial drugs is effective in preventing VAP. However, concerns over antibiotic resistance and narrow spectrum have generally impeded physicians from using these drugs prophylactically. In CF, an inhaled antibiotic, TOBI, has been approved and is used to control the infection associated with the disease. However, chronic and uninterrupted use of TOBI generates resistance, requiring intermittent monthly drug holidays during which the patient s condition regresses. We believe that targeting indications where antimicrobial drugs have already demonstrated their effectiveness may reduce our development risk.

*Target indications where we can obtain direct access to the site or source of infection.* Unlike conventional intravenous delivery of antibiotics to treat disease, which often can lead to poor drug concentrations at the site of infection and high systemic exposures and

Table of Contents

related toxicities, iseganan is delivered directly to the site or source of the infection, i.e., the oral cavity in the case of VAP and the lung in the case of CF. We believe that this strategy may optimize efficacy by maximizing drug concentrations where the drug is needed and reduce potential toxicity by limiting systemic drug exposure.

**Key Features and Benefits of Iseganan**

We believe that there are four features of iseganan that will translate into important clinical benefits.

*Broad Spectrum.* Iseganan kills a diverse range of pathogens. This includes the two major classes of bacteria, Gram-positive and Gram-negative, as well as yeast-like fungi, which are often not naturally susceptible to antibiotics. Treating these three classes of pathogens typically requires two or three antimicrobial drugs. Iseganan is also active against the vast majority of drug-resistant pathogens, including those most commonly found in hospitals. Importantly, iseganan is active against methicillin-resistant *Staphylococcus aureus*, or MRSA, one of the most common hospital-borne resistant microbes, as well as yeast-like organisms such as *Candida albicans*, which are known to cause oral diseases if they become overabundant in the mouth. We are unaware of any other agent on the market or in clinical development that possesses this breadth of antimicrobial activity.

*Low Propensity to Engender Resistance.* Iseganan destroys the cell membranes of microbes, thus damaging their structural integrity. Based on tests we have conducted in the laboratory, iseganan works 100 to 1,000 times faster than conventional antibiotics. Because the cell membrane is a fundamental structure and cannot readily change, and because iseganan destroys membranes so quickly, there is little chance for a microorganism to survive iseganan s killing activity and develop resistance. We conducted several laboratory experiments which were designed to engender resistance. We found that organisms have remained susceptible to the killing effects of iseganan while developing significant resistance to conventional antibiotics. This has been confirmed in both drug-susceptible, as well as multi-drug resistant, strains of pathogens.

There is clinical evidence that antimicrobial peptides may not engender microbial resistance. Colistin, a bacterially derived antimicrobial peptide whose mechanism of action is similar to iseganan, has been used for decades to treat CF, and to date, microbial resistance to colistin has not been seen. We believe that colistin s therapeutic value, however, is limited due to its relatively narrow spectrum of activity.

*Low Propensity to Engender Cross-Resistance.* Cross-resistance arises when an organism develops resistance to a second antibiotic upon exposure to a first, unrelated antibiotic. For example, exposure to amoxocillin may cause resistance to azythromycin. Cross-resistance is particularly problematic because it can severely limit the number of viable therapeutic options a physician has to treat a patient. Organisms treated with iseganan, however, have been shown to remain susceptible to the killing effects of other antimicrobial drugs. As a result, we believe that use of iseganan will preserve therapeutic options.

*Safe and Well-Tolerated.* Based on our experience to date, iseganan appears to be safe and well-tolerated at therapeutically relevant doses when administered to the oral cavity, the planned route of administration for the prevention of VAP. In particular, iseganan has been delivered to the oral cavity of more than 800 patients to date, with no differences in adverse events between the active and placebo groups observed consistently among the trials. Whether delivered to the oral cavity or by inhalation, iseganan is not detectably absorbed into the bloodstream. In CF, based on our completed Phase I studies, we believe we have sufficient safety data to submit to the FDA in support of a Phase II study.

Table of Contents

We believe that these features will provide important benefits to patients and their physicians. Iseganan may allow physicians to effectively prevent and treat infections without:

precisely knowing the offending pathogen;

using multiple antimicrobial drugs;

engendering resistance; and

compromising future use of antimicrobial drugs.

**Our Development Programs**

Iseganan is in clinical development for two indications, ventilator-associated pneumonia and lung infections associated with cystic fibrosis. Several other conditions for which iseganan may have utility are also under investigation, although at an earlier stage of development.

| Indication | Development stage | Our commercial rights |
|---|---|---|
| Ventilator-associated pneumonia | Pivotal trials | Worldwide |
| Cystic fibrosis | Planned Phase II trial in 2nd half 2004 | Worldwide |
| Ear infections | Preclinical | Worldwide |
| Acne and skin infections | Preclinical | Worldwide |
| Vaginitis | Preclinical | Worldwide |

**Iseganan for Ventilator-Associated Pneumonia**

*Background and Market Opportunity*

VAP is the most common infection contracted by patients in the ICU and is a direct result of artificial life support. Artificial life support involves insertion of a tube that connects the patient s lungs to a breathing machine. The tube renders the patient vulnerable to developing pneumonia because it facilitates leakage of microbes from the mouth into the airway of the lungs. The longer the tube is in place, the greater the risk a patient will develop VAP.

There are approximately one million patients annually in the United States, Europe and Japan who are on artificial life support for two or more days and thus are at substantial risk of developing VAP. Approximately 20% of patients who require artificial life support for at least two days develop VAP. Patients who develop VAP are treated with intravenous antibiotics. In spite of this treatment, patients who develop VAP spend, on average, six extra days in the ICU, which adds approximately $40,000 in incremental charges. The Joint Commission on Accreditation of Healthcare Organizations named prevention of VAP as a core ICU performance measure. Performance measurements are used by hospitals to support performance improvements and to demonstrate accountability to external stakeholders including payors. Reimbursements by payors, such as Medicare, do not often cover the costs of VAP and therefore the excess costs of VAP must be borne by hospitals.

There are no approved drugs for the prevention of VAP.

*Oral Decontamination as a Strategy to Prevent VAP*

Given that VAP arises through the aspiration of microbes from the mouth into the lungs, decontaminating the mouth using antimicrobial drugs to prevent VAP is an approach that has received significant medical and scientific interest. Since 1984, there have been more than 30 randomized clinical trials using conventional antimicrobial drugs topically applied in the oral cavity. Most of these trials have independently been statistically significant, and, in the aggregate, they have demonstrated reductions in the incidence of VAP of approximately 50%.

Table of Contents

The following table presents a summary of trials of oral decontamination using conventional antimicrobial drugs conducted and published in peer-reviewed journals in the last ten years. These trials are large, placebo-controlled studies using similar eligibility and diagnostic criteria as our trials of iseganan in preventing VAP.

| Author (Year) | Sample size | VAP rate in placebo group | VAP rate in active group | Reduction in VAP rate | p-value |
|---|---|---|---|---|---|
| Krueger (2002) | 527 | 11% | 2% | 80% | 0.007 |
| Bergmans (2001) | 165 | 31% | 10% | 67% | 0.001 |
| Sanchez Garcia (1998) | 271 | 29% | 11% | 61% | <0.001 |
| Quinio (1996) | 148 | 51% | 25% | 51% | 0.01 |

In general, these studies used combinations of generically available antimicrobial drugs, formulated by hospital staff for oral application. The percentage reduction in the incidence of VAP following the application of topical oral antimicrobial drugs is large, reproducible and statistically significant. Reductions are consistently seen over a wide range of the type of antimicrobial agent used, dosage, formulation or patient population studied. In addition to demonstrating reductions in VAP, several clinical trials have demonstrated that preventing VAP can reduce the use of intravenous antimicrobial drugs for treatment, as well as a patient s time on artificial life support.

Despite these positive results, oral decontamination using conventional antimicrobial drugs generally has not been adopted as a prevention strategy for VAP due to concerns over causing resistance and cross-resistance. Specifically, many of the agents that are effective in preventing VAP are preserved for use in the ICU as systemic agents to treat serious infections. Hence, because of concerns about antimicrobial resistance, prophylactic use is uncommon.

*Iseganan s Profile as an Agent for the Prevention of VAP*

We believe that iseganan has an attractive profile as an agent for the prevention of VAP.

| Attribute | Benefit |
|---|---|
| Broad spectrum of activity<br>Gram-positive bacteria<br>Gram-negative bacteria<br>Drug-resistant microbes<br>Yeast | Kills the vast majority of pathogens known to cause VAP, including microbes not killed by conventional antimicrobial drugs due to resistance |
| Rapidly active in saliva | Acts within minutes, even in the presence of oral secretions |
| Lack of resistance/cross- resistance | Has not been observed to cause resistance in pathogens, including those most commonly responsible for causing VAP |
| Not used systemically for treatment of infection | Appropriate for prophylactic use because it does not limit therapeutic options |

*Clinical Status of Iseganan in VAP*

*Phase I/ II Clinical Trial.* In February 2001, we completed a 42-patient, Phase I/II clinical trial in patients on artificial life support. The trial was designed to demonstrate safety and enable us to select the optimal dose, regimen and formulation of iseganan for use in subsequent clinical trials. Iseganan was