BIODELIVERY SCIENCES INTERNATIONAL INC
Form 10KSB/A
April 29, 2005
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-KSB/A

(Amendment No. 1)

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x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2004

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission file number 0-28931

BioDelivery Sciences International, Inc.

(Name of small business issuer in its charter)

Delaware	**35-2089858**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
2501 Aerial Center Parkway Suite 205	
Morrisville, NC	**27560**
(Address of principal executive offices)	**(Zip Code)**

Issuer s telephone number: (919) 653-5160

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

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

Common Stock, $.001 par value;

Class A common stock purchase warrants

(Title of class)

UMDNJ Medical School

185 South Orange Avenue, Bldg. #4

Newark, New Jersey 07103

(Former name, former address and former fiscal year, if changed since last report)

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

Check if there is no disclosure of delinquent filers in response to Item 405 of Regulation S-B is not contained in this form, and no disclosure will be contained, to the best of issuer s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-KSB or any amendment to this Form 10-KSB. x

Issuer s revenues for fiscal year 2004 were $1,778,898.

The aggregate market value of the voting and non-voting common equity held by non-affiliates as of March 22, 2005 was approximately $8,648,748.20 based on the closing sale price of the company s common stock on such date of U.S. $3.70 per share, as reported by the Nasdaq SmallCap Market.

Transitional Small Business Disclosure Format: Yes ¨ No x

Table of Contents

INTRODUCTORY NOTE

This Report, including the documents incorporated by reference in this Report, includes forward-looking statements. We have based these forward-looking statements on our current expectations and projections about future events. Our actual results may differ materially from those discussed herein, or implied by, these forward-looking statements. Forward-looking statements are identified by words such as believe, expect, anticipate, intend, estimate, plan and other similar expressions. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. Forward-looking statements included in this Report or our other filings with the SEC include, but are not necessarily limited to, those relating to:

- our plans regarding the timing and outcome of research and development relating to the Bioral® and BEMA technology platforms and any proposed formulations or products relating thereto;
- the domestic and international regulatory process relating to our technologies and proposed products and formulations, including the timing and status of our filings with the U.S. Food and Drug Administration, which we refer to herein as the FDA;
- our ability to generate commercial viability and acceptance of our Bioral® and BEMA technology platforms and our proposed formulations and products;
- the protection and control afforded by our interest in licensed patents, or our ability to enforce our rights under such licenses;
- the ability of our sublicense partners to commercially exploit our drug delivery platforms;
- our ability to enter into sublicenses and to receive royalty and other payments from Accentia and other parties to whom we have sublicensed our technologies;
- our ability to retain members of our management team and our employees;
- our ability to receive federal, state, government or private grants and/or attract capital; and
- the competition that may arise in the future.

The foregoing does not represent an exhaustive list of risks. Other sections of this Report include additional risks which could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time and it is not possible for our management to predict all risks, nor can we assess the impact of all risks on our business or the extent to which any risk, or combination of risks, may cause actual results to differ from those contained in any forward-looking statements. All forward-looking statements included in this Report are based on information available to us on the date of this Report. Except to the extent required by applicable laws or rules, we undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements contained throughout this Report.

Table of Contents

PART I

Item 1. Description of Business.

Overview

We are a specialty biopharmaceutical company that is exploiting its licensed and proprietary patented drug delivery technologies to develop and commercialize, or partner with third parties on, clinically-significant new formulations of proven therapeutics, nutraceuticals and micronutrients. Our drug delivery technologies include: (i) the patented Bioral® nanocochleate technology, designed for a potentially broad base of applications, and (ii) the patented BEMA (transmucosal, or applied to the inner cheek membrane) drug delivery technology being developed by our Arius Pharmaceuticals, Inc. subsidiary, which we acquired in August 2004 and which we refer to herein as Arius. Arius is developing products for acute treatment opportunities such as pain, anxiety, nausea and vomiting.

Our Bioral® drug delivery technology encapsulates the selected drug in a nanocrystalline structure termed a cochleate cylinder. We also believe this technology can be applied to micronutrients for use in processed foods and beverages and personal care products. All of the components of the cochleate cylinder are naturally occurring substances. We believe that the cochleate cylinder provides an effective delivery mechanism without forming a chemical bond, or otherwise chemically altering, the drug or micronutrient. Our Bioral® drug delivery technology was developed in collaboration with The University of Medicine and Dentistry of New Jersey and the Albany Medical College (which we refer to herein as the Universities) that have each granted us the exclusive worldwide licenses under applicable patents. Our lead Bioral® formulation is an encochleated version of Amphotericin B, an anti-fungal treatment for treating systemic fungal infections. A Bioral® formulation of Amphotericin B would have the potential for oral delivery of a drug that is currently only given by intravenous injection. A second formulation for intranasal administration Amphotericin B to treat chronic rhinosinusitis is now in development. In April 2004, we licensed this second product to Accentia Biopharmaceuticals, Inc., or Accentia, for the use in the treatment of chronic rhinosinusitis, or CRS, and asthma. We have also explored the creation of cochleate formulations of important nutrients, which we have prepared in kilogram quantities using standard manufacturing processes. We believe these preparations may stabilize the encochleated micronutrients during food processing and may enhance the shelf life of the end product.

Our BEMA drug delivery technology consists of a dissolvable, dime-sized polymer disc for application to mucosal (inner lining of cheek) membranes. BEMA discs deliver a rapid, reliable dose of drug across mucous membranes for time-critical conditions like breakthrough cancer pain, or trauma cases where intravenous lines or injections are unavailable or not practical. Our lead BEMA product under development is BEMA fentanyl, a treatment for breakthrough cancer pain. This product is projected to enter into Phase III trials for breakthrough cancer pain in the second half 2005. A follow on product, BEMA Long Acting Analgesic, is also under development. This is a BEMA formulation of an already approved product in the U.S. that will target a broader range of pain conditions including post operative and chronic pain due to osteoarthritis, lower back disorders and rheumatoid arthritis. We intend to submit an Investigational New Drug Application, or IND, and enter BEMA Long Acting Analgesic into clinical trials in the second half of 2005. Arius licenses the BEMA drug delivery technology on a worldwide exclusive basis from Atrix Laboratories, Inc. (now a wholly-owned subsidiary of QLT Inc.), which we refer to herein as Atrix.

Through Arius, we are also developing Emezine®, which we believe is the first drug to be delivered transmucousally for rapid treatment of nausea and vomiting. In February 2005, we announced that we completed the clinical studies required for our pending New Drug Application, or NDA, on Emezine®. We anticipate filing of the Emezine® NDA in April of this year. Through Arius, we license Emezine® from Reckitt Benckiser Healthcare (UK) Limited, which we refer to herein as Reckitt.

1

Table of Contents

Our development strategy focuses on the utilization of the FDA s 505(b)(2) approval process to obtain more timely and efficient approval of new formulations of previously approved therapeutics which incorporate our licensed drug delivery technologies. Because the 505(b)(2) approval process is designed to address new formulations of previously approved drugs, we believe it has the potential to be more efficient and less time consuming than other FDA approval methods.

In addition to developing and commercializing our drug delivery technologies and initial Bioral® and BEMA products, we are presently in the process of determining the cost and timing of progressing with our autologous HIV therapy to an IND. This technology is being developed as a patient specific, or autologous, therapy for treatment following HIV infection. Our autologous HIV therapy is based upon a patented proteoliposome technology, which we believe facilitates uptake by cells responsible for stimulating immune responses. We believe that the ongoing research and development of this technology will require significant time and resources and we intend to primarily rely upon the availability of grants and corporate support to largely finance further development of this technology, and we may elect not to continue this program. We are also developing a subunit HIV vaccine formulation with our cochleate technology that may have the ability to work following oral administration. This program is currently funded via a National Institutes of Health, or NIH, grant which expires during 2005. We plan on evaluating a potential extension of this grant in 2005.

We intend to finance our research and development, commercialization and distribution efforts and our working capital needs primarily through: (i) applying our licensed technologies to existing therapeutics to create our own proprietary formulations, which we will then seek to obtain FDA approval for and subsequently commercialize and (ii) licensing and joint venture arrangements with pharmaceutical companies, whose own proprietary pharmaceutical products may benefit from our drug delivery technologies. We also have and may continue to raise additional funding from other sources, including debt financing and equity financing. While there can be no assurance that such sources will provide adequate funding for our operations, management believes such sources will be available to us.

In early 2005, we moved our principal executive offices to Arius offices in North Carolina. The new address of our principal executive offices is 2501 Aerial Center Parkway, Suite 205, Morrisville, North Carolina 27560 and our phone number there is (919) 653-5160. Our principal research facilities are in Newark, New Jersey. We also have an administrative office in Tampa, Florida. In this Report, unless the context specifically requires otherwise, the terms BDSI, we, us, our and similar terms refer to BioDelivery Sciences International, Inc., a Delaware corporation, together with its consolidated subsidiaries, Arius and Bioral Nutrient Delivery, LLC, which we refer to herein as BND.

Historical and Recent Events

Public Offering and Financing

On June 24, 2002, the Securities and Exchange Commission, or SEC, declared our Registration Statement on Form SB-2, Registration No. 333-72877, effective. Commencing on June 25, 2002, and pursuant to such Registration Statement, we conducted an offering consisting of 2 million units, which we refer to herein as Units, with each Unit consisting of: (i) one share of common stock, par value $.001 per share, and (ii) one Class A common stock purchase warrant, or Warrants. Each Warrant entitles the owner to purchase one share of our common stock at a price of $6.30 through June 24, 2007. The net offering proceeds we received was $8,226,758. As of the fiscal year ended December 2004, we had exhausted substantially all of the proceeds from our public offering.

Table of Contents

Acquisition of Arius Pharmaceuticals, Inc.

On August 24, 2004, we consummated the acquisition of Arius. As a result of this acquisition, Arius was reorganized with and into a newly formed, wholly-owned subsidiary, which we renamed Arius Pharmaceuticals, Inc. following the closing. Arius is a specialty drug delivery company developing products for the acute treatment opportunities such as pain, anxiety, nausea and vomiting, targeted primarily to surgical and oncology patients. In 2004, Arius acquired an exclusive worldwide license to the BEMA delivery technology developed by Atrix, and also acquired the U.S. rights to a transmucousally delivered tablet formulation of Emezine®, an anti-nausea and vomiting medication. Through Arius, we license Emezine® from Reckitt.

Simultaneously with the closing of the Arius acquisition, Mark A. Sirgo, Pharm.D., a founder and the President and CEO of Arius, entered into an employment agreement with us and was named Senior Vice President of Commercialization and Corporate Development. Andrew L. Finn, Pharm.D., also a founder and the Chief Operating Officer of Arius, also entered into an employment agreement with us and was named Senior Vice President of Product Development at BDSI. Subsequent to the Arius closing, Dr. Sirgo was promoted to the position of Executive Vice President and Chief Operating Officer of our company and, in early 2005, was named President of our company. Dr. Finn was, subsequent to the Arius closing, promoted to the position of Executive Vice President of Clinical Development and Regulatory Affairs.

Hopkins Capital Group Equity Line of Credit

On September 3, 2004, we entered into an Equity Line of Credit Agreement with Hopkins Capital Group II, LLC, which we refer to herein as HCG, a principal stockholder of our company which is controlled and partially-owned by Dr. Francis E. O Donnell, Jr., our Chairman and CEO. Pursuant to the Equity Line Agreement, HCG will, at our request, invest up to $4.0 million in our company from August 23, 2004 through March 31, 2006 in consideration of shares of a newly created class of Series B Convertible Preferred Stock, or Series B Preferred. As of December 31, 2004, $1.45 million has been drawn under the Equity Line Agreement.

Subsequent Events

The following material events occurred subsequent to December 31, 2004:

Sigma-Tau License and Stock Purchase Transaction

On January 20, 2005, we signed a definitive licensing agreement with Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., or Sigma-Tau Pharma, for the application of our Bioral® nanocochleate delivery technology to formulate up to four proprietary pharmaceutical compounds currently under development by Sigma-Tau Pharma. Sigma-Tau Pharma is an affiliate of The Sigma-Tau Group, one of Italy s leading pharmaceutical companies.

Simultaneously with this licensing agreement, we entered into a stock purchase agreement with, and received a non-refundable upfront payment of US$250,000 from, Sigma-Tau Finanziaria S.p.A., or Sigma-Tau, a holding company of The Sigma-Tau Group. This upfront payment was

made in consideration of unregistered shares of our common stock priced at $4.25 a share.

The stock purchase agreement with Sigma-Tau provides for the acquisition by Sigma-Tau, upon the occurrence of specified developmental milestones associated with the license, of additional unregistered shares of our common stock, up to an aggregate potential of $1.5 million worth of such

Table of Contents

shares. These milestones lead up to and include the submission of product INDs by Sigma-Tau Pharma for one or more of the four subject encochleated compounds. Sigma-Tau, through other holding entities, is currently a stockholder of our company. In addition to the milestone payments, we will receive a royalty on future sales of each of the four products which may arise from the encochleated compounds.

Laurus Financing

On February 22, 2005, we consummated a $2.5 million secured convertible debt financing from Laurus Master Fund, Ltd., a Cayman Islands corporation (referred to herein as Laurus). Net proceeds from the financing were used primarily to retire our secured equipment loan with Gold Bank (on which approximately $300,000 was owed and was paid at the closing of the Laurus transaction) and will be used to support our research and development opportunities and for general working capital purposes.

The Laurus investment takes the form of a convertible note secured by certain of our assets. The note has a 3-year term and bears interest at a rate equal to prime plus 2% per annum. The note is convertible, under certain conditions, into shares of our common stock at a price equal to $3.10 per share. In connection with the financing, we also issued Laurus a common stock purchase warrant to purchase up to 350,000 shares of our common stock at a price equal to $3.88 per share. We have agreed, pursuant to a registration rights agreement, to register the shares of common stock underlying the Laurus note and the warrant.

Overview of Specialty Pharmaceuticals

Since our inception, we have focused primarily on research and development of our licensed encochleation technology and the application of such technology to specific drugs and nutraceuticals. The drug delivery industry develops technologies for the improved administration of certain drugs. These technologies, including our own, have focused primarily on safety, efficacy, ease of patient use and patient compliance.

In 2004, however, and in particular as a result of our acquisition of Arius, we have begun to shift our corporate focus to what we call the area of specialty pharmaceuticals : applying our licensed technologies to existing therapeutics to create our own proprietary formulations, for which we then seek to obtain FDA approval and subsequently commercialize. We believe that focusing our drug delivery technologies for use with existing FDA approved drugs to be less risky than attempting to discover new drugs. We are currently seeking to capitalize on the FDA s 505(b)(2) approval process to obtain more timely and efficient approval of new these formulations of previously approved therapeutics which incorporate our licensed drug delivery technologies.

As part of our strategy, however, we will also continue to seek partners, such as Sigma Tau, to whom we can license our delivery technologies so that they may be applied to the proprietary products of such partners. Drug delivery technologies can provide pharmaceutical and biotechnology companies with an avenue for developing new drugs, as well as extending existing drug patent protections. Drug delivery companies can also apply their technologies to drugs no longer patent protected. Pharmaceutical and biotechnology companies view new and improved delivery technology as a way to gain competitive advantage through enhanced safety, efficacy, convenience and patient compliance of their drugs, and we will continue to attempt to leverage this desire in the pharmaceutical industry for improved delivery systems.

We have and intend to continue to primarily target drugs that have large established markets for which there is an established medical need. As a result, doctors are familiar with the drug compounds and are accustomed to prescribing them. As with BEMA fentanyl and Emezine®, we anticipate that many

4

Table of Contents

of the drug candidates we target will have been through the regulatory process and therefore the safety and efficacy of the drug has been previously established. Consequently, we believe that our clinical trials would primarily need to show that our Bioral® or BEMA technologies deliver the drug without harming the patient or changing the clinical attributes of the drug. Focusing on drug delivery compared to drug discovery should allow us to potentially form a number of collaborations to deliver a wide variety of medicines without limiting rights to utilize our proprietary technology with additional drug opportunities.

Pipeline of Proposed Formulations and Products

The following table summarizes the status of our currently proposed formulations and products:

Formulation/Product	Indication	Development Status	Commercial Status
Emezine®	Nausea/Vomiting	Pre-registration	Partnered
BEMA Fentanyl	Breakthrough pain	Clinical Trials	In-house commercialization
BEMA Long Acting Analgesic	Pain	Preclinical	In-house commercialization
Bioral® Amphotericin B	Fungal infections	Preclinical	In-house commercialization
Bioral® NSAID	Pain/inflammation	Preclinical	Available for licensing
Bioral® Paclitaxel	Oncology	Preclinical	Available for licensing
Bioral® siRNA therapeutics	Infectious disease/cancer	Preclinical	Available for licensing
Subunit HIV Vaccine	Encochleated HIV vaccine	Preclinical	Available for licensing
Autologous HIV Vaccine	Therapeutic vaccine for HIV	Preclinical	Available for licensing

We are presently dedicating most of our corporate resources toward the development and commercialization of Emezine®, BEMA Fentanyl, Bioral® Amphotericin B and BEMA Long Acting Analgesic.

Description of Our Drug Delivery Technologies and Proposed Formulations and Products

Encochleation Technology Overview

Our licensed Bioral® drug delivery technology is based upon encapsulating (or encochleating) drugs to potentially deliver the drug safely and effectively. Over the years, biochemists and biophysicists have studied artificial membrane systems to understand their properties and potential applications, as well as to gain insight into the workings of more complex biological membrane systems. In the late 1960 s, scientists began investigating the interactions of divalent cations with negatively charged lipid bilayers. They reported that the addition of calcium ions to small phosphatidylserine vesicles induced their collapse into discs which fused into large sheets of lipid. In order to minimize their interaction with water, these lipid sheets rolled up into nanocrystalline structures, termed cochleates, after the Greek name for a snail with a spiral shell.

Table of Contents

Our licensed Bioral® cochleate technology is based upon components which are believed to be non-toxic. The primary chemical components of our Bioral® cochleate technology are phosphatidylserine, or PS, and calcium. Phosphatidylserine is a natural component of essentially all biological membranes, and is most concentrated in the brain. Clinical studies by other investigators (more than 30 have been published that we are aware of) to evaluate the potential of phosphatidylserine as a nutrient supplement indicate that PS is safe and may play a role in the support of mental functions in the aging brain. As an indication of its nontoxic nature, today phosphatidylserine isolated from soybeans is sold in health food stores as a nutritional supplement.

Research and development of cochleates has been conducted at the Universities for a number of years. Our scientists, some of whom were former researchers and others who still hold teaching positions with these Universities, supervised their cochleate research programs. As a result of the relationship between our scientists and the Universities, we became the exclusive worldwide licensee to develop this cochleate technology and in some cases co-own the patents with them.

Potential Advantages

We believe that our licensed Bioral® drug delivery technology represents a potentially important new delivery mechanism. While the characteristics and benefits of this technology will ultimately be established through FDA clinical trials, our research, based upon pre-clinical studies indicates that our Bioral® technology may have the following characteristics:

All-natural ingredients. Our Bioral® drug delivery technology uses phosphatidylserine, which can be sourced from soy beans, and calcium. Phosphatidylserine from soybeans is available commercially as a nutritional supplement with FDA-allowed health promotion claims.

Encapsulation. Our Bioral® drug delivery encapsulates, or entraps within a crystal matrix, the subject drug, rather than chemically bonding with the drug.

Enhanced Availability. Our Bioral® drug delivery technology is being developed to enable oral availability of a broad spectrum of compounds, such as those with poor water solubility, and protein and peptide biopharmaceuticals, which have been difficult to administer. Our Bioral® drug delivery technology also has the potential to be applied to substances which are not currently deliverable by traditional means so that they may be delivered via injection or orally.

Minimizing Side Effects. Our Bioral® drug delivery technology may reduce toxicity, stomach irritation and other side effects of the encapsulated drug.

Cellular Delivery. Our Bioral® drug delivery technology is being developed as membrane fusion intermediates. We believe that, when drugs encapsulated in our Bioral® drug delivery technology come into close approximation to a target membrane, a fusion event between the outer layer of the cochleate cylinder and the cell membrane may occur. This fusion may result in the delivery of a small amount of the encochleated material into the cytoplasm of the target cell. Further, we believe that drugs encapsulated in our Bioral® drug delivery technology may slowly fuse or break free of the cell and be available for another fusion event, either with this or another cell.

Table of Contents

Stability. Our Bioral® drug delivery technology employs cochleates which consist of multi-layered structures of large, continuous, solid, lipid bilayer sheets, either stacked or rolled up in a spiral, with little or no internal aqueous space. We believe that our cochleate preparations can be stored in cation-containing buffer, or dried, by freezing in a high vacuum environment, to a powder, which is then stored at room temperature and reconstituted with liquid prior to administration. Our cochleate preparations have been shown to be stable for more than two years in cation-containing buffer, and at least one year as a powder at room temperature.

Resistance to Environmental Attack. Our Bioral® drug delivery technology is being developed to provide protection from degradation of the encochleated drug. Traditionally, many drugs can be damaged from exposure to adverse environmental conditions such as sunlight, oxygen, water and temperature. Since the multilayered structure consists of a series of solid layers, we believe that components within the interior of the cochleate structure remain intact, even though the outer layers of the cochleate may be exposed to these conditions.

Patient Compliance. We believe that a potential benefit of our cochleate cylinders may include reducing unpleasant taste, unpleasant intestinal irritation, and in some cases providing oral availability.

Release Characteristics. Our cochleate technology may offer the potential to be tailored to control the release of the drug depending on desired application.

Initial Bioral® Products in Development

We plan a diverse pipeline of products to be developed by applying our Bioral® drug delivery technology to a potentially broad array of established and promising pharmaceuticals. Each intended Bioral® product (i.e., drug and nutraceutical encapsulated with our drug delivery technology) will, upon completion of development, require separate FDA regulatory approval, and accordingly, will be subject to the uncertainty, time and expense generally associated with the FDA regulatory process. Even though we are targeting FDA approved, market-accepted drugs for encapsulation, each of the products currently in development face development hurdles, regulatory requirements and uncertainty before market introduction.

Bioral® Amphotericin B

Systemic fungal infections continue to be a major domestic and international health care problem. In the mid-1990s, Amphotericin B was the most commonly used drug to treat these infections in the United States. Amphotericin B is an established drug which is delivered intravenously. We are currently developing a Bioral® formulation of Amphotericin B for treatment of fungal infections which we expect will be for the treatment of esophageal candidiasis. We plan to submit an IND to the FDA and proceed into clinical trials in late 2005. In the last year, we have successfully sourced phosphatidylserine, or PS, from lecithin derived from soybeans rather than synthetic PS, thereby reducing the costs of goods for our delivery system. In addition, we have simplified our manufacturing approach to Bioral® Amphotericin B, thereby facilitating commercial scale-up. Also, we have changed the ratio of PS to active molecules, thus improving the efficacy while moderating costs. We are currently investigating the pharmacology and

Table of Contents

toxicology in animals. Accordingly, we estimate that the submission of our IND will be made in the fourth quarter of 2005. We estimate that the preclinical and clinical development costs of this formulation will be approximately $7.0 million.

Amphotericin B is an established drug which is used to a disease that frequently strikes patients with AIDS. The use of the conventional injectable Amphotericin B to treat these infections is often limited by its propensity to cause kidney damage which we believe our Bioral® products may minimize. Bioral® Amphotericin B may have uses in other diseases such as Leishmaniasis and Chagas disease.

The primary advantage which we are seeking for our proposed Amphotericin B product is an oral formulation of the drug. Additional potential advantages include improved safety, extended shelf life, improved cellular uptake and reduced dosage. Assuming that we complete development of our proposed Bioral® Amphotericin B formulation and that we obtain FDA approval, we believe that Bioral® Amphotericin B may provide an effective orally administered version of Amphotericin B which may be more effective and less toxic.

According to Visiongain, a market research firm, in 2003, the global antifungal market was approximately $6 billion and is projected to grow to as much as $8 billion by 2009. Annually, there are an estimated 500,000 severe fungal infections globally for which we believe Bioral® Amphotericin B may be an appropriate treatment. Our market research indicates that Bioral® Amphotericin B may be able to achieve peak sales of approximately $400 million annually, although no assurances can be given of this estimation.

In the development of this drug, we have collaborated with the NIH, the Public Health Research Institute of New York and the University of Kentucky. Further, we have been awarded and received all funds under a grant totaling approximately $2.7 million from the NIH to support the further development of this drug formulation.

Separately, on April 12, 2004, we licensed a topical formulation of our encochleated Amphotericin B to Accentia. Accentia is commercializing technology licensed from Mayo Foundation for Medical Education and Research for the treatment of CRS and asthma on a worldwide basis. The technology consists of using low-dose topical antifungals to control the debilitating symptoms of CRS and asthma. The license agreement was amended effective June 1, 2004, then modified in September 2004 by the asset purchase agreement with Accentia describe below, and was twice amended again in 2005 to make certain clarifications. According to the terms of the license as originally entered into, Accentia was to pay us a running royalty of 12-14% on net sales of covered products in the designated field. Accentia estimates that annual prescription cost for its CRS product will be approximately $1,000 per patient. Accentia is responsible for all expenses related to the development of an encochleated BioNasal® Amphotericin B for the indication of CRS and asthma on a worldwide basis, including expenses associated with the provision of supplies, the submission of an IND and clinical trials. We shall retain world-wide rights to the oral and intravenous formulations of encochleated Amphotericin B.

On September 8, 2004, we entered into a definitive Asset Purchase Agreement with Accentia pursuant to which we sold to Accentia an asset consisting of a royalty revenue stream in consideration of a one-time, irrevocable cash payment of $2.5 million. The royalty revenue stream sold was a fifty percent (50%) interest in the future royalties earnable by us on sales by Accentia for products utilizing our topical formulation of our encochleated Amphotericin B for the treatment of CRS, thus effectively reducing our royalty on the sales of such CRS products by 50%. We agreed with Accentia, however, that the future royalty stream sold shall not include royalty payments that are payable by Accentia based on the sale of encochleated products exclusively intended to treat asthma, and the rights to such royalty payments, as originally set forth in the license agreement, shall remain with us.

Table of Contents

Encochleated HIV Subunit Vaccine

Very few vaccine formulations have the ability to work following oral administration. Cochleates have demonstrated the capability in mice to orally deliver DNA, protein immunogens and also small molecules. They have been shown to be effective vehicles for inducing immune responses when administered by parenteral or mucosal routes. Our scientists are working to develop a safe and effective prophylactic/therapeutic HIV subunit vaccine (i.e., a vaccine that creates a bodily immunity to a virus from whose DNA the vaccine is made). The advantages of this potential vaccine may be:

- oral administration because of safety, convenience, lower cost, and the potential to induce systemic and mucosal immunity;
- stability at room temperature;
- induced protective, HIV-specific, antibody and cell mediated immunity; and
- induced systemic and mucosal immune responses.

This program is currently funded via an NIH grant which expires during 2005. We plan on evaluating a potential extension of this grant in 2005.

Bioral® NSAIDS

We have targeted inflammation disorders, such as arthritis, for development of Bioral® products, based upon accepted, unpatented, over-the-counter and prescription anti-inflammatory drugs such as generic aspirin or ibuprofen. Various types of over-the-counter anti-inflammatory compounds are currently available. Nonsteroidal anti-inflammatory drugs, or NSAIDS, significantly decrease inflammation at higher dosages. We believe that Bioral® cochleates may be used to effectively deliver anti-inflammatory drugs with reduced side effects. The primary advantages which we are seeking for our proposed Bioral® anti-inflammatory products include reduced gastrointestinal side effects, reduced required dosage and improved cellular uptake. Anti-inflammatories formulated within cochleates are inside a multi-layered solid particle which we believe may enhance the safety and efficacy profiles and could potentially transform the compounds into an entirely new class of improved anti-inflammatory drugs.

In early 2005, we announced that, in laboratory testing, we applied our licensed Bioral® nanocochleate drug delivery technology to aspirin and traditional NSAIDS that are not selective COX-2 inhibitors. We contracted with an independent testing laboratory to test Bioral® formulations of aspirin and other NSAIDs in a well-established animal model of inflammation. These proof-of-principle animal studies have demonstrated that encochleated NSAIDS enabled a statistically significant reduction in gastro-intestinal toxicity (e.g., ulceration) compared to standard formulations at clinically-relevant high doses of these NSAIDs and aspirin while providing comparable anti-inflammatory effects.

Bioral® Paclitaxel

Paclitaxel is one of the most commonly prescribed chemotherapies for solid tumors such as breast cancer. Paclitaxel is very insoluble in water and is currently available in either a cremophor formulation, which often has significant vehicle-related toxicities, or in a formulation composed as paclitaxel bound to albumin. Both are available as injections. We are working on an oral form of paclitaxel, making therapy for patients more convenient and reducing the risks associated with intravenous therapies.

Table of Contents

Bioral® siRNA

Small interfering RNA, or siRNA, is a new class of oligonucleotides that may offer the ability to identify therapeutics directly based on genomic information of the host or pathogens. Like other oligonucleotide candidates such as antisense, siRNA is very susceptible to degradation by plasma enzymes. In early 2005, we established a collaborative research agreement with a major pharmaceutical company to explore the use of our cochleate delivery technology for systemic and oral delivery of siRNA.

Other Bioral® Projects. We previously targeted the application of our licensed encochleation technology to pharmaceuticals for the treatment of tuberculosis and hereditary lysosomal storage diseases, in particular to Gaucher Disease. We have also pursued collaborative studies with a university for the purpose of determining the feasibility of applying our encochleation technology to create an oral formulation of Apo-A1, a component of HDL. As we are presently focusing our efforts on formulations which are further along in the pre-clinical and clinical stage, we decided in 2004 to place these programs on hold.

BEMA™ Technology Overview

Licensed from a third party to us through our Arius subsidiary, BEMA™ stands for bioerodible mucoadhesive. BEMA™ discs are the size of a dime and are composed of an adhesive layer and a non-adhesive backing layer made of polymers, with both layers capable of holding the desired drug. Upon application, the disc adheres to the mucosal surface (inner lining of the cheek) and delivers the dose of medication rapidly and efficiently, making it an excellent delivery system for time-critical conditions such as nausea, vomiting and breakthrough cancer pain, or trauma cases where IV lines or injections are unavailable or not practical. The BEMA™ system permits control of two critical factors allowing for better dose to dose reproducibility: (i) the contact area for mucosal drug delivery, and (ii) the time the drug is in contact with that area, known as residence time.

In contrast to competing transmucosal delivery systems like lozenges and matrix-based delivery systems placed under the tongue or sprayed in the oral cavity, BEMA™ products:

- Adhere to mucosa in seconds and dissolve in minutes;
- Permit absorption to be determined by the product, with patients not being required to swish or move the product around in the mouth for absorption;
- Have a narrow, reproducible delivery rate, not susceptible to varying or intermittent contact with mucus membranes;
- Dissolve completely, leaving no residual product or waste unlike certain other systems; and
- Cost of goods are relatively inexpensive unlike certain other systems.

Table of Contents

Emezine® and Current BEMA™ Formulations In Development

Emezine®

Through Arius, we have licensed the U.S. rights to a transmucousally delivered formulation of Emezine®, an anti-nausea and vomiting medication used for treating nausea and vomiting which occurs after surgeries and chemotherapy. This is not a BEMA formulation, but rather a formulation administered by placing a tablet between the bridge of the upper front teeth and gum where it dissolves, enabling the active ingredient to be absorbed through the lining of the cheek. We license Emezine® from Reckitt.

Anti-nausea, also known as anti-emetic, products are provided as injectable, oral and rectal formulations. Injectable products require that the patient be in a medical facility and have an intravenous injection line in place. Oral products have limitations because delayed gastric emptying that is associated with nausea and vomiting impedes the absorption of the product and actual product ingestion can be nauseating. Rectal suppositories are inconvenient as well as slow and unpredictable in onset. We believe, therefore, that an alternative delivery system is necessary for anti-emetic products, the market for which we estimate to be approximately $2 billion dollars in the United States.

We believe that our licensed Emezine® tablet:

- Will be the first transmucousally delivered anti-emetic in U.S. market place;
- May offer predictability and speed of onset similar to intravenous injections; and
- Will avoid the discomfort of injections and the inconvenience of suppositories.

Postoperative nausea and vomiting, or PONV, occurs in approximately 30% of patients undergoing operative procedures. Many factors influence the risk and severity of PONV. These include patient specific factors (age, gender), operative procedure (type and duration of procedure) anesthetic related factors (type and duration) and postoperative factors (presence of pain, oral intake). Although significant progress has been made in the prevention of symptoms, patients continue to have difficulty with PONV. Vomiting can result in dehydration, electrolyte imbalances, prolonged recovery room stay, hospital admissions and loss of work.

Anti-emetic, agents are most effective when given prior to the surgical procedure or at cessation of anesthesia and frequently must be continued for several hours after the operative procedure. Products commonly employed for prevention and treatment of PONV are limited to dopamine receptor antagonists (droperidol, prochlorperazine) and serotonin receptor antagonists (ondansetron, granisetron, dolasetron, palonosetron). Dopamine receptor antagonists were the first agents used for PONV and remain the most effective agents.

Chemotherapy induced nausea and vomiting, or CINV, occurs in 70% to 80% of patients receiving different regimes of chemotherapy. CINV is classified five (5) different ways:

Anticipatory: nausea and vomiting occurring as a conditional response from previous chemotherapy;

Acute: acutely within the first 24 hours of the patient receiving their chemotherapy regimen;

Delayed: nausea and vomiting occurring 24 hours after chemotherapy administration (may begin as early as 16 hours after chemotherapy);

Table of Contents

Breakthrough: nausea and vomiting occurring despite preventative therapy; and

Refractory: nausea and vomiting occurring during subsequent cycles of chemotherapy when anti-emetic prophylaxis or rescue therapy (or both) has failed in earlier cycles.

Various classes of drugs have efficacy against acute emetogenic chemotherapy and radiotherapy. These include dopamine receptor antagonists, cannabinoids, corticosteroids and the serotonin (5-HT3) receptor antagonists. Emezine® s active ingredient has activity against Acute, Delayed and Breakthrough CINV. Nausea and vomiting also occur in relation to other conditions such as migraine, vertigo, viral illness and the use of opiod analgesics. Dopamine receptor antagonists are utilized to treat nausea and vomiting caused by many of these conditions.

Based on our market research, we believe that Emezine® may be able to participate in the CINV, PONV and the general nausea and vomiting markets. Such research indicates that Emezine® may be able to achieve peak sales of approximately $25 million annually, although no assurances can be given of this estimation.

In February 2005, we announced that we completed the clinical studies required for our pending FDA new drug application on Emezine®, which we expect to file in the second quarter of 2005. In addition, in March 2005, we received notice from the FDA that it granted, under a small business exception, Arius request for a waiver of the FDA s human drug application fee in connection with our pending NDA for Emezine®. We believe this fee would have been approximately $672,000.

BEMA™ Fentanyl

The global market for pain medication generates annual sales of over $24 billion. Between $2 billion and $4 billion is spent to treat breakthrough pain. Breakthrough episodes of pain are the flares of pain which break through the medication used to control the persistent pain. The leading product for breakthrough cancer pain is the U.S. market is Actiq, which had reported sales of $345 million in 2004 and is projected to exceed sales of $400 million in 2005. We believe there is a clear need and growing market for additional narcotic agents in alternative dosage forms to provide rapid pain relief. Fentanyl belongs to the group of medicines called narcotic analgesics. Narcotic analgesics are used to relieve pain. The transmucosal form of fentanyl is a powerful narcotic used to treat breakthrough cancer pain. Fentanyl applied with our licensed BEMA technology has the potential meet the need for new narcotics and, we believe, will be ideal for breakthrough pain in opioid-tolerant patients.

After receiving approval for the initial indication of break-through cancer pain, we may pursue additional indications for BEMA fentanyl in:

Post-operative patients following step-down from intravenous narcotics;

Hospitalized patients or outpatients without intravenous access; and

Emergency room patients where available intravenous lines are limited or impractical.

We recently announced that we received confirmation from the U.S. Food and Drug Administration that we will be able to utilize the FDA s 505(b)(2) process for regulatory approval consideration of our licensed BEMA fentanyl formulation. As a result of this guidance, we plan to enter BEMA fentanyl into Phase III clinical studies in the second half of 2005. We estimate that the

Table of Contents

clinical development costs of this formulation will be approximately $5.35 million. We believe that BEMA fentanyl may have the potential to capture a significant share of the breakthrough cancer pain market in the U.S., which we estimate could result in annual peak sales of approximately $250 million, although no assurances can be given of this estimation.

BEMA Long Acting Analgesic

In addition to our lead BEMA product, fentanyl, we are also developing a second analgesic product with a longer duration of action suited for a broad range of pain conditions. We are working with this FDA-approved compound that has been shown to produce comparable pain relief to morphine, with an improved safety profile and extended duration of action, but poor oral bioavailability. The BEMA delivery system may enable us to provide this product in a form suitable for ambulatory care and, because of the safety advantage associated with this product, we believe that BEMA long acting analgesic will be an ideal next step product for patients with incomplete pain relief on non-narcotic analgesics.

Our proposed BEMA formulation of this long acting analgesic is intended to meet the need for a new narcotic and will be ideally used for:

- Post-operative pain; and
- Chronic pain, including lower back, osteoarthritis and rheumatoid arthritis.

We expect to submit an IND for BEMA Long Acting Analgesic in the second half of 2005. Entrance into clinical trials will follow immediately thereafter. We estimate that the clinical development costs of this formulation will be approximately $5.5 million.

Due to the ability of BEMA Long Acting Analgesic being able to participate in all four of the key pain markets (chronic pain, post-operative pain, breakthrough malignant pain, breakthrough non-malignant pain), we believe that BEMA Long Acting Analgesic has the potential to achieve a 1-2% share of the total worldwide pain market which is valued at approximately $24 billion. This would translate into an estimated $250-500 million in peak annual sales, although no assurances can be given of this estimation.

Other Projects

Autologous HIV Therapy

As part of our research and development activities, we have developed and are investigating our patented autologous (patient-specific) HIV therapy for AIDS which uses a cochleate related (proteoliposome) delivery vehicle. This immunotherapeutic is autologous meaning that it contains the specific patient s virus or membrane protein. Our autologous HIV therapy is intended to boost or alter the immune response in patients already infected with HIV.

We are currently investigating the potential cost for the research and administrative efforts that would be necessary to obtain an FDA approved IND necessary to continue this program. If these costs turn out to be prohibitively high, we may elect to not pursue this program or seek a development and commercial partner. We believe that the time, expense and risk to market for this program is substantial and uncertain, particularly when compared to that which we anticipate for the potentially broad-base of pharmaceuticals and vaccines which may ultimately be encapsulated in our cochleate drug delivery technology.

Table of Contents

Bioral Nutrient Delivery, LLC

On January 8, 2003, we formed Bioral Nutrient Delivery, LLC, a Delaware limited liability company, as a majority-owned subsidiary. BND presently has two classes of equity interests: Class A Shares and Class B Shares. As of the date of this Report, we own approximately 94.5% of BND s Class B Shares and all 708,586 of BND s Class A Shares. During 2003, we made plans to distribute to our stockholders 3,545,431 of BND s Class B Shares, or approximately 43% of BND s currently outstanding equity interests, including the Class A Shares. In early 2005, after having reevaluated this strategic opportunity, we decided to forego the planned distribution of Class B Shares and withdrew the registration statement relating to the distribution from the SEC. We presently have no intention of effecting any such distribution.

Effective April 1, 2003, we entered into an agreement with BND pursuant to which BND sublicenses from us, on an exclusive world-wide perpetual basis, our proprietary encochleation technology for use in processed food and beverages and personal care products. BND s early-stage business opportunity is based solely upon our licensed encochleation technology platform, which we utilize as a drug delivery system. Our preliminary findings suggest that, by using our encochleation technology, a variety of nutrients, which are substances with potentially beneficial properties, might be protected from degradation during the manufacturing process and delivered with substantially all of the characteristics of the nutrient intact, although no assurances can be given that we will be able to accomplish this on a large-scale basis. BND was formed to identify licensees who will apply our sublicensed technology to nutrients, and BND will seek to commercialize our delivery technology through a combination of licensing programs to manufacturing, marketing and distribution companies within food, beverage and personal care product industries. BND does not intend to manufacture market or distribute products itself.

In consideration of the sublicense grant, BND shall pay us a royalty of 8% on all revenue which BND receives from third parties. Among other things, failure to make the payment of the royalties on a timely basis shall be cause for termination of the sublicense. In addition, we may terminate the sublicense subsequent to BND s entering into sublicenses in consideration of a payment equal to six (6) times our trailing twelve (12) months gross revenues. We also reserve the right to use the technology in all ways except those covered by our sublicense agreement with BND. In order to keep our operating expenses manageable, effective April 1, 2003, BND entered into a management services and administrative agreement with us, under which we provided BND with certain resources, including use of our office in Tampa, Florida. The management services agreement with BND terminated on December 31, 2004, and given that the BND opportunity is not presently a high priority for us, we opted not to renew such agreement.

Relationship with The University of Medicine and Dentistry of New Jersey and Historical Relationship with Albany Medical College

We have had and continue to have critical relationships with UMDNJ and Albany Medical College. Some of our scientists were former researchers and educators at these Universities researching cochleate technology. All of our current research and development is done using facilities provided to us on the campus of UMDNJ, pursuant to a lease, or at the facilities of our contractors or collaborators. Both of these Universities are stockholders in our company and have a substantial financial interest in our business.

In September 1995, we entered into a license agreement with the Universities to be the exclusive worldwide developer and sub-licensor of the cochleate technology. Under the license agreement, we and the Universities have also jointly patented certain aspects of the cochleate technology and co-own such patents with them.

Table of Contents

Pursuant to the license agreement, we agreed that each University would be issued an equity interest in our capital stock, originally equal to 2% of our outstanding capital stock. These arrangements were subsequently revised in December, 2002. On December 16, 2002, we amended our license agreement with the Universities to provide for a decrease in the royalty payments to be paid to the Universities on sublicenses in consideration of an increase in the royalty on product sales and the issuance to the Universities of options to purchase shares of our common stock. As of December 31, 2004, UMDNJ owns 139,522 shares (including shares issued under a research agreement) and warrants to purchase 8,951 shares of our common stock at $3.05 and 75,000 options to purchase our common stock at a price per share of $2.37. As of December 31, 2004, Albany Medical College owns 2,222 shares of our common stock and warrants to purchase 9,951 shares of our common stock at $3.05 and 75,000 options to purchase our common stock at a price per share of $2.37. There are no further requirements to provide either University any additional equity interests in our company.

The license agreement, as amended, grants us an exclusive license to the cochleate technology owned by these Universities and obligates us to pay a royalty fee structure as follows:

(a) For commercial sales made by us or our affiliates, we shall pay to the Universities a royalty equal to 5% of net sales of cochleate products; and

(b) For commercial sales of cochleate products made by any of our sublicensees, we shall pay to the Universities royalties up to 5% of our revenues received from the sublicensee from the sale of such products.

Our royalty payments to the Universities will be divided equally among them pursuant to the license. In 2004, we accrued a $125,000 royalty payment to the Universities in connection with our $2.5 million asset sale to Accentia.

In April 2001, we entered into a research agreement with UMDNJ whereby we agreed with UMDNJ to share the rights to new research and development that jointly takes place at UNDNJ s facilities until December 31, 2005. We also agreed to provide UNDNJ with progress and data updates and allow its researchers to publish certain projects. We lease our research facilities totaling approximately 8,000 square feet located on their campus pursuant a lease agreement ending December 31, 2005. The monthly rent was $3,340 for 2001, $3,840 for 2002, $4,340 for 2003, $4,840 for 2004 and $5,340 for 2005. We plan to enter into discussions with UMDNJ during 2005 regarding a possible extension or renewal of this lease. No assurances can be given that we will be able to extend or renew the lease, and we may decide to relocate, scale back and/or outsource such operations.

In addition to our rent payments, we have also agreed to pay for certain other services provided by UNDNJ. These include two employees from UNDNJ for a total of $209,811.45, a budget to purchase supplies and chemicals (adjusted to exact cost), and an indirect cost factor constituting 8% for 2001 (12% in 2002, 16% in 2003, 20% for 2004 and 24% for 2005) of the direct costs of the employee costs and chemicals.

Collaborative and Supply Relationships

We are a party to collaborative agreements with universities, government agencies, corporate partners, and contractors. Research collaboration may result in new inventions which are generally considered joint intellectual property. Our collaboration arrangements are intended to provide us with access to greater resources and scientific expertise in addition to our in-house capabilities. We also have supply arrangements with a few of the key component producers of our delivery technology. Our relationships include:

15

Table of Contents

Atrix Laboratories, Inc. On May 27, 2004, Arius entered into a worldwide, exclusive royalty-bearing license agreement with Atrix to develop, market, and sell products incorporating Atrix s BEMA technology, including its BEMA fentanyl product, and to use the BEMA trademark in conjunction therewith. The BEMA delivery technology consists of an easy to use, dissolvable, dime-sized polymer disc that is applied to the mucus membrane of the mouth. All research and development related to the BEMA technology, including three existing Investigational New Drug Applications, have been transferred to Arius in accordance with the Atrix license agreement.

Under the terms of the Atrix license agreement, Arius is required to pay Atrix: (i) an upfront licensing fee of $1 million, which was paid in August 2004, (ii) additional cash payments upon achievement of certain developmental and regulatory milestones, (iii) for reimbursement for research and development support, and (iv) royalties on commercial sales of all BEMA products. A joint development management committee comprised of representatives of Arius and Atrix oversees product development. Arius is responsible for the research and development of the products, including costs and expenses, and for their sale, marketing, manufacture, and distribution, provided that, under the terms of a clinical supply agreement between Atrix and Arius entered into pursuant to the license agreement, Atrix shall provide Arius with certain supplies of BEMA fentanyl product for clinical trials for a limited period of time, at Arius expense. Atrix retains certain co-promotion rights to the BEMA fentanyl product.

Reckitt Benckiser Healthcare (UK) Limited. Effective January 6, 2004, Arius entered into an exclusive royalty-bearing license with Reckitt Benckiser Healthcare (UK) Limited to develop, market, and sell Reckitt s Emezine® (buccal prochlorperazine maleate) product for the treatment of nausea and vomiting in the United States, and to use the Emezine® trademark in conjunction therewith. Under the terms of the license agreement, Arius is required to pay Reckitt: (i) an upfront licensing fee, which has been previously paid in accordance with the Reckitt agreement, (ii) an additional cash payment upon achievement of a certain developmental and regulatory milestone, and (iii) royalties on commercial sales of the licensed product. Arius will be responsible for the development of the product, including costs and expenses, and for its sale, marketing, and distribution in the United States. In addition, Arius shall be required to obtain from Reckitt, and Reckitt shall be required to supply to Arius, at Arius expense, all product to be sold under the license.

Sigma-Tau. In January 2005, we signed a definitive licensing agreement with Sigma-Tau Pharma for the application of our Bioral® nanocochleate delivery technology to formulate up to four proprietary pharmaceutical compounds currently under development by Sigma-Tau Pharma. Simultaneously with this licensing agreement, we entered into a stock purchase agreement with, and received a non-refundable upfront payment of US$250,000 from, Sigma-Tau. This upfront payment was made in consideration of unregistered shares of our common stock priced at $4.25 a share. The stock purchase agreement with Sigma-Tau provides for the acquisition by Sigma-Tau, upon the occurrence of specified developmental milestones associated with the license, of additional unregistered shares of our common stock, up to an aggregate potential of $1.5 million worth of such shares. These milestones lead up to and include the submission of product INDs by Sigma-Tau Pharma for one or more of the four subject encochleated compounds.

Table of Contents

PPDI. On December 31, 2002, we entered into an agreement with PPDI, pursuant to which PPDI was granted a license to apply our Bioral® nano-delivery technology to two therapeutic products. In connection therewith, we received a $2 million up-front royalty payment. In addition, the terms of the license require additional royalty payments based on regulatory milestones and a running royalty rate based on worldwide sales.

Potential siRNA Partner. We have entered into a pre-evaluation agreement with a major pharmaceutical company focusing on siRNA targets. The goal of the agreement is to generate proof of concept of the ability of our nanochocleates to successfully formulate the siRNA targets. After proof of concept is achieved, the agreement has an option to progress these targets to therapeutics at which time royalties will be discussed.

National Institutes of Health. To investigate the properties of new antifungal cochleate formulations. Grants totaling approximately $2.7 million have been awarded to us by NIH for the development of our proposed Amphotericin B product. Additionally, we are conducting anti-fungal studies using our Bioral® drug delivery technology through NIH selected and paid contractors. The NIH has reserved broad and subjective authority over future disbursements under the grant. While no objective or specific milestones for future disbursements have been established by the NIH, we must generally demonstrate to the satisfaction of the NIH that our research and use of proceeds are consistent with the goal of developing a formulation for the oral delivery of Amphotericin B. Furthermore, we are required to submit to the NIH an annual report of activities under the grant. To date we have received all expected disbursements under the NIH grant and anticipate that no future disbursements will be made by the NIH under the terms of the grant.

Public Health Research Institute of New York. To investigate our proposed Amphotericin B product and other anti-fungal applications of our drug delivery technology. This relationship may involve shared expense reimbursement and shared intellectual property with regard to joint inventions.

We also have agreements with entities that are affiliated with and partially-owned by key members of our board of directors and management to conduct research and license certain proposed drugs. See Certain Relationships and Related Transactions for affiliations with our management.

As of December 31, 2001, our board of directors appointed an audit committee consisting of independent directors to review all agreements and transactions which have been entered into with related parties, as well as all future related party transactions. At the meeting the independent board members, with Dr. O Donnell abstaining, and after seeking and reviewing advice from an independent valuation firm and inquiring about the details of the various transactions, ratified all prior related party transactions. Subsequent to this meeting, the audit committee independently ratified these agreements. During 2004, after compliance with our internal policies and procedures, we also entered into several new related party contracts. The following are the related-party agreements entered into prior to our initial public offering and subsequently:

Accentia Biopharmaceuticals, Inc. We have several business relationships with Accentia Biopharmaceuticals, Inc. and its affiliates. HCG, which is controlled by Dr. Frank O Donnell, our Chairman and CEO and which owns a significant percentage of our common stock as of the date of this Report, as well as all of our Series B Convertible Preferred Stock, is a significant stockholder of Accentia. In addition, Dr. O Donnell is also the Chairman and CEO of Accentia. Also, Alan Pearce, a member of our board of directors, is the CFO of Accentia and James A. McNulty, our Secretary, Treasurer and CFO, is the Treasurer and Corporate Secretary of Accentia.

Table of Contents

Amphotericin B License. On April 12, 2004, we licensed a topical formulation of our encochleated Amphotericin B to Accentia. Accentia is commercializing technology licensed from Mayo Foundation for Medical Education and Research for the treatment of CRS and asthma on a worldwide basis. The technology consists of using low-dose topical antifungals to control the debilitating symptoms of CRS and asthma. Accentia is responsible for all expenses related to the development of an encochleated BioNasal® Amphotericin B for the indications of CRS and asthma on a worldwide basis, including expenses associated with the provision of supplies, the submission of an IND and clinical trials. We shall retain world-wide rights to the oral and intravenous formulations of encochleated Amphotericin B.

Arius/TEAMM Distribution Agreement. On March 17, 2004, Arius granted exclusive marketing and sales rights in the United States to TEAMM Pharmaceuticals, Inc., or TEAMM, with respect to Arius licensed Emezine® product for the treatment of nausea and vomiting. TEAMM is a specialty pharmaceutical company and wholly-owned subsidiary of Accentia. As part of this agreement, TEAMM has agreed to pay for the development costs of Emezine®. We received development cost reimbursements of $1.0 million in 2004 from Accentia in connection with this agreement.

Analytica International Market Studies. During 2004, Analytica International, a provider of research, commercialization, and communications services to the pharmaceutical and biotechnology industries and a subsidiary of Accentia, performed two market studies for us. We paid Analytica $47,800 for these reports, some of which we paid in 2005.

RetinaPharma Technologies, Inc. We previously entered into a license agreement with this development-stage biotechnology company to use our delivery technology in connection with their proposed nutraceutical product with potential application for macular degeneration and retinitus pigmentosa, a disease affecting the retina, and through an agreement with Tatton Technologies, LLC (which subsequently merged into RetinaPharma), certain apoptotic drugs and apoptotic naturally occurring substances to treat certain neuro-degenerative diseases. This exclusive worldwide right to use our Bioral® drug delivery technology in conjunction with their effort to develop, commercialize and manufacture their proposed products, or to sublicense to a third party, is only for the purpose of treating antiapoptotic pharmaceutical and nutraceutical treatment of retinal disease and glaucoma. These licenses shall remain in effect as long as RetinaPharma remains in compliance with the terms of the agreements. HCG, one of our significant stockholders, and Dr. Francis E. O Donnell, Jr., our Chief Executive Officer and Chairman, are affiliated as stockholders and a director of RetinaPharma.

Biotech Specialty Partners, LLC. We have entered into a non-exclusive distribution agreement with Biotech Specialty Partners, LLC, or BSP, a development-stage distribution company, to market and distribute our proposed products once we have completed the commercialization of our products. Our financial arrangement with BSP requires us to sell to BSP all of our proposed products, as and when purchased by with BSP at a cost which is the lesser of:

(i) ten percent (10%) below the lowest wholesale acquisition cost, inclusive of rebates, quantity discounts, etc.; and

Table of Contents

(ii) the lowest cost at which we are then selling the product(s) to any other purchaser. The term of the agreement shall be for a term of five years once a product becomes available for distribution. BSP is a start-up enterprise, which to date has not distributed any pharmaceutical products.

These agreements generally provide that, except for on-going development costs related to our cochleate drug delivery technology, we are not required to share in the costs of the development of the pharmaceutical product or technologies of these companies. In connection with our acquisition of Arius, BSP waived its rights under its distribution agreement with us with respect to all of Arius products. HCG, which is affiliated with Dr. Francis E. O Donnell, Jr., our Chairman and CEO, are affiliated as stockholders, and a member of the management, of

We are entitled to receive the following royalty and other payments:

Accentia Biopharmaceuticals, Inc. Under our license agreement with Accentia as originally entered into, Accentia was to pay us a running royalty of 12-14% on net sales in the U.S. of its CRS and asthma products in the designated field. On September 8, 2004, we entered into a definitive Asset Purchase Agreement with Accentia pursuant to which we sold to Accentia an asset consisting of a royalty revenue stream in consideration of a one-time, irrevocable cash payment of $2.5 million. The royalty revenue stream sold was a fifty percent (50%) interest in the future royalties earnable by us on sales by Accentia for products utilizing our topical formulation of our encochleated Amphotericin B for the treatment of CRS, thus effectively reducing our royalty on the sales of such CRS products by 50%. We agreed with Accentia, however, that the future royalty stream sold shall not include royalty payments that are payable by Accentia based on the sale of encochleated products exclusively intended to treat asthma, and the rights to such royalty payments, as originally set forth in the license agreement, shall remain with us.

TEAMM Pharmaceuticals, Inc. Under Arius distribution agreement with TEAMM, TEAMM: (i) has previously paid to Arius an upfront fee, (ii) has previously paid to Arius an initial milestone payment and shall in the future pay to Arius certain additional milestone payments upon achievement of certain developmental and regulatory milestones, (iii) shall support Arius clinical development costs with respect to such product, and (iv) shall pay royalties to Arius based on the sales of such product. In addition, Arius shall be obligated to supply TEAMM, at TEAMM s expense, with such products for sale and promotional use. We received development cost reimbursements of $1.0 million in 2004 from Accentia in connection with this agreement.

RetinaPharma Technologies, Inc. We are entitled to 10% of all net revenue from the sale for the authorized use of our technology incorporated into the proposed products with potential application to various neuro-degenerative diseases. The planned RetinaPharma products are in early stage development and no sales of such products or royalty revenue therefrom is anticipated in the foreseeable future. We are also entitled to 10% of all net revenue from the sale for the authorized use of our technology incorporated into RetinaPharma s proposed product with potential application to various neuro-degenerative diseases. This latter product (which was transferred to RetinaPharma in its merger with Tatton Technologies, LLC) is in its early stage of development and no sales of such product or royalty revenue therefrom is anticipated in the foreseeable future.

Table of Contents

In pursuing potential commercial opportunities, we intend to seek and rely upon additional collaborative relationships with corporate partners. Such relationships may include initial funding, milestone payments, licensing payments, royalties, access to proprietary drugs or potential applications of our drug delivery technologies or other relationships. Our agreements with PPDI, Accentia and Sigma-Tau are examples of these types of relationships, and we will continue to seek other similar arrangements.

Licenses, Patents and Proprietary Information

Our interest in the intellectual property is subject to and burdened by various royalty payment obligations and by other material contractual or license obligations.

In general, the patent position of biotechnology and pharmaceutical firms is frequently considered to be uncertain and involve complex legal and technical issues. There is considerable uncertainty regarding the breadth of claims allowed in such cases and the degree of protection afforded under such patents. While we believe that our intellectual property position is sound and that we can develop our new drug delivery technologies and our HIV therapies, we cannot provide any assurances that our patent applications will be successful or that our current or future intellectual property will afford us the desired protection against competitors. It is possible that our intellectual property will be successfully challenged or that patents issued to others may preclude us from commercializing our drugs.

Other parties could have patent rights which may block our products. We are aware of two issued United States patents dealing with lipid formulations of Amphotericin B products. The first of these patents, United States Patent No. 4,978,654, claims an Amphotericin B liposome product. We do not believe that our patent or technology are in conflict with this existing patent, although there can be no assurance that a court of law in the United States patent authorities might determine otherwise. Our belief is based upon the fact that our cochleate product does not contain liposomes, which is required by the issued claims of this patent. The second of these patents, United States Patent No. 5,616,334, claims a composition of a lipid complex containing Amphotericin B defined during prosecution as a ribbon structure. Our Bioral® nano-encapsulation technology uses cochleates which are not ribbon structures. Accordingly, we do not believe that we require a license under this patent. We are also aware of United States Patent No. 6,585,997, related to mucoadhesive erodible drug delivery devices. We do not believe that our BEMA fentanyl product is in conflict with the existing patent, at least because there are limitations recited in the issued claims that are not met by our product. Accordingly, we do not believe that we require a license under this patent. If a court were to determine that we infringe any of these patents and that these patents are valid, we might be required to seek one or more licenses to commercialize our Bioral® formulation of Amphotericin B and/or our BEMA products. There can be no assurance that we would be able to obtain such licenses from the patent holders. In addition, if we were unable to obtain a license, or if the terms of the license were onerous, there may be a material adverse effect upon our business plan to commercialize these products.

Most of the inventions claimed in our cochleate patents were made with the United States government support. Therefore, the United States government has certain rights in the technology, and we have certain obligations to the U.S. government, which could be inconsistent with our plans for commercial development of products and/or processes. We believe to the extent the United States government would have rights in our licensed Bioral® technology due to their funding, we have to either obtain a waiver from the United States government relating to the United States government s rights in the technology, or have agreements with the United States government which would grant us exclusive rights.

Table of Contents

We rely on trade secrets and confidentiality agreements with collaborators, advisors, employees, consultants, vendors and other service providers. We cannot assure you that these agreements will not be breached or that our trade secrets will not otherwise become known or be independently discovered by competitors. Our business would be adversely affected if our competitors were able to learn our secrets or if we were unable to protect our intellectual property.

Cochleate Technology

With respect to our cochleate technology and liposome technology related to our autologous HIV therapy, we are the owner and/or the exclusive licensee of nine issued United States patents and five foreign issued patents owned by the parties listed in the chart below. We believe that our licenses to this intellectual property will enable us to develop this new drug delivery technology based upon cochleate and cochleate related technology. Our intellectual property strategy is intended to maximize our potential patent portfolio, license agreements, proprietary rights and any future licensing opportunities we might pursue. With regard to our Bioral® cochleate technology, we intend to seek patent protection for not only our delivery technology, but also potentially for the combination of our delivery technology with various drugs no longer under patent protection. Below is a table summarizing patents we believe are currently important to our business and technology position.

Patent Number	Issued	Expires	Title	Owner
EUR0722338	07/25/2001	09/30/2014	Protein - and peptide cochleate vaccines methods of immunizing using the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US06,165,502	12/26/2000	09/11/2016	Protein-lipid vesicles and autogenous immunotherapeutic comprising the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US06,153,217	11/28/2000	01/22/2019	Nanocochleate formulations, process of preparation and method delivery of pharmaceutical agents	BioDelivery Sciences International, Inc., The University of Medicine and Dentistry of New Jersey and Albany Medical College
US06,592,894	07/15/2003	01/22/2019	Nanocochleate formulations, process of preparation and method delivery of pharmaceutical agents	BioDelivery Sciences International, Inc., The University of Medicine and Dentistry of New Jersey and Albany Medical College
AUS722647	11/23/2000	09/02/2017	Protein-lipid vesicles and autogenous immunotherapeutic comprising the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College

Table of Contents

Patent Number	Issued	Expires	Title	Owner
US05,994,318	11/30/1999	11/24/2015	Cochleate delivery vehicles	The University of Medicine and Dentistry of New Jersey and Albany Medical College
EUR 812209	05/06/2004	02/22/2016	Cochleate delivery vehicles for biologically relevant molecules	The University of Medicine and Dentistry of New Jersey and Albany Medical College
CA 2,246,754	10/22/2002	02/21/2017	Cochleate delivery vehicles	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US05,840,707	11/24/1998	11/24/2015	Stabilizing and delivery means of biological molecules	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US05,834,015	11/10/1998	9/11/2016	Protein-lipid vesicles and autogenous immunotherapeutic comprising the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College
AUS689505	02/02/1998	09/30/2014	Protein - or peptide - cochleate immunotherapeutics and methods of immunizing using the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US05,643,574	07/01/1997	07/01/2014	Protein - or peptide - cochleate immunotherapeutics methods of immunizing using the same	The University of Medicine and Dentistry of New Jersey and Albany Medical College
US04,871,488	10/03/1989	10/03/2006	Reconstituting viral glycoproteins into large phospholipid vesicles	Albany Medical College
US04,663,161	05/05/1987	04/22/2005	Liposome methods and compositions	Albany Medical College

Through Arius, we license from Atrix the following U.S. and foreign patents and patent applications relating to the BEMA™ technology:

Application Number	Country	Application Date	Patent Number	Grant Date	Expiration Date	Title
08/734,519	US	10/18/1996	5,800,832	09/01/1998	10/18/2016	Bioerodable Film for Delivery of Pharmaceutical Compounds to Mucosal Surfaces

Table of Contents

Application Number	Country	Application Date	Patent Number	Grant Date	Expiration Date	Title
09/144,827	US	09/01/1998	6,159,498	12/12/2000	10/18/2006	(same as above)
09/069,703	US	04/29/1998	Pending			Pharmaceutical Carrier Device Suitable for Delivery of Pharmaceutical Compounds to Mucosal Surfaces
09/684,682	US	10/04/2000	Pending			(same as above)
10/962,833	US	10/12/2004	Pending			(same as above)
10/763,063	US	01/22/2004	Pending			Bioerodible Film for Delivery of Pharmaceutical Compounds to Mucosal Surfaces
10/706,603	US	11/12/2003	Pending			Adhesive Bioerodible Ocular Drug Delivery System
60/495,356	US	08/15/2003				Adhesive Bioerodible Transmucosal Drug Delivery System
US97/18605	PCT	10/16/1997	N/A	N/A	N/A	Pharmaceutical Carrier Device Suitable for Delivery of Pharmaceutical Compounds to Mucosal Surfaces
4757497	Australia	10/16/1997	729516	05/17/2001	10/16/2017	(same as above)
2,268,187	Canada	10/16/1997	Pending		10/16/2017	(same as above)
2001508037	Japan	10/16/1997	Pending		10/16/2017	(same as above)
9791047	EP*	10/16/1997	0973497	12/11/02	10/16/2017	(same as above)
US99/09378	PCT	04/29/1999	N/A	N/A	N/A	(same as above)
3967899	Australia	04/29/1999	746339		04/29/2019	(same as above)
2,329,128	Canada	04/29/1999	Pending		04/29/2019	(same as above)
2002512950	Japan	04/29/1999	Pending		04/29/2019	(same as above)
99922753	EP	04/29/1999	1079813	02/09/05	04/29/2019	(same as above)
10/121,430	US	04/11/2002	Pending			Process for Loading a Drug Delivery Device
US03/11313	PCT	04/11/2003	N/A	N/A	N/A	(same as above)

* Validated in the following European countries: Austria, Belgium, Switzerland, Germany, Denmark, Spain, France, United Kingdom, Greece, Ireland, Italy, Netherlands, Sweden.

Emezine®

With respect to Emezine®, through Arius, we license from Reckitt U.S. Patent No. 4,717,723, issued January 5, 1988, entitled Pharmaceutical Compositions.

Table of Contents

BEMA Trademark

In addition, in March 2005, we received notification from Atrix, from whom we license the trademark BEMA , that Atrix received an office action from the U.S. Patent and Trademark Office rejecting their application for such mark. Based on our discussions with Atrix, we believe it may be possible to overcome any objections that the trademark examiner may have, and we have requested that Atrix continue to pursue the mark aggressively. No assurances can be given, however, that Atrix will be able to overcome such objections, and if such objections are not resolved to the examiner s satisfaction, we may be denied federal trademark protection for this mark.

Competition

The biopharmaceutical industry in general is competitive and subject to rapid and substantial technological change. Developments by others may render our proposed Bioral® or BEMA technologies, proposed drug formulations (including Emezine®) and HIV therapies under development noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Below are some examples of companies seeking to develop potentially competitive technologies. Many of these entities have significantly greater research and development capabilities than do we, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. In addition, acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors research, financial, marketing, manufacturing and other resources. Such potential competitive technologies may ultimately prove to be safer, more effective or less costly than any drugs which we are currently developing or may be able to develop. Additionally, our competitive position may be materially affected by our ability to develop or successfully commercialize our drugs and technologies before any such competitor.

Cochleate Technology

While many development activities are private, and therefore we cannot know what research or progress has actually been made, we are not aware of any other drug delivery technology using a naturally occurring drug delivery vehicle or carrier that can be used to simultaneously address two important clinical goals: oral delivery of drugs that normally require injection and targeted cell delivery once the drug is in the body.

Included among the companies which we believe are developing potentially competitive technologies are Emisphere Technologies, Inc. (NASDAQ: EMIS) and Novavax, Inc. (NASDAQ: NVAX), each a publicly traded company, and CyDex, Inc and NOBEX Corporation, each a privately-held company. We believe that these potential competitors are seeking to develop and commercialize technologies for the oral delivery of drugs which may require customization for various therapeutics or groups of therapeutics. While our information concerning these competitors and their development strategy is limited, we believe our technology can be differentiated because our cochleate technology is seeking to deliver a potential broad base of water soluble and water insoluble (fat or lipid soluble) compounds with limited customization for each specific drug.

We believe that our technology may have cell-targeted delivery attributes as well. Additional companies which are developing potentially competitive technologies in this area may include Valentis

Table of Contents

Inc. (NASDAQ: VLTS) and Enzon Pharmaceuticals Inc. (NASDAQ: ENZN), both publicly traded companies, and Flamel Technologies and Inex Pharmaceuticals Corporation, both of which are privately-held companies, which we believe may be seeking to develop technologies for cell-targeted delivery of drugs. American Pharmaceutical Partners (NASDAQ: APPX) has recently received approval for Abraxane, which is a formulation of paclitaxel, which is bound to albumin. This provides for cellular delivery via the gp60 receptor. While we have limited information regarding these potential competitors and their development status and strategy, we believe that our technology may be differentiated because unlike these potential competitors, we seek to use our cochleate to encapsulate the therapeutic to achieve drug delivery into the interior of the cells such as inflammatory cells.

Although the competitors mentioned above are developing drug delivery techniques conceptually similar to ours with respect to encapsulation, or more specifically nano-encapsulation, we believe that our approach is different, proprietary and protected under our licensed and patented technology. One primary way we can be differentiated from our competitors is in our approach of using naturally occurring substances to form a cochleate which encapsulates the drug in a scroll-like multilayered delivery vehicle.

BEMA

Included among the companies which we believe are developing potentially competitive technologies to BEMA are Hollis Eden (NASDAQ: HEPH), a publicly traded company, and TransOral Pharmaceuticals, a privately-held company. We believe that these potential competitors are seeking to develop and commercialize technologies for the buccal delivery for various therapeutics or groups of therapeutics. While our information concerning these competitors and their development strategy is limited, we believe our technology can be differentiated because the BEMA technology provides for a consistent dose based on how the BEMA technology adheres to the buccal membrane and dissolves over a predetermined rate. We are aware that Access Pharmaceuticals is developing a technology which is similar to BEMA. We are exploring options in defense of our patent position in regard to this technology.

For BEMA fentanyl, in the breakthrough cancer pain area, we believe the most advanced competitors are Cephalon (NASDAQ: CEPH) and Endo Pharmaceutical Holdings (NASDAQ: ENDP) both publicly traded companies. Cephalon s lead product for this indication is Actiq which generated $345 million in sales in 2004. Cephalon will license this product to Barr Laboratories upon approval of OraVescent Fentanyl. This product utilizes an effervescent tablet which is administered buccally. Endo has licensed, from Orexo Pharmaceuticals AB, Rapinyl, which is a polymer formulated sublingual fentanyl tablet indicated for breakthrough cancer pain. This product is administered sublingually. Generex Biotechnology and Arakis, Ltd. are developing sublingual spray formulations of opioids for breakthrough pain. LAB International, Inc. and Delex Therapeutics, Inc are developing inhaled formulations of fentanyl for administration either nasally or across the alveoli in the lungs. While we have limited information regarding these potential competitors and their development status and strategy, we believe that our technology may be differentiated because unlike these potential competitors, BEMA fentanyl has a predefined residence time on the buccal membrane providing for consistent drug delivery from dose to dose. We believe that all of the competitive formulations fentanyl will have intra-dose variability.

Emezine®

The nausea and vomiting market is well established with many established pharmaceutical companies marketing products as well as generic versions of older, non patent protected products. The primary classes are the 5HT3 antagonists, the dopamine antagonists, the substance P antagonists, and the antihistamines. The 5HT3 antagonists account for the largest share of the market with

Table of Contents

GlaxoSmithKline s (NSYE: GSK) Zofran(tablets, injection and solution), which presently accounts for the largest share of the market. MGI Pharma s (NASDAQ: MOGN) Aloxiinjection is the newest entry into the market and has gained significant share in a short period of time in the CINV market. Merck s (NYSE: MRK) Emendtablet has the highest revenue of the non 5HT3 drugs. Emend is available by tablet. The rest of the market is covered by the phenothiazines (dopamine antagonists) and antihistamines. These are generically available by injection, tablet or suppository. Emezine will be differentiated in this market due to the buccal route of administration.

Autologous HIV Therapy

In terms of our Autologous HIV therapy, we believe that competitors may also be working on patient-specific therapies for cancer. However, we are not aware of any competitors currently attempting to develop patient-specific therapies for HIV. This does not, however, mean that there are not any now or that there will not be in the future. Vaccines can be used for prophylactic (prevention of infection), or therapeutic (treatment following infection) applications. The patient-specific therapeutic, which we are attempting to develop, is intended to boost or alter the immune response in patients already infected with HIV. For the most part, HIV vaccines in development, about which we are aware, are being targeted specifically to prevent infection. However, some of these vaccines may also prove useful for therapeutic applications. As such, these could prove to be competitive with our autologous therapeutic. We are aware of a product in development, EradicAide, by Adventrx Pharmaceuticals (AMEX: ANX) which utilizes a similar mechanism to elicit a cellular based response to attack HIV infected cells. We believe our therapeutic HIV vaccine is superior due to it being tailored to each patient. With the advent of multiple mutations giving the virus resistance to conventional HIV therapies, our product is intended to be tailored to attack that particular virus potentially, thus potentially allowing for a higher degree of efficacy through this specificity.

Manufacturing

During drug development and the regulatory approval process, we plan to rely on third-party manufacturers to produce our compounds for research purposes and for pre-clinical and clinical trials. Except as provided for under our license agreement with Reckitt for Emezine®, we do not presently have manufacturing arrangements with respect to our intended product. Emezine® will be manufactured by Reckitt in Hall, England. This facility has been inspected by the FDA and is currently used for the manufacture of other products sold in the U.S. The formulation for BEMA fentanyl development, and initial clinical trial material for the manufacturer, will be done by Dow Pharmaceutical Sciences and Atrix, respectively. We are in the process of finalizing an agreement for the manufacture of large scale clinical trial suppliers and a NDA stability batch with a commercial scale manufacturer that currently produces products for the US market on identical equipment to that planned for BEMA manufacture. As our intended products near market introduction, we intend to outsource manufacturing to third party manufacturers, which comply with the FDA s applicable Good Manufacturing Practices. While we believe that such commercial manufacturing arrangements may be available, no such relationships have been establish to date.

We have and intend to purchase component raw materials from various suppliers. As our intended products near market introduction, we intend to seek multiple suppliers of all required components although there may not actually be more than one at that time.

Sales and Marketing

Our marketing strategy, assuming completion of our drug delivery technologies, product and formulation development and regulatory approval, are to market and sell our approved formulations and

26

Table of Contents

products under the Bioral®, BEMA or other brand names which we either own or license from third parties through our Arius subsidiary. The Arius commercial efforts will be primarily focused on the hospital/oncology/surgery areas to maintain cost efficiency. We plan to initiate the sales organization around the launch of BEMA fentanyl with 75-100 representatives focused on physicians, hospitals and groups who treat cancer patients. For sales and marketing into primary care and geographies outside of the United States, we will explore a wide range of potential arrangements, such as licensing, direct sales, co-marketing, joint venture and other arrangements. Such arrangements may be with large or small pharmaceutical companies, general or specialty distributors, biotechnology companies, physicians or clinics, or otherwise. We have licensed the commercial rights to Emezine® to TEAMM Pharmaceuticals, a subsidiary of Accentia. TEAMM is responsible for the sales and marketing of Emezine®. We have a non-exclusive distribution arrangement with Biotech Specialty Partners, LLC, an early-stage alliance of specialty pharmaceutical and biotechnology companies, although BSP has waived its rights with respect to Arius products.

Government Regulation

The manufacturing and marketing of any drug or nutraceutical which we formulate with our licensed encochleation or BEMA technologies, our autologous HIV therapeutic and Emezine®, as well as our related research and development activities, are subject to regulation for safety, efficacy and quality by numerous governmental authorities in the United States and other countries. We anticipate that these regulations will apply separately to each drug formulation with our drug delivery technologies. We believe that complying with these regulations will involve a considerable level of time, expense and uncertainty.

In the United States, drugs are subject to rigorous federal regulation and, to a lesser extent, state regulation. The Federal Food, Drug and Cosmetic Act, as amended, and the regulations promulgated thereunder, and other federal and state statutes and regulations govern, among other things, the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising and promotion of our drugs. Drug development and approval within this regulatory framework is difficult to predict and will take a number of years and involve the expenditure of substantial resources.

The steps required before a pharmaceutical agent may be marketed in the United States include:

1. Laboratory and clinical tests for safety and small scale manufacturing of the agent;

2. The submission to the FDA of an IND which must become effective before human clinical trials can commence;

3. Clinical trials to characterize the product and establish its safety and efficacy in the intended patient population;

4. The submission of a NDA or Biologic License Application to the FDA; and

5. FDA approval of the NDA or Biologic License Application prior to any commercial sale or shipment of the product.

In addition to obtaining FDA approval for each product, each product-manufacturing establishment must be registered with, and approved by, the FDA. Manufacturing establishments are subject to biennial inspections by the FDA and must comply with the FDA s Good Manufacturing Practices for products, drugs and devices.

27

Table of Contents

Pre-clinical Trials

Pre-clinical testing includes laboratory evaluation of chemistry and formulation, as well as tissue culture and animal studies to assess the safety and potential efficacy of the product. Pre-clinical safety tests must be conducted by laboratories that comply with FDA regulations regarding Good Laboratory Practices. No assurance can be given as to the ultimate outcome of such pre-clinical testing. The results of pre-clinical testing are submitted to the FDA as part of an IND and are reviewed by the FDA prior to the commencement of clinical trials. Unless the FDA objects to an IND, clinical studies may begin thirty (30) days after the IND is submitted.

We intend to largely rely upon contractors to perform pre-clinical trials.

Clinical Trials

Clinical trials involve the administration of the investigational product to healthy volunteers or to patients under the supervision of a qualified investigator. Clinical trials must be conducted in accordance with Good Clinical Practices under protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol must be submitted to the FDA prior to its conduct. Further, each clinical study must be conducted under the auspices of an independent institutional review board at the institution where the study will be conducted. The institutional review board will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution. The drug product used in clinical trials must be manufactured according to Good Manufacturing Practices.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the product into healthy human subjects, the drug is tested for safety (adverse side effects), absorption, dosage tolerance, metabolism, bio-distribution, excretion and pharmacodynamics (clinical pharmacology). Phase II is the proof of principal stage and involves studies in a limited patient population in order to:

Asses the potential efficacy of the product for specific, targeted indications;

Identify the range of doses likely to be effective for the indicator; and

Identify possible adverse side effects and safety risks.

When there is evidence that the product may be effective and has an acceptable safety profile in Phase II evaluations, Phase III trials are undertaken to establish the clinical efficacy and the safety profile of the product within a larger population at geographically dispersed clinical study sites. Phase III frequently involves randomized controlled trials and, whenever possible, studies are conducted in a manner so that neither the patient nor the investigator knows what treatment is being administered. We, or the FDA, may suspend clinical trials at any time if it is believed that the individuals participating in such trials are being exposed to unacceptable health risks.

We intend to rely upon third party contractors to advise and assist us in the preparation of our INDs and clinical trials that will be conducted under the INDs. Two (2) studies were conducted in 2004 under the Emezine® IND. Multiple studies will be conducted in 2005 under the IND for

BEMA fentanyl and for Bioral® Amphotericin B.

Table of Contents

New Drug Application and FDA Approval Process

The results of the manufacturing process development work, pre-clinical studies and clinical studies are submitted to the FDA in the form of a New Drug Application for approval to market and sale of the product. The testing and approval process is likely to require substantial time and effort. In addition to the results of preclinical and clinical testing, the NDA applicant must submit detailed information about chemistry, manufacturing and controls that will describe how the product is made. The approval process is affected by a number of factors, including the severity of the disease, the availability of alternative treatments and the risks and benefits demonstrated in clinical trials. Consequently, there can be no assurance that any approval will be granted on a timely basis, if at all. The FDA may deny a New Drug Application if applicable regulatory criteria are not satisfied, require additional testing or information or require post-marketing testing (Phase IV) and surveillance to monitor the safety of a company s product if it does not believe the NDA contains adequate evidence of the safety and efficacy of the drug. Moreover, if regulatory approval of a drug is granted, such approval may entail limitations on the indicated uses for which it may be marketed. Finally, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. Post approval studies may be conducted to explore further intervention, new indications or new product uses.

Among the conditions for NDA approval is the requirement that any prospective manufacturer s quality control and manufacturing procedures conform to Good Manufacturing Practices and the specifications approved in the NDA. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of drug and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, also are subject to inspections by or under the authority of the FDA and by other federal, state or local agencies. Additionally, in the event of non-compliance, FDA may issue warning letters and seek criminal and civil penalties, enjoin manufacture, seize product or revoke approval.

International Approval

Whether or not FDA approval has been obtained, approval of a product by regulatory authorities in foreign countries must be obtained prior to the commencement of commercial sales of the drug in such countries. The requirements governing the conduct of clinical trials and drug approvals vary widely from country to country, and the time required for approval may be longer or shorter than that required for FDA approval. Although there are some procedures for unified filings for certain European countries, in general, each country at this time has its own procedures and requirements.

Other Regulation

In addition to regulations enforced by the FDA, we are also subject to regulation under the Controlled Substances Act, the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential future federal, state or local regulations. Our research and development may involve the controlled use of hazardous materials, chemicals, and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of any accident, we could be held liable for any damages that result and any such liability could exceed our resources.

Table of Contents

Employees

As of March 21, 2005, we had 22 full-time employees, of which 10 are laboratory scientists and 12 are involved in our operations, administration, accounting and IT. Eight of our scientists have Ph.D. degrees and two have medical degrees. None of our employees are covered by collective bargaining agreements. From time to time, we also employ independent contractors to support our engineering and support and administrative functions. We consider relations with our employees to be good. Each of our current scientific personnel has entered into confidentiality and non-competition agreements with us.

Risk Factors

An investment in our company is extremely risky. You should carefully consider the following risks, in addition to the other information presented in this Report before deciding to buy or exercise our securities. If any of the following risks actually materialize, our business and prospects could be seriously harmed, the price and value of our securities could decline and you could lose all or part of your investment.

Risks Related to Our Technologies

The failure to complete development of our drug delivery technologies, obtain government approvals, including required FDA approvals, or to comply with ongoing governmental regulations could delay or limit introduction of our proposed formulations and products and result in failure to achieve revenues or maintain our ongoing business.

Our research and development activities and the manufacture and marketing of our proposed formulations and products are subject to extensive regulation for safety, efficacy and quality by numerous government authorities in the United States and abroad. Before receiving FDA clearance to market our proposed formulations and products, we will have to demonstrate that our formulations and products are safe and effective on the patient population and for the diseases that are to be treated. Clinical trials, manufacturing and marketing of drugs are subject to the rigorous testing and approval process of the FDA and equivalent foreign regulatory authorities. The Federal Food, Drug and Cosmetic Act and other federal, state and foreign statutes and regulations govern and influence the testing, manufacture, labeling, advertising, distribution and promotion of drugs and medical devices. As a result, clinical trials and regulatory approval can take a number of years or longer to accomplish and require the expenditure of substantial financial, managerial and other resources.

In order to be commercially viable, we must successfully research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute formulations or products incorporating our technologies. For each drug or nutraceutical that we formulate with our drug delivery technologies and for our HIV therapies, as the case may be, we must successfully meet a number of critical developmental milestones, including:

- demonstrate benefit from delivery of each specific drug through our drug delivery technologies;
- demonstrate through pre-clinical and clinical trials that our drug delivery technologies and our HIV therapies are safe and effective; and

30

Table of Contents

establish a viable Good Manufacturing Process capable of potential scale-up.

The time-frame necessary to achieve these developmental milestones may be long and uncertain, and we may not successfully complete these milestones for any of our proposed formulations or products in development.

In addition to the risks previously discussed, our HIV immunotherapeutic is subject to additional developmental risks, which include the following:

uncertainties arising from the rapidly growing scientific aspects of HIV and potential treatments;

uncertainties arising as a result of the broad array of potential treatments related to HIV;

anticipated expense and time believed to be associated with the development and regulatory approval of treatments for HIV; and

availability of corporate resources to dedicate to this project and the potential that this project will not be a priority for us.

In order to conduct clinical trials that are necessary to obtain approval by FDA to market a formulation or product, it is necessary to receive clearance from the FDA to conduct such clinical trials. The FDA can halt clinical trials at any time for safety reasons or because we or our clinical investigators do not follow the FDA s requirements for conducting clinical trials. If we are unable to receive clearance to conduct clinical trials or the trials are halted by the FDA, we would not be able to achieve any revenue from such product as it is illegal to sell any drug or medical device for human consumption without FDA approval.

Moreover, it is our stated intention to attempt to avail ourselves of the FDA s 505(b)(2) approval procedure, which we believe is less costly and time consuming. If this approval pathway is not available to us with respect to a particular formulation or product, the time and cost associated with developing and commercialize such formulations or product may be prohibitive.

Data obtained from clinical trials are susceptible to varying interpretations, which could delay, limit or prevent regulatory clearances.

Data already obtained, or in the future obtained, from pre-clinical studies and clinical trials do not necessarily predict the results that will be obtained from later pre-clinical studies and clinical trials. Moreover, pre-clinical and clinical data is susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. A number of companies in the pharmaceutical industry including those involved in competing drug delivery technologies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to adequately demonstrate the safety and effectiveness of a proposed formulation or product under development could delay or prevent regulatory clearance of the potential drug, resulting in delays to commercialization, and could materially harm our business. Our clinical trials may not demonstrate sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our drugs, and thus our proposed drugs may not be approved for marketing.

Table of Contents

Competitors in the drug development industry may develop competing technology.

Drug companies and/or other technology companies may seek to develop and market nanoencapsulation or mucosal adhesive technologies which may compete with our technologies. While we believe that our technologies have certain advantages over potential competitors, competitors may develop similar or different technologies which may become more accepted by the marketplace.

Our HIV therapies may not gain FDA approval in clinical trials or be effective as a therapeutic against the HIV virus which could affect our future profitability.

In order to obtain regulatory approvals of our autologous and subunit HIV therapies, we must demonstrate that these procedures are safe and effective for use in humans and function as therapeutics against the HIV virus. We may not be able to demonstrate that our proposed HIV therapies are safe or effective in advanced clinical trials that involve human patients. We are also not able to assure that the results of the clinical trials already conducted and which we intend to conduct will support our applications for regulatory approval. As a result, our HIV therapy programs may be curtailed, redirected or eliminated at any time. The HIV virus is very complex and may be prone to genetic mutations. These mutations have produced strains of HIV that are resistant to currently approved therapeutics. Even if we gain regulatory approval for our autologous or subunit HIV therapies, the virus may develop similar resistance to our treatment. This could have a material adverse effect on our business, financial condition and results of operations.

Moreover, to date, we have only conducted a pilot study pursuant to Institutional Review Board oversight in anticipation of our initial FDA submission for our autologous HIV therapy. We are currently investigating the potential cost for the research and administrative efforts that would be necessary to obtain the FDA approved IND necessary to continue this program. If these costs turn out to be prohibitively high, we may elect to not pursue this program. In addition, our subunit HIV vaccine program is currently funded via an NIH grant which expires during 2005. We plan on evaluating a potential extension of this grant in 2005. We may be unsuccessful is securing additional grant money or other funds to continue this program.

Risks Relating to Our Business

Since we have a limited operating history and have not generated any revenues from the sale of products to date, you cannot rely upon our limited historical performance to make an investment decision.

Since our inception in January 1997 and through December 31, 2004, we have recorded accumulated losses totaling $13,495,104. As of December 31, 2004, we had a working capital deficit of $357,000. Our ability to generate revenue and achieve profitability depends upon our ability, alone or with others, to complete the development of our proposed formulations and products, obtain the required regulatory approvals and manufacture, market and sell our proposed formulations and products.

Although we have earned some licensing-related revenue to date, we have not generated any revenue from the commercial sale of our proposed formulations or products or any drugs or nutraceuticals to which we have applied our technologies. Since our inception, we have engaged primarily in research and development, licensing technology, seeking grants, raising capital and recruiting scientific and management personnel, although we have more recently begun to focus on commercialization activities as well with the acquisition of Arius. We have not generated revenues to date other than research grants, limited licensing or royalty revenues and a $2.5 million sale of a royalty revenue stream to Accentia.

This limited history may not be adequate to enable you to fully assess our ability to develop and commercialize our technologies and proposed formulations or products, obtain FDA approval and achieve market acceptance of our proposed formulations or products and respond to competition. No assurances can be given as to exactly when, if at all, we will be able to fully develop, commercialize, market, sell and derive material revenues from our proposed formulations or products in development.

Table of Contents

We will need to raise additional capital to continue our operations or we may be unable to fund our operations, promote our formulations or products or develop our technologies.

Our operations have relied almost entirely on external financing to fund our operations. Such financing has historically primarily come from the sale of common and preferred stock and convertible debt to third parties and to a lesser degree from loans and revenue from license and royalty fees. We anticipate, based on our current proposed plans and assumptions relating to our operations (including the timetable of, and costs associated with, new product development) and financings we have undertaken subsequent to December 31, 2004, that our current working capital will be sufficient to satisfy our contemplated cash requirements at least through December 31, 2005. We will need to raise additional capital to fund our anticipated operating expenses and future expansion. Among other things, external financing will be required to cover our operating costs. We cannot assure you that financing whether from external sources or related parties will be available if needed or on favorable terms. If additional financing is not available when required or is not available on acceptable terms, we may be unable to fund our operations and planned growth, develop or enhance our technologies, take advantage of business opportunities or respond to competitive market pressures. Any negative impact on our operations may make capital raising more difficult and may also result in a lower price for our securities.

We may have difficulty raising needed capital in the future because of our limited operating history and business risks associated with our company.

Our business currently does not generate any sales, and revenue from grants and collaborative agreements may not be sufficient to meet our future capital requirements. We do not know when this will change. We have expended and will continue to expend substantial funds in the research, development and clinical and pre-clinical testing of our drug delivery technologies and, potentially, our autologous HIV immunotherapeutic. We will require additional funds to conduct research and development, establish and conduct clinical and pre-clinical trials, commercial-scale manufacturing arrangements and to provide for the marketing and distribution. Additional funds may not be available on acceptable terms, if at all. If adequate funds are unavailable from any available source, we may have to delay, reduce the scope of or eliminate one or more of our research, development or commercialization programs or product launches or marketing efforts which may materially harm our business, financial condition and results of operations.

During 2004, we exhausted substantially all of the proceeds from our June 2002 initial public offering. Our long term capital requirements are expected to depend on many factors, including:

- number of potential formulations and technologies in development;
- continued progress and cost of our research and development programs;
- progress with pre-clinical studies and clinical trials;
- time and costs involved in obtaining regulatory clearance;
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

costs of developing sales, marketing and distribution channels and our ability to sell our drug or nutraceutical formulations or products;

Table of Contents

costs involved in establishing manufacturing capabilities for commercial quantities of our drug or nutraceutical formulations or products;

competing technological and market developments;

market acceptance or our drug or nutraceutical formulations or products;

costs for recruiting and retaining employees and consultants; and

costs for training physicians.

We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. We may seek to raise any necessary additional funds through the exercising of our public warrants, equity or debt financings, collaborative arrangements with corporate partners or other sources, which may be dilutive to existing stockholders or otherwise have a material effect on our current or future business prospects. If adequate funds are not available, we may be required to significantly reduce or refocus our development and commercialization efforts with regards to our delivery technologies and our proposed formulations and products.

Our additional financing requirements could result in dilution to existing stockholders.

The additional financings which we have undertaken and which we will require have and may in the future be obtained through one or more transactions which have or will effectively dilute the ownership interests of our stockholders. Further, we may not be able to secure such additional financing on terms acceptable to us, if at all. We have the authority to issue additional shares of common stock and preferred stock, as well as additional classes or series of ownership interests or debt obligations which may be convertible into any one or more classes or series of ownership interests. We are authorized to issue 45 million shares of common stock and 5 million shares of preferred stock. Such securities may be issued without the approval or other consent of our stockholders.

We currently rely on the facilities of the University of Medicine and Dentistry of New Jersey for all of our research and development activities, which activities could be materially delayed should we lose access to those facilities.

We have no research and development facilities of our own. As of the date of this Report, we are entirely dependent on third parties to use their facilities to conduct research and development. To date, we have relied on the University of Medicine and Dentistry of New Jersey and Albany Medical College for this purpose, as well as third party providers of testing and trial services. Additionally, the Universities own certain of the patents to our encochleation drug delivery technology. Our inability to conduct research and development, or our inability to find suitable third party providers of research and development services on an outsourcing basis, may delay or impair our ability to gain FDA approval and commercialization of our drug delivery technologies, formulations and products.

We plan to enter into discussions with UMDNJ during 2005 regarding a possible extension or renewal of this lease. No assurances can be given that we will be able to extend or renew the lease, and we may decide to relocate, scale back and/or outsource such operations. Should the lease expire or if we are otherwise are required to relocate on short notice, we do not currently have an alternate facility where we could relocate. The cost and time to establish or locate an alternative research and development facility to develop our technologies, other than through the

Universities, or to find suitable third party

Table of Contents

providers of research and development services on an outsourcing basis, could be substantial and might delay gaining FDA approval and commercializing our formulations and products, assuming that we have not defaulted on the terms of our intellectual property licenses and can continue with our approval process.

We are dependent on our collaborative agreements for the development of our drug delivery technologies and business development which exposes us to the risk of reliance on the viability of third parties.

In conducting our research and development activities, we rely upon numerous collaborative agreements with universities, governmental agencies, manufacturers, contract research organizations and corporate partners. The loss of or failure to perform under any of these arrangements, by any of these entities, may substantially disrupt or delay our research and development and commercialization activities, including our in-process and anticipated clinical trials. This loss may also increase our expenses and materially harm our business, financial condition and results of operation.

We have a license agreement with the University of Medicine and Dentistry of New Jersey and Albany Medical College in which they grant us exclusive license to conduct research and development of the encochleation drug delivery technology. Our research facilities are also located on the premises of the University of Medicine and Dentistry of New Jersey pursuant to a research agreement. In addition, our BEMA technology and Emezine® product are licensed from third parties.

To date, almost all of our funding for research and operations have come from grants and other types of funding from corporate sponsors and the NIH. We will continue to be dependent upon the NIH, in particular, to develop our Bioral® Amphotericin B. Furthermore, we anticipate that research and development of our HIV therapy will primarily depend on funding from the federal government.

Our two National Institutes of Health grants have either expired or are set to expire, which could deny us important funding.

In 2001, the National Institutes of Health awarded us a Small Business Innovation Research Grant (SBIR) which we utilized in our research and development efforts relating to our Bioral® Amphotericin B formulation. We have received all anticipated funding under this grant to date, and this grant expired in August 2004. In 2002, the NIH awarded us a second SBIR grant which we have utilized in our research and development efforts relating to our encochleated HIV subunit vaccine. We have received anticipated funding under this second grant to date, and the grant is set to expire on July 31, 2005. Although we may seek additional NIH funding for either of these programs, we may choose not to seek such funding or such funding may be unavailable to us. The absence of additional funding from the NIH could impair our ability to further develop our Bioral® Amphotericin B formulation or our encochleated HIV subunit vaccine. Furthermore, as a result of these expirations, we are anticipating a decline in sponsored research revenue with associated NIH grant expenditures in 2005.

We are exposed to product liability, clinical and preclinical liability risks which could place a substantial financial burden upon us, should we be sued, because we do not currently have product liability insurance above and beyond our general insurance coverage.

Our business exposes us to potential product liability and other liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical formulations and products. Such claims may be asserted against us. In addition, the use in our clinical trials of pharmaceutical formulations and products that our potential collaborators may develop and the subsequent sale of these formulations or

35

Table of Contents

products by us or our potential collaborators may cause us to bear a portion of or all product liability risks. A successful liability claim or series of claims brought against us could have a material adverse effect on our business, financial condition and results of operations.

Since we do not currently have any FDA-approved products or formulations, we do not currently have any product liability insurance, and we maintain liability insurance relating only to clinical trials on Emezine®. We cannot assure you that we will be able to obtain or maintain adequate product liability insurance on acceptable terms, if at all, or that such insurance will provide adequate coverage against our potential liabilities. Furthermore, our current and potential partners with whom we have collaborative agreements with or our future licensees may not be willing to indemnify us against these types of liabilities and may not themselves be sufficiently insured or have sufficient liquidity to satisfy any product liability claims. Claims or losses in excess of any product liability insurance coverage that may be obtained by us could have a material adverse effect on our business, financial condition and results of operations.

Acceptance of our formulations or products in the marketplace is uncertain and failure to achieve market acceptance will prevent or delay our ability to generate revenues.

Our future financial performance will depend, at least in part, upon the introduction and customer acceptance of our proposed pharmaceutical or nutraceutical formulations or products. Even if approved for marketing by the necessary regulatory authorities, our formulations or products may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

- receipt of regulatory clearance of marketing claims for the uses that we are developing;
- establishment and demonstration of the advantages, safety and efficacy of our technologies;
- pricing and reimbursement policies of government and third-party payors such as insurance companies, health maintenance organizations and other health plan administrators;
- our ability to attract corporate partners, including pharmaceutical companies, to assist in commercializing our proposed formulations or products; and
- our ability to market our formulations or products.

Physicians, patients, payors or the medical community in general may be unwilling to accept, utilize or recommend any of our proposed formulations or products. If we are unable to obtain regulatory approval, commercialize and market our proposed formulations or products when planned, we may not achieve any market acceptance or generate revenue.

We may be sued by third parties who claim that our drug or nutraceutical formulations or products infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of medical patents.

We may be exposed to future litigation by third parties based on claims that our technologies, formulations, products or activities infringe the intellectual property rights of others or that we have misappropriated the trade secrets of others. This risk is exacerbated by the fact that the validity and breadth of claims covered in medical technology patents and the breadth and scope of trade secret protection involve complex legal and factual questions for which important legal principles are unresolved. Any litigation or claims against us, whether or not valid, could result in substantial costs,

Table of Contents

could place a significant strain on our financial resources and could harm our reputation. Most of our license agreements require that we pay the costs associated with defending this type of litigation. In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease selling, making, using, importing, incorporating or using any of our technologies and/or formulations or products that incorporate the challenged intellectual property, which would adversely affect our revenue;

- obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or

- redesign our formulations or products, which would be costly and time-consuming.

Other parties could have patent rights which may block our products. We are aware of two issued United States patents dealing with lipid formulations of Amphotericin B products. The first of these patents, United States Patent No. 4,978,654, claims an Amphotericin B liposome product. We do not believe that our patent or technology are in conflict with this existing patent, although there can be no assurance that a court of law in the United States patent authorities might determine otherwise. Our belief is based upon the fact that our cochleate product does not contain liposomes, which is required by the issued claims of this patent. The second of these patents, United States Patent No. 5,616,334, claims a composition of a lipid complex containing Amphotericin B defined during prosecution as a ribbon structure. Our Bioral® nano-encapsulation technology uses cochleates which are not ribbon structures. Accordingly, we do not believe that we require a license under this patent. We are also aware of United States Patent No. 6,585,997, related to mucoadhesive erodible drug delivery devices. We do not believe that our BEMA fentanyl product is in conflict with the existing patent, at least because there are limitations recited in the issued claims that are not met by our product. Accordingly, we do not believe that we require a license under this patent. If a court were to determine that we infringe any of these patents and that these patents are valid, we might be required to seek one or more licenses to commercialize our Bioral® formulation of Amphotericin B and/or our BEMA products. There can be no assurance that we would be able to obtain such licenses from the patent holders. In addition, if we were unable to obtain a license, or if the terms of the license were onerous, there may be a material adverse effect upon our business plan to commercialize these products.

Most of the inventions claimed in our Bioral® patents were made with the United States government support. Therefore, the United States government has certain rights in the technology, and we have certain obligations to the U.S. government, which could be inconsistent with our plans for commercial development of products and/or processes. We believe to the extent the United States government would have rights in our licensed Bioral® technology due to their funding, we have to either obtain a waiver from the United States government relating to the United States government s rights in the technology, or have agreements with the United States government which would grant us exclusive rights.

In addition, in March 2005, we received notification from Atrix, from whom we license the trademark BEMA , that Atrix received an office action from the U.S. Patent and Trademark Office rejecting their application for such mark. Based on our discussions with Atrix, we believe it may be possible to overcome any objections that the trademark examiner may have, and we have requested that Atrix continue to pursue the mark aggressively. No assurances can be given, however, that Atrix will be able to overcome such objections, and if such objections are not resolved to the examiner s satisfaction, we may be denied federal trademark protection for this mark.

Table of Contents

As of the date of this Report, and except as discussed above, we have not engaged in discussions, received any communications, nor do we have any well-founded reason to believe that any third party is challenging or has the right proper legal authority to challenge our intellectual property rights or those of the actual patent holders.

If we are unable to adequately protect or enforce our rights to intellectual property or secure rights to third-party patents, we may lose valuable rights, experience reduced market share, assuming any, or incur costly litigation to protect such rights.

Our ability to obtain license to patents, maintain trade secret protection and operate without infringing the proprietary rights of others will be important to our commercializing any formulations or products under development. The current and future development of our drug delivery technologies is contingent upon whether we are able to maintain a license to access the patents. Without this license, the technologies would be protected from our use and we would not be able to even conduct research without prior permission from the patent holder. Therefore, any disruption in access to the technologies could substantially delay the development of our technologies.

The patent positions of biotechnology and pharmaceutical companies, including ours which involves licensing agreements, are frequently uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications and any issued and licensed patents may not provide protection against competitive technologies or may be held invalid if challenged or circumvented. Our competitors may also independently develop drug delivery technologies or products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. law.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements provide that all materials and confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual s relationship with us shall be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology. We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology.

Although our trade secrets and technical know-how are important, our continued access to the patents is a significant factor in the development and commercialization of our drug delivery technologies. Aside from the general body of scientific knowledge from other drug delivery processes and lipid technology, these patents, to the best of our knowledge and based upon our current scientific data, are the only intellectual property necessary to develop and apply our Bioral® and BEMA drug delivery systems to the drugs or nutraceuticals to which we are attempting to apply them. We do not believe that we are violating any other patents in developing our technologies.

We may have to resort to litigation to protect our rights for certain intellectual property, or to determine their scope, validity or enforceability. Enforcing or defending our rights is expensive, could cause diversion of our resources and may not prove successful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technologies to develop or sell competing products.

Table of Contents

Key components of our cochleate drug delivery technologies may be provided by sole or limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs.

Certain components used in our research and development activities, such as lipids, are currently purchased from a single or a limited number of outside sources. For example, we currently purchase our lipid supplies from Chemi, a subsidiary of Italfarmico. The reliance on a sole or limited number of suppliers could result in:

potential delays associated with research and development and clinical and pre-clinical trials due to an inability to timely obtain a single or limited source component;

potential inability to timely obtain an adequate supply of required components; and

potential for reduced control over pricing, quality and timely delivery.

We do not have long-term agreements with any of our suppliers, and therefore the supply of a particular component could be terminated without penalty to the supplier. Any interruption in the supply of components could cause us to seek alternative sources of supply or manufacture these components internally. If the supply of any components is interrupted, components from alternative suppliers may not be available in sufficient volumes within required timeframes, if at all, to meet our needs. This could delay our ability to complete clinical trials, obtain approval for commercialization or commence marketing; or cause us to lose sales, incur additional costs, delay new product introductions or harm our reputation. Furthermore, components from a new supplier may not be identical to those provided by the original supplier. Such differences if they exist could affect product formulations or the safety and effectiveness of our products that are being developed.

We have limited manufacturing experience and once our drug or nutraceutical formulations or products are approved, we may not be able to manufacture sufficient quantities at an acceptable cost.

We remain in the research and development and clinical and pre-clinical trial phase of product commercialization. Accordingly, once our proposed formulations or products are approved for commercial sale, we will need to establish the capability to commercially manufacture our formulations or products in accordance with FDA and other regulatory requirements. We have limited experience in establishing, supervising and conducting commercial manufacturing. If we fail to adequately establish, supervise and conduct all aspects of the manufacturing processes, we may not be able to commercialize our formulations or products. We do not presently own manufacturing facilities necessary to provide clinical or commercial quantities of our proposed formulations or products.

We presently plan to rely on third party contractors to manufacture part or all of our proposed formulations or products. This may expose us to the risk of not being able to directly oversee the production and quality of the manufacturing process. Furthermore, these contractors, whether foreign or domestic, may experience regulatory compliance difficulty, mechanic shut downs, employee strikes, or any other unforeseeable acts that may delay production.

Table of Contents

Due to our limited marketing, sales and distribution experience, we may be unsuccessful in our efforts to sell our formulations or products, enter into relationships with third parties or develop a direct sales organization.

Except for our non-exclusive distribution agreement with BioTech Specialty Partners, Inc., a development-stage company affiliated with Dr. Francis E. O Donnell, a member of our management and significant beneficial owner of our securities, and the agreement between Arius and TEAMM Pharmaceuticals, also an affiliate of Dr. O Donnell, relating to Emezine®, we have yet to establish marketing, sales or distribution capabilities for our proposed formulations or products. Until such time as our proposed formulations or products are further along in the regulatory process, we will not devote any meaningful time and resources in this regard. At the appropriate time, we intend to enter into agreements with third parties to sell our proposed formulations or products, or we may develop our own sales and marketing force. We may be unable to establish or maintain third-party relationships on a commercially reasonable basis, if at all. In addition, these third parties may have similar or more established relationships with our competitors.

If we do not enter into relationships with third parties for the sales and marketing of our proposed formulations or products, we will need to develop our own sales and marketing capabilities. We have limited experience in developing, training or managing a sales force. If we choose to establish a direct sales force, we may incur substantial additional expenses in developing, training and managing such an organization. We may be unable to build a sales force on a cost effective basis or at all. Any such direct marketing and sales efforts may prove to be unsuccessful. In addition, we will compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts may be unable to compete against these other companies. We may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all.

We may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our formulations or products;
- cease operations with little or no notice to us; or
- offer, design, manufacture or promote competing formulations or products.

If we fail to develop sales, marketing and distribution channels, we would experience delays in generating sales and incur increased costs, which would harm our financial results.

If we are unable to convince physicians as to the benefits of our proposed formulations or products, we may incur delays or additional expense in our attempt to establish market acceptance.

Broad use of our drug delivery technologies may require physicians to be informed regarding our proposed pharmaceutical formulations or products and the intended benefits. The time and cost of such an educational process may be substantial. Inability to successfully carry out this physician education process may adversely affect market acceptance of our proposed formulations or products. We may be unable to timely

educate physicians regarding our intended pharmaceutical formulations or products in sufficient numbers to achieve our marketing plans or to achieve product acceptance. Any delay in physician education may materially delay or reduce demand for our formulations or products. In addition, we may expend significant funds toward physician education before any acceptance or demand for our formulations or products is created, if at all.

Table of Contents

If an event of default occurs under the convertible note issued to Laurus, it could seriously harm our operations.

On February 22, 2005, we issued a $2.5 million secured convertible term note to Laurus. The note and related agreements contain numerous events of default which include:

- failure to pay interest, principal payments or other fees when due;
- breach by us of any material covenant or term or condition of the note or any agreement made in connection therewith;
- breach by us of any material representation or warranty made in the note or in any agreement made in connection therewith;
- default on any indebtedness exceeding, in the aggregate, $100,000, to which we or our subsidiaries are a party;
- assignment for the benefit of our creditors, or a receiver or trustee is appointed for us;
- bankruptcy or insolvency proceeding instituted by or against us and not dismissed within 30 days;
- money judgment entered or filed against us for more than $100,000 and remains unresolved for 30 days;
- failure to timely deliver shares of common stock when due upon conversions of the note;
- common stock suspension for 10 consecutive days or 10 days during any 30 consecutive days from a principal market, provided that we are unable to cure such suspension within 30 days or list our common stock on another principal market within 60 days; and
- loss, damage or encumbrance upon collateral securing the Laurus debt which is valued at more than $100,000 and is not timely mitigated.

If we default on the note and the holder demands all payments due and payable, the cash required to pay such amounts would most likely come out of working capital, which may not be sufficient to repay the amounts due. In addition, since we rely on our working capital for our day to day operations, such a default on the note could materially adversely affect our business, operating results or financial condition to such extent that we are forced to restructure, file for bankruptcy, sell assets or cease operations. Further, our obligations under the note are secured by substantially all of our assets. Failure to fulfill our obligations under the note and related agreements could lead to loss of these assets, which would be detrimental to our operations.

Table of Contents

The restrictions on our activities contained in the Laurus financing documents could negatively impact our ability to obtain financing from other sources.

So long as 25% of the principal amount of the Laurus note is outstanding, the Laurus financing documents restrict us from obtaining additional debt financing without Laurus approval and subject to certain specified exceptions. To the extent that Laurus declined to approve a debt financing that does not otherwise qualify for an exception to the consent requirement, we would be unable to obtain such debt financing. In addition, subject to certain exceptions, we have granted to Laurus a right of first refusal to provide additional financing to us in the event that we propose to engage in additional debt financing or to sell any of our equity securities. Laurus right of first refusal could act as a deterrent to third parties which may be interested in providing us with debt financing or purchasing our equity securities. To the extent that such a financing is required for us to conduct our operations, these restrictions could materially adversely impact our ability to achieve our operational objectives.

Low market prices for our common stock would result in greater dilution to our shareholders, and could negatively impact our ability to convert the Laurus debt into equity.

The market price of our common stock significantly impacts the extent to which the Laurus debt is convertible into shares of our common stock. The lower the market price of our common stock as of the respective times of conversion, the more shares we will need to issue to Laurus to convert the principal and interest payments then due. If the market price of our common stock falls below certain thresholds, we will be unable to convert any such repayments of principal and interest into equity, and we will be required to make such repayments in cash. Our operations could be materially adversely impacted if we are required to make repeated cash payments on the unrestricted portion of the Laurus debt.

Risks Related to Our Industry

The market for our proposed formulations and products is rapidly changing and competitive, and new drug delivery mechanisms, drug delivery technologies, new HIV therapeutics, new drugs and new treatments which may be developed by others could impair our ability to maintain and grow our business and remain competitive.

The pharmaceutical and biotechnology industries are subject to rapid and substantial technological change. Developments by others may render our technologies and proposed formulations or products noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities and budgets than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors financial, marketing, manufacturing and other resources.

We are engaged in the development of drug delivery technologies. As a result, our resources are limited and we may experience technical challenges inherent in such technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competition. Some of these technologies may have an entirely different approach or means of accomplishing similar therapeutic effects compared to our technology. Our competitors may develop drug delivery technologies and drugs that are safer, more effective or less costly than our proposed formulations or products and, therefore, present a serious competitive threat to us.

42

Table of Contents

The potential widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our formulations or products, even if commercialized. Many of our targeted diseases and conditions can also be treated by other medication or drug delivery technologies. These treatments may be widely accepted in medical communities and have a longer history of use. The established use of these competitive drugs may limit the potential for our technologies, formulations and products to receive widespread acceptance if commercialized.

If users of our proposed formulations or products are unable to obtain adequate reimbursement from third-party payors, or if new restrictive legislation is adopted, market acceptance of our proposed formulations or products may be limited and we may not achieve revenues.

The continuing efforts of government and insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

Our ability to commercialize our proposed formulations or products will depend in part on the extent to which appropriate reimbursement levels for the cost of our proposed formulations and products and related treatments are obtained by governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payors are increasingly challenging the prices charged for medical drugs and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and drugs, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices for or rejection of our drugs.

We could be exposed to significant drug liability claims which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.

The testing, manufacture, marketing and sale of our proposed drug or nutraceutical formulations involve an inherent risk that product liability claims will be asserted against us. We currently have a general liability policy with an annual aggregate limit of $2 million with a $1 million limit per occurrence which does not provide coverage for product liability. All of our pre-clinical trials have been and all of our proposed clinical and pre-clinical trials are anticipated to be conducted by collaborators and third party contractors. We currently have insurance relating to product liability or insurance related to clinical or pre-clinical trials only with respect to our Emezine® formulation, for which we have a clinical trial liability policy providing for a $2 million aggregate limit. We intend to seek additional insurance against such risks before our product sales are commenced, although there can be no assurance that such insurance can be obtained at such time, or even if it is available, that the cost will be affordable. Even if we obtain insurance, it may prove inadequate to cover claims and/or litigation costs. The cost and availability of such insurance are unknown. Product liability claims or other claims related to our proposed formulations and products, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant settlement amounts or judgments. Any successful product liability or other claim may prevent us from obtaining adequate liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be

Table of Contents

available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our drug delivery technology. A product liability claim could also significantly harm our reputation and delay market acceptance of our proposed formulations and products.

Our business involves environmental risks related to handling regulated substances which could severely affect our ability to conduct research and development of our drug delivery technology

In connection with our research and development activities and our manufacture of materials and drugs, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development may in the future involve the controlled use of hazardous materials, including but not limited to certain hazardous chemicals and narcotics. The current hazardous chemicals that we currently use, which may change as our research progresses, are chloroform and methanol. We are authorized to use these and other hazardous chemicals in our facilities through our affiliation with the University Medicine and Dentistry of New Jersey. The university also disposes these chemicals from our premises as part of our agreement to use the facilities and carries general liability insurance in this regard.

Although we believe that our safety procedures for storing, handling and disposing of such materials will comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

Risks Related to Our Management and Key Employees

We depend upon key personnel who may terminate their employment with us at any time, and we will need to hire additional qualified personnel.

Our success will depend to a significant degree upon the continued services of key management, technical, and scientific personnel, including Drs. Francis O Donnell, Mark Sirgo, Andrew Finn, Raphael Mannino and Mr. James McNulty. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to development or approval, loss of sales and diversion of management resources. In addition, our success will depend on our ability to attract and retain other highly skilled personnel, including research scientists. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all.

We have key man life insurance policy for Dr. Raphael Mannino in the amount of $2.0 million. This insurance may not adequately compensate us for the loss of Dr. Mannino s services. Additionally, neither our Chairman and CEO, Dr. Frank O Donnell, our President and Chief Operating Officer, Dr. Mark Sirgo, nor any of our other executives currently has this coverage. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

Table of Contents

Executive officers, directors and entities affiliated with them have substantial control over, which could delay or prevent a change in our corporate control favored by our other stockholders.

As of the date of this Report, our directors, executive officers and principal stockholders, together with their affiliates, will beneficially own, in the aggregate, approximately 68.0% of our outstanding common stock. These figures do not reflect our outstanding shares of Series A Preferred, the vast majority of which is held by Drs. Sirgo and Finn, our outstanding shares of Series B Preferred, all of which is held by HCG, an affiliate of Dr. O Donnell or our convertible note with Laurus. Additionally, these figures do not reflect any future potential exercise of our Class A warrants or other outstanding warrants into shares of common stock or the increased percentages that our officers and directors may have in the event that they exercise any of the options granted to them under our Amended and Restated 2001 Stock Option Plan or if they otherwise acquire additional shares of common stock generally. The interests of our current officer and director stockholders may differ from the interests of other stockholders. As a result, these current officer and director stockholders would have the ability to exercise control over all corporate actions requiring stockholder approval, irrespective of how our other stockholders may vote, including the following actions:

election of directors;

adoption of or amendments to stock option plans;

amendment of charter documents;

issuance of blank check preferred stock; or

approval of certain mergers and other significant corporate transactions, including a sale of substantially all of our assets.

Certain of our management team have relationships which may potentially result in conflicts of interests.

Dr. O Donnell, who is an executive officer, on our board of directors and also is a substantial beneficial owner of our securities, including all of our outstanding shares of Series B Preferred, has a financial interest in a number of other companies which have business relationships with us. These companies include Accentia, RetinaPharma Technologies, Inc., Biotechnology Specialty Partners, Inc, and American Prescription Partners, Inc. We have entered into license agreements with Accentia and RetinaPharma International, Inc. with regard to proposed products incorporating our Bioral® technology. We have entered into a non-exclusive distribution with Biotechnology Specialty Partners, Inc. Each of these business arrangements was approved (with Dr. O Donnell abstaining) by our Board of Directors and our predecessor s board of directors. These agreements or any future agreements may involve conflicting interests between our interests, the interests of the other entities and Dr. O Donnell.

Risks Related to Our Publicly-Traded Securities

Our stock price is subject to market factors, and your investment in our securities could decline in value.

Since our initial public offering in June 2002, there has only been a limited public market for our securities and there can be no assurance that an active trading market in our securities will be maintained. In addition, the overall market for securities in recent years has experienced extreme price and volume

Table of Contents

fluctuations that have particularly affected the market prices of many smaller companies. In particular, the market prices of securities of biotechnology and pharmaceutical companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our securities, which could cause a decline in the value of your securities. These fluctuations, as well as general economic and market conditions, may have a material or adverse effect on the market price of our common stock.

If we cannot meet the Nasdaq SmallCap Market s continuing listing requirements and Nasdaq rules, Nasdaq may delist our securities, which could negatively affect our company, the price of our securities and your ability to sell our securities.

In 2004, according to rules of the Nasdaq SmallCap Market, our shares of common stock were subject to potential delisting from such market because we did not meet certain requirements. Although, as of the date of this prospectus, our shares are still listed on the Nasdaq SmallCap Market, in the future, we may not be able to meet the listing maintenance requirements of the Nasdaq SmallCap Market and Nasdaq rules, which require, among other things, minimum stockholders equity of $2.5 million. If we are unable to satisfy the Nasdaq criteria for maintaining listing, our securities could again be subject to delisting. Trading, if any, of our securities would thereafter be conducted in the over-the-counter market, in the so-called pink sheets or on the National Association of Securities Dealers, Inc. s electronic bulletin board. As a consequence of any such delisting, an event of default may be called under our Laurus note and, regardless of whether such an event of default is called, a stockholder would likely find it more difficult to dispose of, or to obtain accurate quotations as to the prices of our securities.

The redemption of our public warrants may adversely affect potential investors.

Our publicly-traded warrants, which expire on June 24, 2007, are redeemable, in whole or in part, for $.10 per warrant upon 30 days written notice to the warrant holder; provided that: (i) there is then an effective registration statement under the Securities Act covering the shares issuable upon exercise of the warrants and (ii) the average closing sale price of our common stock equals or exceeds $7.87 for the 10 trading days prior to the date of the notice of redemption.

Notice of redemption of the warrants could force holders to exercise the warrants and pay the exercise price therefore at the time when it may be disadvantageous for them to do so, sell the warrants at the current market price when they might otherwise wish to hold the warrants or accept the redemption price which is likely to be substantially less than the market value of the warrants at the time of redemption.

Current prospectus and state blue sky registration required to exercise warrants.

Holders of our warrants will be able to exercise their warrants only if a current registration statement relating to such shares is then in effect and only if the shares are qualified for sale under the securities laws of the applicable state or states. We do not currently have an effective registration statement covering the shares of common stock issuable upon exercise of the warrants. The warrants may be deprived of any value if the a registration statement covering the shares underlying the warrants is not effective and available or such underlying shares are not or cannot be registered in the applicable states.

Table of Contents

Additional authorized shares of our common stock and preferred stock available for issuance may adversely affect the market for our common stock.

We are authorized to issue 45 million shares of our common stock. As of December 31, 2004, there were 7,245,863 shares of common stock issued and outstanding. However, the total number of shares of our common stock issued and outstanding does not include shares reserved in anticipation of the exercise of options or warrants. To the extent such options or warrants are exercised, the holders of our common stock may experience further dilution. In addition, as in the case of the Laurus financing, in the event that any future financing should be in the form of, be convertible into or exchangeable for, equity securities, and upon the exercise of options and warrants, investors may experience additional dilution.

In addition to the above referenced shares of common stock which may be issued without stockholder approval, we have 5 million shares of authorized preferred stock, the terms of which may be fixed by our Board. We have issued preferred stock in the past, and our board of directors has the authority, without stockholder approval, to create and issue one or more additional series of such preferred stock and to determine the voting, dividend and other rights of holders of such preferred stock. The issuance of any of such series of preferred stock may have an adverse effect on the holders of common stock.

Shares eligible for future sale may adversely affect the market.

From time to time, certain of our stockholders may be eligible to sell all or some of their shares of common stock by means of ordinary brokerage transactions in the open market pursuant to Rule 144, promulgated under the Securities Act, subject to certain limitations. In general, pursuant to Rule 144, a stockholder (or stockholders whose shares are aggregated) who has satisfied a one year holding period may, under certain circumstances, sell within any three month period a number of securities which does not exceed the greater of 1% of the then outstanding shares of common stock or the average weekly trading volume of the class during the four calendar weeks prior to such sale. Rule 144 also permits, under certain circumstances, the sale of securities, without any limitation, by our stockholders that are non-affiliates that have satisfied a two year holding period. Any substantial sale of our common stock pursuant to Rule 144 or pursuant to any resale prospectus may have material adverse effect on the market price of our securities.

Our certificate of incorporation, our bylaws and Delaware law contain provisions that preserve our current management.

Our certificate of incorporation and by-laws may discourage, delay or prevent a change in our management team that stockholders may consider favorable. These provisions include:

authorizing the issuance of blank check preferred stock without any need for action by stockholders;

eliminating the ability of stockholders to call special meetings of stockholders;

permitting stockholder action by written consent; and

establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

Table of Contents

These provisions could allow our board of directors to affect your rights as a stockholder since our board of directors can make it more difficult for common stockholders to replace members of the board. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt to replace our current management team.

Item 2. Description of Property.

In early 2005, we relocated our principal executive offices to Arius offices in Morrisville, North Carolina. Arius lease for this approximately 2000 square foot space terminates in September 2007. Rental payment due on this space are: (i) from February 1, 2005 through September 30, 2005, $2,733.50 per month; (ii) From October 1, 2005 through September 30, 2006, $2,816.33 per month; and (ii) from October 1, 2006 through September 30, 2007, $2,900.82 per month. The landlord for this space is Pizzagalli Properties, LLC. We believe this space is presently adequate for use as our principal executive office.

We conduct our research operations a single site located on the campus of UMDNJ. Pursuant to a five year lease agreement with UMDNJ ending December 31, 2005, we occupy a total of approximately 8,000 square feet. The monthly rent was $3,340 in 2001, $3,840 in 2002, $4,340 in 2003, $4,840 in 2004 and is $5,340 in 2005 plus agreed payments for graduate student assistants, two BDSI executives and supplies used by us. The payments to UMDNJ for certain executive salaries totaled $211,747 for 2004. Historically, the payments for rent and supplies have averaged approximately $75,000 annually. The terms of the lease allows us flexibility of terminating the lease arrangement and relocating to a new space better suited for our long-term space requirements. Our ability to terminate is without a penalty provided that we give prior written notice. We plan to enter into discussions with UMDNJ during 2005 regarding a possible extension or renewal of this lease. No assurances can be given that we will be able to extend or renew the lease, and we may decide to relocate, scale back and/or outsource such operations.

Item 3. Legal Proceedings.

On or about April 19, 2004, we were named as the defe