launch

NITROMED, INC.
ANNUAL REPORT 2005
2005 HIGHLIGHTS

BiDil® (isosorbide dinitrate/hydralazine hydrochloride) is approved for use in black patients in addition to standard heart medications to:

:: treat heart failure,
:: extend life,
:: improve heart failure symptoms, and
:: help heart failure patients stay out of the hospital longer.

There is little experience in patients with heart failure who experience significant symptoms while at rest.

:: The unanimous recommendation for approval of BiDil by the Cardiovascular and Renal Drugs Advisory Committee of the U.S. Food and Drug Administration (FDA) on June 16

:: The approval of BiDil by the FDA on June 23

:: The nationwide commercial launch of BiDil in mid-July

:: The introduction of NitroMedCares™, an industry leading patient assistance program, in July

:: The cumulative sales of approximately 14,000 BiDil prescriptions by year end, written by over 3,600 physicians

:: The inclusion of BiDil in the heart failure treatment guidelines issued jointly by the American College of Cardiology and American Heart Association

:: The presentation of new BiDil clinical trial data at major cardiovascular medical meetings in September and November

:: The availability of BiDil through all state Medicaid formularies except Maine by October

:: The publication of a cost-effectiveness analysis of BiDil in December issue of Circulation: Journal of the American Heart Association

:: The formation of a strategic alliance with the National Association for the Advancement of Colored People (NAACP) aimed at narrowing health care disparities that exist between African Americans and Caucasians
On behalf of the management, board of directors and employees of NitroMed, I’m pleased to report to you on our Company’s progress during the year 2005, and into 2006. We make this year’s report with a combined sense of pride for our important accomplishments, urgency with respect to our commercial objectives, and confidence in our ability to drive our first marketed product, BiDil® (isosorbide dinitrate/hydralazine hydrochloride), to success.

The year 2005 was highlighted by the unanimous advisory committee recommendation for BiDil, and its unprecedented approval by the U.S. Food and Drug Administration (FDA) in June. BiDil was approved for the treatment of self-identified black patients with symptomatic heart failure. Only two weeks later, in mid-July, we launched BiDil in target markets across the nation with a contracted cardiovascular sales force. This “first of its kind” drug approval – for treatment of a specific racial group – would not have been possible without the commitment and expertise of an outstanding team of NitroMed employees, BiDil clinical investigators and advocates. As the FDA stated in its June 23, 2005 press release on the subject, the approval of BiDil represents “a striking example of how a treatment can benefit some patients even if it does not help all patients. The information presented to the FDA clearly showed that blacks suffering from heart failure will now have an additional safe and effective option for treating their condition.

In the future, we hope to discover characteristics that identify people of any race who might be helped by BiDil.” NitroMed shares this vision and commitment to the development of increasingly “personalized” medicine. We view the African American Heart Failure (A-HeFT) trial that served as the basis for BiDil’s approval as an important victory in addressing racial disparities within our nation’s healthcare system, and we view the current BiDil label a significant step towards the ultimate goal of individual-based treatment.

As pleased as we are with the approval of BiDil and the skillful way in which that process was managed, we are not satisfied with BiDil’s commercial performance to date; NitroMed recognized $4.5 million in revenue for the first six months of BiDil sales; $1.1 million during the third quarter and $3.3 million during the fourth quarter of 2005. As board chairman and recently appointed interim Chief Executive Officer for the Company, it is my unequivocal priority to unlock the greater value that I believe is inherent in BiDil for shareholders and patients alike.

Medically speaking, clinical evidence and support for BiDil has been very positive, and the BiDil label is exceptionally strong. BiDil was shown in A-HeFT to provide significant increases in survival, decreases in first hospitalizations, and improvements in functional status for black heart failure patients who were treated with BiDil as adjunctive treatment to other standard heart failure medications, as compared to patients receiving standard treatment alone. Outcomes from the 1,050-patient A-HeFT trial have since led to the inclusion of BiDil in both sets of major cardiovascular guidelines referenced by primary care physicians and cardiovascular specialists: those jointly issued in August 2005 by the American College of Cardiology and the American Heart Association; and, those issued in February 2006 by the Heart Failure Society of America (HFSA). The
HFSA guidelines recommend the combination of isosorbide dinitrate and hydralazine hydrochloride (BiDil’s components) as a new standard treatment for symptomatic heart failure in African Americans. We believe that external validation of BiDil’s medical benefits is an important factor in influencing physician adoption and prescribing of BiDil.

Commercially, we have identified fundamental obstacles that, once removed, should accelerate the BiDil sales trajectory. For example, improving managed care reimbursement of BiDil is key in addressing the issue of patient co-pay affordability. A generous sampling program during the first four months of launch, while successful in providing patients with BiDil at no cost as we launched our NitroMedCares™ patient assistance program and secured broad Medicaid reimbursement, did not yield the level of prescriptions through private payors that we expected. Since the majority of African Americans with heart failure are insured through managed care providers, working with these private payors to implement lower co-pays for BiDil is a priority for NitroMed. In addition to removing reimbursement obstacles to BiDil sales, we are also proceeding with transitioning the contracted BiDil sales force into NitroMed. We believe that direct management, accountability and common goals can drive increased productivity. As well, we are exploring partnering and/or co-promotion opportunities that can expand BiDil’s marketing reach.

We look forward to welcoming the BiDil sales force to NitroMed under the leadership of Gerald Bruce, who joined NitroMed as Vice President of Sales in January 2006. With over twenty combined years of cardiovascular sales, marketing and managed care operations experience at Johnson & Johnson and Bristol-Myers Squibb, Gerald brings a critical and timely expertise to the Company. Kenneth Bate, who joined NitroMed in March 2006 as Chief Operating Officer and Chief Financial Officer, also brings timely competencies. He offers over fifteen years of executive level experience in the areas of sales and marketing, finance, and commercial operations at both Millennium Pharmaceuticals and Biogen (now Biogen IDEC), as well as venture capital, investment banking and transaction advisory expertise.

With BiDil’s commercial success as the company’s priority, it is necessary to periodically evaluate and align our operational costs with current BiDil sales projections. To this end, research and development activities were scaled back in March 2006, preserving only those projects determined to be core to the growth and sustainability of the BiDil-based cardiovascular franchise. In particular, work will continue to develop a controlled release formulation of BiDil that is expected to increase patient convenience and compliance via once- or twice-daily dosing (the current dosing regimen is three times daily), and strategically, would help secure incremental patient demand and patent protection for BiDil. With respect to other projects, we are seeking to out-license or otherwise monetize various assets, including development stage compounds such as NMI 3377, a nitric oxide-enhancing cardiovascular agent for which we have already completed preclinical development. While these are difficult steps for NitroMed, which was built on the foundation of its proprietary nitric oxide-enhancing technology, they are currently necessary for maximizing our opportunities for commercial success and future growth.

GUIDANCE
We will be providing an updated liquidity statement with our first quarter of 2006 financial report, as well as an updated estimate of projected expenses for 2006 after giving effect to the restructuring of the BiDil sales force in January, the downsizing of our research and development group in March, and cost efficiencies related to the internalization of the BiDil sales force, which is projected to be completed by July 2006.

With respect to the Company’s cash position, as of December 31, 2005, our cash, cash equivalents and marketable securities totaled $61.5 million. Subsequent to the end of the year, the Company raised $58.6 million net of expenses in a registered direct offering that closed on January 26, 2006. We will be providing an updated liquidity statement with our first quarter of 2006 financial report.

With prudent fiscal management, our mid-launch course correction, and clear, attainable goals, we are well prepared to drive value for BiDil and NitroMed. I look forward to reporting to you again on our progress.

Sincerely,

Argeris N. Karabelas, Ph.D.
Chairman and interim Chief Executive Officer
ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2005

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

Delaware  22-3159793
(State or other jurisdiction of incorporation or organization) (IRS Employer Identification No.)

125 Spring Street, Lexington, Massachusetts  02421
(Address of principal executive offices) (Zip Code)

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☑ No ☐.

Indicate by check mark whether the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☑.

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of “accelerated filer and large accelerated filer” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☑ Accelerated filer ☐ Non-accelerated filer ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑.

The aggregate market value of the registrant’s common stock held by nonaffiliates of the registrant was approximately $299,486,000, based on the price at which the registrant’s common stock was last sold on June 30, 2005.

As of February 23, 2006, there were 36,632,342 shares of the registrant’s common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant’s proxy statement for the annual meeting of stockholders to be held on May 17, 2006, which are to be filed pursuant to Regulation 14A within 120 days after the end of the registrant’s fiscal year ended December 31, 2005, are incorporated by reference into Item 5 of Part II and Part III of this report.
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PART I

This annual report on Form 10-K contains forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including any projections of revenue, expenses, earnings or losses from operations, or other financial items; any statements of the plans, strategies and objectives of management for future operations; any statements concerning product research, development and commercialization timelines or outcomes; any statements of expectation or belief; and any statements of assumptions underlying any of the foregoing. The risks, uncertainties and assumptions referred to above include risks that are described in “Risk Factors” and elsewhere in this annual report and that are otherwise described from time to time in our Securities and Exchange Commission reports filed after this report.

The forward-looking statements included in this annual report represent our estimates as of the date of this annual report. We specifically disclaim any obligation to update these forward-looking statements in the future, except as specifically required by law or the rules of the Securities and Exchange Commission. These forward-looking statements should not be relied upon as representing our estimates or views as of any date subsequent to the date of this annual report.

ITEM 1. BUSINESS

Overview

We are an emerging pharmaceutical company with substantial expertise and intellectual property in nitric oxide-based drug development. Our goal is to become a leading, multi-product pharmaceutical company by developing innovative nitric oxide-based products and by building on our BiDil® development experience and commercialization infrastructure to identify and market additional products for cardiovascular and metabolic diseases. We have devoted substantially all of our efforts towards the research and development of our product candidates and the commercialization of our currently marketed product, BiDil. Since our inception, we have funded our operations mainly through the sale of equity securities, debt financings, license fees, research and development funding and milestone payments from our collaborative partners. We have never been profitable and have incurred an accumulated deficit of $242.5 million as of December 31, 2005.

In June 2005, the U.S. Food and Drug Administration, or FDA, approved our first commercial product, BiDil, for the treatment of heart failure in self-identified black patients as an adjunct to current standard therapies. BiDil is an orally administered fixed-dose combination of isosorbide dinitrate and hydralazine hydrochloride. We commercially launched BiDil in July 2005 and generated product sales of $4.5 million during the year ended December 31, 2005. We market BiDil primarily to cardiologists and primary care physicians who treat African Americans with heart failure. Our sales and marketing organization is comprised internally of a senior vice president of sales and marketing, a vice president of sales, a vice president of marketing, three regional sales directors and fifteen district sales managers. In addition, we have an agreement with Publicis Selling Solutions pursuant to which, on our behalf, Publicis has employed and trained a cardiovascular specialty sales force currently consisting of 144 sales representatives to sell BiDil to our target prescriber markets. We have also engaged Schwarz Pharma under a five-year exclusive manufacturing and supply agreement for the three times daily immediate release dosage formulation of BiDil.

We are also applying our nitric oxide technology to develop additional novel pharmaceuticals, as well as safer and more effective versions of existing drugs, to target significant diseases that are characterized by a deficiency in nitric oxide and to treat underserved patient populations. Our nitric oxide-development strategy involves the internal development of proprietary nitric oxide-enhancing product candidates, such
as BiDil, the co-development of nitric oxide-enhancing drugs with collaborators and the out-licensing of our nitric oxide-enhancing technology in exchange for potential milestone payments and royalties on sales.

We expect that research, development and commercialization expenses relating to our products and product candidates and to enhancing our core technologies will continue to fluctuate in the near-term and may vary significantly from our current estimates. Our operating expenses related to our research and development efforts and our sales, general and administrative costs for the year ended December 31, 2005, total $105.9 million. We currently estimate that our operating expenses for fiscal year 2006 will range between $95.0 and $110.0 million, excluding cost of product sales and expenses related to the adoption of Statement of Financial Accounting Standards (“SFAS”) No. 123R, Share-Based Payment. We believe that our existing cash, cash equivalents and marketable securities, together with the proceeds from our recent equity offering in January 2006, will be sufficient to fund our current operating plan, including operating expenses in support of the launch and commercialization of BiDil, for at least the next 21 months.

In the near-term, a key driver of our success will be our ability to successfully launch, commercialize and achieve market penetration of BiDil. We will need to generate significant revenues to achieve profitability. At the present time we are unable to estimate the level of revenues that we will realize from sales of BiDil or the commercialization of other product candidates that we may successfully develop and commercialize. We are therefore unable to estimate when we will achieve profitability, if at all.

We were incorporated in Delaware in 1992. Our principal executive office is located at 125 Spring Street, Lexington, Massachusetts 02421, and our telephone number is (781) 266-4000. Our Internet address is www.nitromed.com. The information on our website is not incorporated by reference into this annual report on Form 10-K and should not be considered to be a part of this annual report. Our website address is included in this annual report on Form 10-K as an inactive technical reference only.

When used in this annual report on Form 10-K, the terms “NitroMed,” “we,” “our” and “us” refer to NitroMed, Inc., unless otherwise specified. We own the trademarks NitroMed®, NitRx®, BiDil®, and NitroMed’s logo “N.” Other trademarks and service marks appearing in this annual report on Form 10-K are the property of their respective holders.

Our Nitric Oxide-Enhancing Medicines

Nitric oxide is a naturally occurring compound that is synthesized in cells to regulate a broad range of cellular reactions. Many disease states are associated with a deficiency in nitric oxide and might benefit from nitric oxide-enhancing medicines. For example, depleted levels of nitric oxide have been implicated in diseases such as heart failure, pulmonary hypertension and sexual dysfunction. Additionally, nitric oxide-enhancing medicines have been shown to reduce side effects associated with a variety of medications, including a broad range of anti-inflammatory medications.

BiDil: Treatment for Heart Failure in African Americans

Heart Failure in African Americans

Heart failure, also called congestive heart failure or dilated cardiomyopathy, is a progressively worsening condition that occurs when the heart muscle weakens and cannot pump blood efficiently enough to meet the metabolic needs of the body. The loss of pump function is usually caused by an underlying condition, such as hypertension or coronary artery disease, which weakens the heart muscle and increases a person’s risk of heart failure. The most common symptoms of heart failure include shortness of breath from congestion in the lungs, fatigue, sleeping problems due to the inability to lay flat, sudden awakening with shortness of breath and swelling in the feet, ankles and other parts of the body.

Heart failure affects approximately five million Americans and there is currently no cure for the disease. After a patient is diagnosed with heart failure, their prognosis is generally poor, with approximately 50 percent of patients dying within five years. Heart failure is the primary reason for
hospitalizations among people over the age of 65 and is one of the most expensive diseases faced by Americans, costing more than all cancers combined.

An estimated 750,000 African Americans are currently diagnosed with heart failure, with the number expected to increase to nearly 900,000 by 2010, based on data from the U.S. census bureau and the Centers for Disease Control and Prevention. African Americans between the ages of 45 and 64 are 2.5 times more likely to die from heart failure than Caucasians in the same age range. The African American community also presents with the disease at a younger age than their white counterparts, resulting in earlier disability, and higher rates of both hospitalization and premature death. In addition, some medicines approved for the treatment of heart failure appear to be less effective in controlling high blood pressure in African American patients. Ethnic disparities in the prevalence of heart failure have been attributed to a variety of factors, including access to medical care, disease management, socioeconomic factors, lifestyle habits and a higher incidence of diabetes, hypertension and metabolic syndrome.

**African American Heart Failure Trial (A-HeFT)**

In 2001, we partnered with the Association of Black Cardiologists, Inc. to conduct the African American Heart Failure Trial (A-HeFT), the first trial conducted in a heart failure population in which all of the participants identified themselves as black. A retrospective analysis of an earlier study with a combination of isosorbide dinitrate and hydralazine hydrochloride had suggested a trend for improved survival in the subset of patients with mild to moderate heart failure who self-identified as black. The randomized, double-blind, placebo-controlled A-HeFT study enrolled 1,050 self-identified black patients with New York Heart Association, or NYHA, class III or IV heart failure at 169 clinical research sites. The classification system means that patients had marked limitation of physical activity (class III) or were unable to carry out any physical activity without discomfort (class IV). Participants in A-HeFT were required to be stable while receiving standard heart failure therapy at the time of the beginning of the trial, per their physicians. The primary end point for the trial was a composite score made up of weighted values for death from any cause, a first hospitalization for heart failure, and change in the quality of life.

After a unanimous recommendation from the independent A-HeFT Data and Safety Monitoring Board and Steering Committee in July 2004, A-HeFT was halted early due to a significant survival benefit seen with the drug. Patients taking BiDil in addition to current therapies experienced a significant 43% decrease in the risk of mortality (p=0.012) (absolute mortality rate: BiDil, 6.2% vs. placebo, 10.2%), a 39% reduction in the risk of first hospitalization for heart failure (p<0.001) (absolute first hospitalization rate: BiDil, 16.4% vs. placebo, 24.4%) and a statistically significant improvement at most time points in response to the Minnesota Living with Heart Failure Questionnaire, which is a self-report of the patient’s functional status, versus patients taking placebo in addition to current standard therapies. Adverse events reported in the trial included symptoms of headache and dizziness, which were significantly more frequent in the group given BiDil, and exacerbations of congestive heart failure, both moderate and severe, which were significantly more frequent in the placebo group.

**BiDil: Launch and Commercialization Strategy**

BiDil, an orally administered fixed-dose combination of isosorbide dinitrate and hydralazine hydrochloride, was approved by the FDA in June 2005 for the treatment of heart failure in self-identified black patients. BiDil is indicated for the treatment of heart failure as an adjunct to standard therapy in self-identified black patients to improve survival, to prolong time to hospitalization for heart failure, and to improve patient-reported functional status. There is little experience in patients with NYHA class IV heart failure. Most patients in the clinical trial supporting effectiveness, referred to as A-HeFT, received, in addition to BiDil or placebo, a loop diuretic, an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker, and a beta blocker, and many also received a cardiac glycoside or an aldosterone antagonist. BiDil is a fixed-dose combination of isosorbide dinitrate, a vasodilator with effects on arteries
and veins, and hydralazine hydrochloride, a predominantly arterial vasodilator. The mechanism of action underlying the beneficial effects of BiDil in the treatment of heart failure has not been established.

Since launch in July 2005, our sales strategy for BiDil has been focused on:

- concentrated sales efforts through a dedicated sales force:
- ensuring patient access through
  - efforts to obtain public and private insurance coverage and to secure preferable reimbursement status among third-party payors,
  - our patient assistance program, and
  - coalition building with advocacy organizations; and
- creating physician awareness through our publications strategy.

We market BiDil to cardiologists, primary care physicians and other caregivers who treat African Americans with heart failure through a dedicated sales and marketing organization. Our sales and marketing organization is comprised internally of a senior vice president of sales and marketing, a vice president of sales, a vice president of marketing, three regional sales directors and fifteen district sales managers. In addition, we have an agreement with Publicis Selling Solutions pursuant to which, on our behalf, Publicis has employed and trained a specialty sales force currently consisting of 144 sales representatives to sell BiDil to our target prescriber markets. Under this agreement, we have the right to hire some or all of the Publicis representatives directly at any time upon the payment to Publicis of an agreed upon fee and after July 2006 without penalty. Under separate agreements, Publicis has recruited, hired and trained seven account executives and one national director who are assisting us in gaining formulary access and preferential reimbursement treatment for BiDil, and has hired five medical science liaisons to report into our medical affairs group.

We launched BiDil in July 2005 with 195 sales territories that were estimated to account for 90% of African American patients with heart failure, covering approximately one-third of the nation’s postal zip codes. Based on six-month post-launch experience, we have found that the African American heart failure market is more concentrated than projected, with approximately 90% of BiDil prescriptions coming from only 141 of these 195 territories. With this knowledge, we have reduced our sales force representation to approximately 144 sales representatives in order to further focus our sales force efforts and to generate greater cost-effectiveness in our sales strategy. As part of our effort to make our sales force more effective and cost-efficient, we intend to transition the sales force from contractors to NitroMed employees by the third quarter of 2006, as permitted under our existing Publicis contract.

With respect to manufacturing, we have engaged Schwarz Pharma under a five-year exclusive manufacturing and supply agreement for the three times daily immediate release dosage formulation of BiDil. Under the supply agreement, we have the right to engage a backup manufacturer. As part of the manufacturing process, we order bulk materials of hydralazine hydrochloride from Flavine International, Inc., the U.S. representative of Sumitomo Corp., and isosorbide dinitrate from Dottikon ES Holding AG, and have them delivered directly to Schwarz Pharma for manufacturing.

Our current efforts to expand patient access to BiDil focus on gaining improved insurance coverage. We obtained approximately 100% private insurance coverage at launch at Tier III, a term generally used to denote the level of reimbursement at which access to a product is approved by a third-party payor but at which patient co-pays are at their highest level, ranging from approximately $30.00 to $50.00. We are currently seeking to secure Tier II reimbursement, a term generally used to denote a preferential level of reimbursement at which patient co-pays range from approximately $15.00 to $25.00, for 35% of privately covered lives during the first quarter of 2006, and 50% of privately covered lives by July 2006. With respect to Medicare Part D, a Medicare prescription drug plan, as of February 2, 2006, in the 21 states that comprise 90% of the African American patient population, BiDil was listed on 38% of existing plans. Out
of all such plans on which BiDil was listed, 24% listed BiDil at a Tier II preferential reimbursement level. BiDil is currently covered under Medicaid plans covering 99% of the African American patient population covered under Medicaid plans.

With respect to our coalition-building efforts, we recently announced a strategic alliance with the National Association for the Advancement of Colored People (NAACP) to implement measures to narrow health care disparities that exist between African Americans and Caucasians in areas of access, affordability, quality, infrastructure and compliance. As part of the partnership, NitroMed is providing a $1.5 million grant to establish an organizational infrastructure to allow the NAACP to develop the necessary grass roots health advocacy initiatives. We have also developed coalitions with other advocacy and professional organizations as part of our efforts to address racial and ethnic disparities in cardiovascular disease, including the Association of Black Cardiologists and the Congressional Black Caucus.

In 2006, our efforts to continue to enhance physician awareness of BiDil and its effectiveness will be supported by the expected submission of up to 6 primary publications related to BiDil based on data from the A-HeFT trial.

**Internal Development Programs**

**BiDil XR and BiDil Combination**

The current formulation of BiDil is an immediate-release tablet that must be taken three times daily. We are currently pursuing the development of an extended release formulation of BiDil (BiDil XR) that could be taken either once or twice a day, depending on the particular formulation we pursue. BiDil XR could enhance the BiDil market by facilitating greater compliance by patients with their medications schedule, an issue which is more pronounced in a patient population already on a substantial number of concomitant medications.

We are also engaging in research and development efforts to develop BiDil Combination products which would combine BiDil with existing, marketed medicines, such as ACE inhibitors, beta blockers, or aldosterone receptor blockers. BiDil and the existing medicines can be combined together through either a chemical linkage to potentially create a proprietary new chemical entity or through the direct mixing of the medicines and BiDil to potentially create a patentable new use and dosage form. We generally pursue development opportunities with respect to nitric oxide-enhancing drugs from among those marketed medicines whose safety and efficacy we believe can be improved by increased nitric oxide levels in the body. We believe that the probability of clinical success for our next-generation BiDil Combination product candidates is increased because regulatory approvals have already been achieved for the existing medicines that we are seeking to improve. We also believe that the commercial risk associated with these product candidates is mitigated because many of these existing medicines have already generated significant sales in their markets.

**Cardiovascular Portfolio**

We are utilizing our nitric oxide expertise and proprietary position to develop product candidates for a variety of additional medical conditions. As part of this effort, we recently announced that we expect to file an Investigational New Drug Application for NMI 3377, a proprietary nitric oxide-enhancing cardiovascular agent, in the second quarter of 2006. We currently have retained all development rights to this product candidate.

**Other Nitric Oxide Enhancing Product Candidates**

**Overview**

In the 1980s, nitric oxide was identified as a significant molecule that regulates a wide range of important cellular functions. Professor Robert R. Furchgott, a member of our scientific advisory board
until his retirement in 2005, and two other individuals were awarded the Nobel Prize in Physiology and Medicine in 1998 for this discovery.

Recent research has shown that nitric oxide also plays important biochemical and physiological roles in many diseases or medical conditions, including the following:

**Cardiovascular Disease.** The formation of nitric oxide in the cells that line the inner walls of blood vessels, referred to as the endothelium, has been found to play a crucial role in maintaining the dilation of the blood vessels, a process essential for the regulation of blood pressure. Nitric oxide produced by the endothelium also inhibits the clumping of platelets, which are cells in the blood that promote clotting, and the adhesion of platelets and white blood cells to the blood vessels’ inner walls, thereby significantly reducing the obstruction of blood vessels that is associated with blood clots and stroke. Numerous other cardiovascular actions of nitric oxide have been reported, including maintaining sufficient blood flow to the heart muscle and regulation of the contraction of the heart muscle. Cardiovascular diseases associated with nitric oxide imbalance include atherosclerosis, high cholesterol levels, high blood pressure, pulmonary hypertension and heart failure.

**Gastrointestinal and Inflammatory Disease.** Nitric oxide is capable of influencing many of the biochemical and physiological reactions that are key to preventing or repairing injury to the gastrointestinal tract, such as stimulating mucus secretion from the mucus membrane lining the stomach and intestines and regulating the blood flow feeding the wall of the gastrointestinal tract and the mucus membrane. Nitric oxide can control inflammatory cell activation and is active on other chemical mediators in the inflammatory process. Gastrointestinal diseases in which nitric oxide has potential beneficial actions include gastric injury, inflammatory bowel disease, and peptic ulcer induced by non-steroidal anti-inflammatory drugs, or NSAID’s.

**Central Nervous System Disorders.** Nitric oxide is also synthesized in nerve cells, or neurons, of the central nervous system, where it performs many physiological functions, including the formation of memory and the modulation of pain. Nitric oxide-based therapies for diseases such as epilepsy, stroke, neuroinflammatory disorders and trauma may be able to provide protection to neurons.

**Sexual Dysfunction.** In the peripheral nervous system, nitric oxide is now known to play a role in regulating some forms of vasodilation and certain gastrointestinal, respiratory and genito-urinary functions. For example, male penile erection is dependent upon nitric oxide-relaxation of genital smooth muscles, and drugs like Viagra enhance the nitric oxide-signaling pathway.

**Respiratory Disease.** Nitric oxide inhalation reduces pulmonary hypertension and improves oxygenation, the absorption of oxygen by the lungs. In inflammatory pulmonary diseases, such as asthma and chronic obstructive pulmonary disease, nitric oxide has the potential to promote airway dilation and reduce inflammation, thus reducing airway sensitivity to airborne irritants and allergens.

We estimate that candidate medicines for our nitric oxide technology have current annual worldwide sales in excess of $30 billion. We seek to produce our nitric oxide-enhancing drug candidates by combining an existing, marketed medicine with a nitric oxide donor, which is a molecule capable of increasing nitric oxide levels in the body. The nitric oxide donor and the existing medicine can be combined together through either a chemical linkage to potentially create a proprietary new chemical entity or through the direct mixing of the medicine and the nitric oxide enhancing compound to potentially create a patentable new use and dosage form. We believe that the probability of clinical success for our drug candidates is increased because regulatory approvals have already been achieved for the existing medicines that we are seeking to improve. We also believe that the commercial risk associated with these drug candidates is mitigated because many of these existing medicines have already generated significant sales in their markets.
We have generated significant intellectual property rights for our nitric oxide technology and compounds to protect our interests and support our discovery and development of additional product candidates.

**Nitric Oxide Enhancing Medicines for the Treatment of Cardiovascular Disease**

We have initiated several new and novel cardiovascular drug discovery programs based on the therapeutic potential of nitric oxide-enhancing drugs in the treatment of diseases associated with Endothelial Dysfunction. Endothelial Dysfunction is recognized as one of the common denominators underlying many cardiovascular diseases including atherosclerosis, hypertension, heart failure, diabetes, pulmonary hypertension and metabolic syndrome. Abnormal function of the endothelium precedes vascular morphological changes in the early stages of cardiovascular disease. Nitric oxide has many important roles in maintaining the function of normal endothelium. These include vasodilatation, inhibition of platelet adhesion and activation, inhibition of smooth muscle growth, inhibition of leukocyte adhesion and a reduction in chemotactic factor expression. Loss of nitric oxide therefore is a primary feature of endothelial dysfunction. Restoration of nitric oxide from the endothelium has been clinically demonstrated to reduce cardiovascular risk in many disease states. We therefore are using our nitric oxide expertise and proprietary patent position to add nitric oxide-donating capacity to existing classes of drugs which have been shown to have clinical utility in the treatment of cardiovascular diseases where endothelial dysfunction plays a critical role.

The following table highlights those classes of nitric oxide-enhancing cardiovascular medicines where we have created, or are seeking to create, intellectual property rights, and where we believe we may offer a clinical benefit compared to existing FDA-approved medicines.

<table>
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<tr>
<th>Product Candidate and Therapeutic Area</th>
<th>Potential Clinical Benefit</th>
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| **Nitric Oxide-Enhancing Angiotensin Receptor Blockers**  
  • Hypertension | - Improved endothelial function; accelerated blood pressure lowering; enhanced renal protection |
| **Nitric Oxide-Enhancing Beta Blockers**  
  • Hypertension, Heart Failure | - Better tolerated (reduction in impotence, insulin resistance); improved endothelial function |
| **Nitric Oxide-Enhancing Diuretics**  
  • Hypertension, Heart Failure, Edema | - Better side effect profile; enhanced diuresis/natriuresis; enhanced renal protection |
| **Nitric Oxide-Enhancing Angiotensin-Converting Enzyme Inhibitors**  
  • Hypertension | - Improved efficacy; enhanced renal protection |
| **Nitric Oxide-Enhancing Renin Inhibitors**  
  • Hypertension | - Improved efficacy |
| **Nitric Oxide-Enhancing Statins**  
  • Hypertension | - Enhanced activity; faster onset |
| **Nitric Oxide-Enhancing Aldosterone Antagonists**  
  • Hypertension | - Improved blood pressure control |
Nitric Oxide-Based Medicines for Acute Renal Failure

Acute renal failure is characterized as a sudden deterioration in kidney function and affects about 5% of all hospitalized patients. The condition is often associated with trauma, burns, systemic infections and shock. It is a serious and life threatening condition from which more than half of the affected patients die. Currently, there are no effective drug therapies for acute renal failure. Disease management is costly and includes kidney dialysis and transplantation. Nitric oxide plays a pivotal role in kidney homeostasis at the level of the renal vasculature, glomerulus, and renal tubule. All three subtypes of nitric oxide synthase (endothelial, neuronal and inducible) are expressed in various kidney structures and participate in the control of glomerular and medullary hemodynamics, tubuloglomerular feedback responses, the renin-angiotensin system, and electrolyte/fluid balance through endogenous generation of nitric oxide.

In February 2004, we signed a licensing and commercialization agreement with the University of Edinburgh and the University of St. Andrews in Scotland to research nitric oxide-based medicines with the goal of identifying treatment of acute renal failure. Our agreement with the universities supports a healthcare innovations technology transfer program funded by the Wellcome Trust, which is focused on the development of early stage projects to a point where they can be further developed by the commercial sector.

Other Development Programs

We are utilizing our nitric oxide expertise and proprietary position to develop product candidates for a variety of additional medical conditions. The following table highlights those classes of nitric oxide-enhancing medicines where we have created, or are seeking to create, intellectual property rights and where we believe we may offer a clinical benefit compared to existing FDA-approved medicines. Our efforts in these areas primarily consist of discovery-stage research primarily directed to establishing our intellectual property position.

Product Candidate and Therapeutic Area | Potential Clinical Benefit
--- | ---
Nitric Oxide-Enhancing NSAID’s | • Pain, inflammation, cancer and central nervous system diseases
• Improved gastrointestinal tolerance; accelerated ulcer healing; reduced kidney damage and hypertension

Nitric Oxide-Enhancing Phosphodiesterase Inhibitors | • Pain, inflammation, cancer and central nervous system diseases
• Asthma
• Male erectile dysfunction
• Pulmonary hypertension
• Chronic obstructive airway disease
• Anti-nociceptive; anti-inflammatory; enhanced efficacy; fewer side effects
• Increased airway circulation; reduced lung inflammation and decreased sensitivity to airborne allergens
• Increased response rate; rapid onset of action
• Increased efficacy; longer duration of action
• Increased airway circulation

Nitric Oxide-Enhancing Steroids | • Allergy and Asthma
• Dermatology
• Faster onset of action; increased airway circulation
• Faster onset of action; increased efficacy

Nitric Oxide-Enhancing Gastrointestinal Protectants | • Peptic ulcer
• Improved efficacy; faster onset of action
Nitric Oxide-Enhancing Arginines

- Kidney failure
- Improved sodium and water balance

Nitric Oxide-Enhancing Antibiotics

- Cystic Fibrosis
- Improved antibacterial activity; increased mucus production

Corporate Collaborations

As part of our strategy to accelerate our product development efforts, we established collaborations with Boston Scientific Corporation in the area of nitric oxide-enhancing paclitaxel-coated stents to reduce restenosis and with Merck Frosst Canada & Co., a Merck & Co., Inc. subsidiary, in the area of nitric oxide-enhancing COX-2 inhibitors for use in the treatment of various diseases. In November 2004, we agreed to terminate our collaboration with Merck. In addition, on December 31, 2005, the research term under our agreement with Boston Scientific expired. These collaborations were designed to provide us with capital and research, development and marketing capabilities. We intend to pursue other collaborations, as appropriate. Since inception, a substantial portion of our revenue has been derived from our collaborations with third parties. For the years ended December 31, 2005, 2004 and 2003, our collaboration with Boston Scientific accounted for $1,592,000, $1,592,000 and $442,000 in revenue.

Boston Scientific Agreement

In November 2001, we entered into a research, development and license agreement with Boston Scientific in the field of restenosis. We granted Boston Scientific an exclusive worldwide license to develop and commercialize nitric oxide-enhancing cardiovascular stents. We also granted to Boston Scientific a right of first refusal to obtain an exclusive license under our nitric oxide technologies to commercialize products for restenosis, which right of first refusal is for a period of three years after the end of the research term. In December 2003, we agreed to extend the agreement to continue the research and development collaboration through December 2005.

Boston Scientific made an up-front license payment of $1.5 million to us in 2001, and made an additional payment of $3.0 million in December 2003 in connection with the extension of the research and development collaboration. In the event that specified research, development and commercialization milestones were achieved, Boston Scientific would have been obligated to make milestone payments to us. In addition, Boston Scientific would have been obligated to pay royalties to us on the sale of any products resulting from the collaboration. Boston Scientific made a $3.5 million equity investment in our stock in 2001. In August 2003, in connection with a private placement, Boston Scientific made an additional $500,000 equity investment in our stock.

The research term of the Boston Scientific agreement expired on December 31, 2005, although certain rights extend beyond this term. We intend to evaluate the continued development of this technology and in the future may seek collaboration with other potential partners.

Merck Agreement

In December 2002, we entered into a research, development and license agreement with Merck to jointly develop pharmaceutical products containing nitric oxide-enhancing COX-2 inhibitors. Under the terms of the agreement, we granted Merck an exclusive worldwide, royalty-bearing license to develop, make and sell nitric oxide-enhancing COX-2 inhibitors for use in the treatment or prevention of various diseases, conditions or disorders.
Merck paid an up-front license fee of $10.0 million under the agreement and also made research and development payments over the three-year term of the research program totaling $7.2 million. In 2003, Merck made two payments, each of $5.0 million, for achieving the first two milestones.

On September 30, 2004, Merck halted the phase II trial of our lead candidate in nitric oxide-enhancing COX-2 inhibitors. This lead nitric-oxide candidate is composed of a derivative of rofecoxib. Rofecoxib is the active ingredient in Vioxx, a COX-2 inhibitor which Merck voluntarily withdrew from worldwide markets on September 30, 2004. In November 2004, we agreed with Merck to terminate the collaboration agreement. Merck paid us a lump sum of $1.8 million, representing the full amount of the research funding owed to us for 2005, but is not required to provide us with any further funding. We retain all rights to our technology in the field of nitric oxide-enhancing COX-2 inhibitors, and intend to evaluate the continued development of this technology in collaboration with other potential partners.

Our Strategy

Our goal is to become a leading, multi-product pharmaceutical company by developing additional innovative nitric oxide products and by building on our BiDil development experience and commercialization infrastructure to identify and market additional products for cardiovascular and metabolic diseases. Key elements of our strategy include:

Successfully commercializing BiDil. We currently have an internal marketing and sales infrastructure and a dedicated contract sales force, which sales force we intend to internalize by the third fiscal quarter of 2006, to promote BiDil for the treatment of heart failure in African Americans. Based on the number of physicians serving the African American heart failure market and the experience we have gained six months into BiDil’s launch, we believe we can successfully promote BiDil with approximately 144 sales representatives, a reduction of over fifty sales representatives from our initial pre-launch estimates. This reduction in sales force representatives could result in our failure to realize certain market potential in areas in which we have chosen not to provide representation.

We have also seen steady prescription growth for BiDil since launch, with total prescriptions for BiDil increasing from an average of approximately 1,100 per month in the third quarter of 2005 to an average of approximately 3,500 per month in the fourth quarter of 2005, with December 2005 at approximately 4,700, based on aggregate weekly data derived from Source Projected Launchtrac, Wolters Kluwer Health. We will need to substantially increase the number of prescriptions being written for BiDil in order to successfully commercialize this product. Because BiDil is the only heart failure treatment specifically indicated to treat African Americans with heart failure, we believe that we will continue to achieve market acceptance and penetration in this population.

In addition, we believe that the documented efficacy and cost-effectiveness of BiDil will bolster our continuing efforts to expand the level of preferential reimbursement treatment received by BiDil both from public and private payors. Our failure to achieve preferential reimbursement treatment for BiDil in the near term could significantly hinder market acceptance of BiDil by physicians and patients.

Successfully leveraging our BiDil sales force. Our sales force targets high prescribing physicians who treat African Americans with cardiovascular and metabolic diseases. We believe the African American community is an underserved patient population and suffers a disproportionate incidence of cardiovascular and other diseases. We believe that we can in-license or otherwise acquire rights to drugs and drug candidates to further serve this population.

Capitalizing on our clinical development expertise. We believe the experience we gained in designing and executing our BiDil clinical trial program makes us an attractive clinical development partner for companies developing product candidates in the cardiovascular field.
Focusing our internal development projects and potential collaborations on nitric oxide-enhancing versions of existing medicines. We believe that many pharmaceutical companies have currently marketed drugs and products that can benefit from the therapeutic attributes and the potential patent protection of our nitric oxide-enhancing technology. We are currently conducting research and development on several drug classes and have consolidated an intellectual property position from which we believe we can generate significant value. We intend to pursue collaborations with leading health care companies where our product candidates will benefit from the marketing reach, clinical expertise and technology of the partner.

Continuing to protect and enhance our product-specific and nitric oxide intellectual property rights and capabilities. Because of its critical role in our on-going product development efforts, we intend to aggressively pursue the protection of our intellectual property. In order to protect and expand our current intellectual property position, we intend to invest significantly in nitric oxide-related research and development efforts, including attracting and retaining highly talented and experienced personnel.

Research and Development

As of December 31, 2005, our research and development group consisted of 45 employees, including 19 biologists, 11 medicinal chemists, 9 persons engaged in clinical development and 6 persons engaged in patent and other research and development-related functions. Our research and development group is focusing on the continuous improvement of our core technology, the development of new materials and platforms, complementary products and new initiatives aimed at leveraging our core technology in new market areas.

During the fiscal years ended December 31, 2005, 2004 and 2003, we estimate that our total company-sponsored research and development expenses were $29.6 million, $23.0 million, and $15.1 million, respectively, and that our collaborator-sponsored research and development expenses were $2.3 million, $5.0 million, $3.8 million, respectively.

Proprietary Rights and Licensing

Our policy is to prosecute and enforce our patents and proprietary technology. We intend to continue to file United States and foreign patent applications to protect technology, inventions and improvements that are considered important to the development of our business. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets.

As of December 31, 2005, we have 86 issued U.S. patents and 62 pending U.S. patent applications. We also have 66 issued patents and 122 pending patent applications in certain major industrial countries, including Canada, the major European market countries, Australia and Japan. Our issued U.S. and foreign patents expire on various dates between 2007 and 2025.

BiDil. We have three U.S. patents, one expiring in 2007 and the other two in 2020, and one Canadian patent expiring in 2008, which relate to co-administration of the components of BiDil. The first U.S. patent and the Canadian patent cover methods for reducing mortality associated with chronic congestive heart failure. The second U.S. patent covers methods for reducing mortality associated with chronic congestive heart failure, for improving the quality of life, for improving oxygen consumption or improving exercise tolerance in black patients. The third U.S. patent covers additional claims to specific indications and dosing ranges for the treatment of heart failure and other conditions in black patients. We have not filed any patent applications outside of the United States and Canada for BiDil, as pertains to the patent expiring in 2007. We have filed applications claiming priority relative to the patents expiring in 2020 in Canada and Europe. In addition, we have filed ten additional U.S. patent applications and corresponding foreign patent applications that could provide additional patent protection for BiDil.
Nitric Oxide Stents. We have seven U.S. patents expiring on dates between 2013 and 2021 which cover the coating of medical devices with nitric oxide compounds, prevention of adverse effects associated with the use of a medical device, treatment of a damaged vessel or treatment of a damaged vascular surface in a patient by administration of a nitric oxide compound. We have five pending U.S. patent applications which, if issued, will have expiration dates between 2021 and 2025 and which cover the composition of matter of specific nitric oxide donors or nitric oxide-linked compounds and their methods of use for the treatment of restenosis. We have filed additional patent applications worldwide. We have been issued one Australian patent, one European patent, and one Canadian patent, all of which expire in 2014.

Nitric Oxide-Enhancing COX-2 Inhibitors and Nitric Oxide-Enhancing NSAID’s for Inflammation. We have three issued and nine pending U.S. patent applications, which, if issued, will have expiration dates between 2020 and 2026 and which disclose and claim novel nitric oxide-enhancing COX-2 inhibitors. These applications also disclose kits and methods of use for the treatment of pain, inflammation and fever, gastrointestinal disorders, disorders resulting from elevated levels of COX-2 inhibitors, for reducing renal and respiratory toxicity, for facilitating wound healing and for improving the cardiovascular profile of COX-2 inhibitors. We have also filed additional foreign patent applications relating to this technology. We have three U.S. patents expiring in 2015, two U.S. patents expiring in 2018, and one patent application which, if issued, will expire in 2018, which cover different compositions of matter and methods of use for the treatment of pain, inflammation, fever and gastrointestinal disorders with novel nitric oxide-enhancing NSAID’s. One pending patent application, which, if issued, will expire in 2023, discloses specific composition of matter and methods of use for the treatment of pain, inflammation and gastrointestinal disorders of novel nitric oxide-enhancing NSAID’s.

We have filed additional patent applications worldwide and have been issued four Australian patents, three of which expire in 2016 and one in 2019, and one issued Canadian patent, which expires in 2016.

Nitric Oxide Enhancing Cardiovascular Compounds. We have nine pending U.S. patent applications and five pending Patent Cooperation Treaty, or PCT, patent applications, which if issued, will have expiration dates between 2024 and 2026 and which disclose and claim novel nitric oxide-enhancing cardiovascular compounds. These applications also disclose kits and methods of use for the treatment of several diseases and disorders.

Other Development Programs. We also have a U.S. patent and a pending U.S. patent application, both of which expire in 2019, which disclose the methods of use of N-hydroxyguanidines in the treatment of renal failure. We have also filed additional foreign patents applications covering this technology.

License, Manufacturing and Commercialization Agreements

Schwarz Pharma Manufacturing, Inc. In February 2005, we entered into a five-year exclusive manufacturing and supply agreement with Schwarz Pharma for the three times daily immediate release dosage formulation of BiDil. Under the supply agreement, we have the right to engage a backup manufacturer but do not currently have any backup manufacturing agreement in place. The agreement renews automatically upon the expiration of the then-current term for successive one year terms unless either party provides written notice of termination at least six months prior to the expiration of the then-current term. The agreement is also terminable upon the occurrence of certain specified events.

Cardinal Health PTC, LLC. In June 2005, we entered into a three-year exclusive distribution agreement with Cardinal Health for the distribution of BiDil in all formulations. We are obligated to pay Cardinal Health fees for the services provided under the agreement. Pursuant to the terms of the agreement, Cardinal Health has the right of first negotiation for any new pharmaceutical product to be sold by us during the term. The agreement renews automatically unless either party provides written notice.
of termination at least ninety days prior to the expiration of the then-current term. The agreement is terminable without cause upon 120-days notice. However, we are obligated to pay certain fees if we exercise this termination right during the initial term of the agreement. The agreement is also terminable upon the occurrence of certain specified events.

**Publicis Selling Solutions, Inc.** In November 2004, as amended in May 2005, we entered into an agreement with Publicis, a contract sales organization, pursuant to which, on our behalf, Publicis has employed and trained a specialty sales force currently consisting of approximately 144 sales representatives to sell BiDil to our target prescriber markets. The agreement is for a current term of 24 months beginning on January 31, 2005, with our option to continue the agreement beyond this term. We have the right to terminate this agreement upon 90 days written notice to Publicis. If we had terminated this agreement during the period between January 31, 2005 and January 30, 2006, we would have been required to pay a termination fee in the amount of $1.0 million. If we terminate during the period between January 31, 2006 and July 31, 2006, the termination fee will be $750,000. If we terminate the agreement after July 31, 2006, Publicis is not eligible for a termination fee.

**Dr. Jay N. Cohn.** In January 1999, as amended in January 2001 and March 2002, we entered into a collaboration and license agreement with Dr. Jay N. Cohn. Under the agreement, Dr. Cohn licensed to us exclusive worldwide royalty-bearing rights to technology and inventions owned or controlled by Dr. Cohn and that relate to BiDil for the treatment of cardiovascular disease. We have made milestone and are currently making royalty payments to Dr. Cohn since FDA approval and since first commercial sale of BiDil. The agreement imposes upon us an obligation to use reasonable best efforts to develop and, upon receipt of regulatory approval, manufacture, market and commercialize products based upon the licensed rights. If we fail to meet this obligation, Dr. Cohn has the right to terminate the agreement and the license granted to us under the agreement. Dr. Cohn also has the right to terminate the agreement if we materially breach the agreement and fail to remedy the breach within 30 days. We have the right to terminate the agreement at any time upon 30 days’ prior written notice. Unless earlier terminated, the agreement continues in perpetuity. Pursuant to the agreement, Dr. Cohn was appointed to our scientific advisory board, entered into a consulting agreement with us and was granted an option to purchase 10,000 shares of our common stock.

**The Brigham and Women’s Hospital.** In August 1992, as amended in November 1996, we entered into a research and license agreement with The Brigham and Women’s Hospital, Inc (BWH). Under the agreement, we sponsored a research program at BWH for a period of approximately two years relating to the diagnostic, therapeutic and prophylactic use of nitric oxide and related compounds. Under the agreement, in exchange for our sponsored research funding, BWH granted us exclusive worldwide royalty-bearing rights to technology and inventions owned at the effective time of, or developed in the course of, the sponsored research program. We were applying the patents, patent applications and other intellectual property rights licensed to us by the BWH in our former nitric oxide-stent program. The agreement imposes on us due diligence obligations with respect to the research, development and commercialization of products based upon the licensed rights. If we fail to meet these obligations, then upon written notice the license will become non-exclusive. BWH has the right to terminate the agreement if we materially breach the agreement and fail to remedy the breach within 60 days.

**Boston University.** In June 1993, as amended in July 1997, January 1999, December 2002 and February 2005, we entered into a research and license agreement with the Trustees of Boston University (BU). Under the agreement, we have agreed to sponsor a multi-year research program at BU in the area of nitric oxide-enhancing medicines. Under the agreement, in exchange for our sponsored research funding, BU has granted us exclusive worldwide royalty-bearing rights to technology and inventions owned by BU and/or for the principal investigator named in the research proposal at the effective time of, or developed in the course of, the sponsored research program. We have agreed to pay royalties to BU on all products sold or distributed by us or our affiliates which incorporate or utilize inventions, material or
information specified in the agreement. The agreement imposes on us due diligence obligations with respect to the development and commercialization of products based upon the licensed rights. If we fail to meet these obligations, then upon notice by BU, the parties are required to enter into good faith negotiations, and if the parties cannot reach resolution, the license will become non-exclusive without the right to sublicense. BU has the right to terminate the agreement if we materially breach the agreement and fail to remedy the breach within 60 days. We may terminate funding of any sponsored research program on three months’ prior written notice.

**FoxKiser.** In connection with our efforts to obtain the approval of BiDil from the FDA, we entered into an agreement with the law firm of FoxKiser LLC (FoxKiser) for services related to the regulatory approval process for BiDil. The agreement provided for payment of legal consulting fees upon receipt of written FDA approval of BiDil. In addition, the agreement requires us to pay royalties to FoxKiser on commercial sales of BiDil. The royalty term ends six months after the date of market introduction of an FDA-approved generic version of BiDil. During the third quarter of 2005, we entered into a separate consulting agreement with FoxKiser following the approval by the FDA of BiDil. During the years ended December 31, 2005 and 2004, we recorded charges of $1.6 and $1.9 million, respectively, pertaining to the legal consulting fees related to these agreements. On June 23, 2005, we received written FDA approval of BiDil, and in July 2005, we paid $2.4 million pursuant to the terms of these agreements.

**Dr. John D. Folts.** In March 1995, as amended in November 1996 and December 1998, we entered into an agreement with Dr. John D. Folts, pursuant to which Dr. Folts assigned to us his rights to any pending patent applications and issued patents relating to the use of nitric oxide adducts in exchange for a royalty on any products, methods or services sold or distributed by us or our licensees that are covered by the assigned patents. These patents cover technologies that were used in our former nitric oxide-coated stent development program with Boston Scientific.

**Trademarks, Trade Secrets and Other Proprietary Information**

We also currently own the following U.S. trademarks:

- BiDil;
- NitroMed;
- NitRx; and
- NitroMed “N” logo.

In addition, we depend upon trade secrets, know-how and continuing technological improvements to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

**Competition**

We face intense competition from a wide range of pharmaceutical and life science companies, as well as academic and research institutions and government agencies. These competitors include organizations that are pursuing the same or similar technologies to those which constitute our technology platform and organizations that are developing and commercializing pharmaceutical products that may be competitive with our product or product candidates.
We believe that competition for BiDil and our other nitric oxide-enhancing cardiovascular medicines that we may develop will initially come from companies currently marketing and selling therapeutics to treat heart failure in the general population. These competitors include GlaxoSmithKline, plc, Merck & Co., Inc., Pfizer Inc. and AstraZeneca plc.

We also face competition from other companies that are active in or entering into the area of nitric oxide-based therapeutics. We are aware of six companies working in the area of nitric-oxide therapeutics: Angiogenix, Inc., GB Therapeutics, NicOx S.A., OxoN Medica, RenoPharm and Vasopharm BIOTECH GmbH.

We intend to compete with these companies on the basis of BiDil’s strong label and documented efficacy and cost-effectiveness, our intellectual property portfolio, the expertise of our scientific and marketing and sales personnel and our nitric oxide technologies. Principal competitive factors in our industry include:

- improved patient outcomes;
- cost-effectiveness;
- acceptance by patients, physicians, other health care providers and third-party public and private payors;
- the quality and breadth of an organization’s technology;
- the skill of an organization’s employees and its ability to recruit and retain skilled employees;
- an organization’s intellectual property protection;
- development, sales and marketing capabilities; and
- the availability of substantial capital resources to fund development and commercialization activities.

Many of the companies competing against us have financial and other resources substantially greater than our own. In addition, many of our competitors have significantly greater experience in marketing and selling pharmaceutical products, including cardiovascular medicines, testing pharmaceutical and other therapeutic products, and obtaining FDA and other regulatory approvals of products for use in health care. Accordingly, our competitors may succeed more rapidly than we will in obtaining FDA approval for product candidates and achieving widespread market acceptance of products. In addition, we also compete with these companies with respect to manufacturing efficiency and marketing capabilities with respect to BiDil, our only approved product. We have no internal manufacturing capabilities, and our marketing and sales resources may be significantly more limited than those of our competitors.

**Government Regulation and Reimbursement**

**FDA Requirements for New Drug Compounds**

The research, testing, manufacture and marketing of drug products are extensively regulated by numerous governmental authorities in the United States and other countries. In the United States, drugs are subject to rigorous regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, labeling, promotion and marketing and distribution of pharmaceutical products. Failure to comply with applicable regulatory requirements may subject a company to a variety of enforcement actions, including:

- product seizures;
- voluntary or mandatory recalls;
• voluntary or mandatory patient or physician notification;
• withdrawal of product approvals;
• restrictions on, or prohibitions against, marketing our products;
• fines;
• restrictions on importation of our products;
• injunctions;
• debarment;
• civil and criminal penalties; and
• suspension of review, refusal to approve pending applications.

The steps ordinarily required before a new pharmaceutical product may be marketed in the United States include pre-clinical laboratory tests, animal tests and formulation studies, the submission to the FDA of a notice of claimed investigational exemption or an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes several years, and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of potential candidates for a considerable period of time and impose costly procedures upon a manufacturer’s activities. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Pre-clinical tests include laboratory evaluation of product chemistry and formulation, as well as animal trials to assess the potential safety and efficacy of the product. The conduct of the pre-clinical tests and formulation of compounds for testing must comply with federal regulations and requirements. The results of pre-clinical testing are submitted to the FDA as part of an IND.

A 30-day waiting period after the filing of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not commented on or questioned the IND within this 30-day period, clinical trials may begin. If the FDA has comments or questions, the questions must be answered to the satisfaction of the FDA before initial clinical testing can begin. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. In some instances, the IND process can result in substantial delay and expense.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and requirements, under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. subjects must be submitted to the FDA as part of the IND. The study protocol and informed consent information for patients in clinical trials must be submitted to institutional review boards for approval.
Clinical trials to support a New Drug Application, or NDA, for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In phase I, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess safety, including side effects associated with increasing doses, metabolism, pharmacokinetics and pharmacological actions. Phase II usually involves trials in a limited patient population, to determine dosage tolerance and optimum dosage, identify possible adverse effects and safety risks, and provide preliminary support for the efficacy of the drug in the indication being studied.

If a compound demonstrates evidence of effectiveness and an acceptable safety profile in phase II evaluations, phase III trials are undertaken to further evaluate clinical efficacy and to further test for safety within an expanded patient population, typically at geographically dispersed clinical trial sites. Phase I, phase II or phase III testing of any product candidate may not be completed successfully within any specified time period, if at all.

After successful completion of the required clinical testing, generally an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of extensive clinical and other testing and a compilation of data relating to the product’s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. Under Federal law, the submission of NDAs are additionally subject to substantial application user fees, currently exceeding $750,000, and the manufacturer and/or sponsor under an approved application are also subject to annual product and establishment user fees, currently exceeding $30,000 per product and $200,000 per establishment. Additional user fees exceeding $300,000 apply for NDA supplements containing clinical data. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency’s threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under federal law, the FDA has agreed to certain performance goals in the review of NDAs. Most such applications for non-priority drug products are reviewed within ten months. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee.

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, an approvable letter followed by an approval letter. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA’s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require post approval testing and surveillance to monitor the drug’s safety or efficacy and may impose other conditions, including labeling restrictions which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing. On July 20, 2004, the FDA issued a proposed rule that would replace not approvable and approvable letters with complete response letters. Complete response letters would describe all specific deficiencies in an NDA but would not characterize the application as approvable or not.
Once the NDA is approved, a product will be subject to certain post-approval requirements, including requirements for adverse event reporting and submission of periodic reports and/or supplemental NDA’s for approval of changes to the originally approved prescribing information, product formulation, and manufacturing and testing requirements. Following approval, drug products are required to be manufactured and tested for compliance with NDA and/or compendial specifications prior to release for commercial distributions. The manufacture and testing must be performed in approved manufacturing and testing sites complying with current Good Manufacturing Practice requirements and subject to FDA inspection authority.

Approved drug products must be promoted in a manner which is consistent with their terms and conditions of approval. In addition, the FDA requires substantiation of any claims of superiority of one product over another including, in many cases, requirements that such claims be proven by adequate and well controlled head-to-head clinical trials. To the extent that market acceptance of our product candidates may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively affect the sales of our products and/or our expenses.

If the FDA’s evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter. A not approvable letter outlines the deficiencies in the submission and often requires additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, the FDA may withhold approval of an NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

Once an NDA is approved, the product covered thereby becomes a “listed drug” which can, in turn, be cited by potential competitors in support of approval of an abbreviated NDA. An abbreviated NDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. There is no requirement, other than the requirement for bioequivalence testing, for an abbreviated NDA applicant to conduct or submit results of pre-clinical or clinical tests to prove the safety or efficacy of its drug product. Drugs approved in this way are commonly referred to as “generic equivalents” to the listed drug, are listed as such by the FDA, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor. During this three year period, the FDA cannot grant effective approval of an abbreviated NDA based on that listed drug. Federal law also provides a period of five years following approval of a drug containing no previously approved active ingredients, during which abbreviated NDAs for generic versions of those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval. Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an abbreviated NDA referencing that drug are required to certify whether they intend to market their generic products prior to expiration of those patents. If an abbreviated NDA applicant certifies that it believes all listed patents are invalid or not infringed, it is required to provide notice of its filing to the NDA sponsor and the patent holder. If the patent holder then initiates a suit for patent infringement against the abbreviated NDA sponsor within 45 days of receipt of the notice, the FDA cannot grant effective approval of the abbreviated NDA until either 30 months has passed or there has been a court decision holding that the patents in
question are invalid or not infringed. If the abbreviated NDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then the FDA cannot grant effective approval of the abbreviated NDA until those patents expire. The first abbreviated new drug applicant(s) submitting substantially complete applications certifying that all listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days against other generics after a final court decision of invalidity or non-infringement or after it begins marketing its product, whichever occurs first, during which subsequently submitted abbreviated NDA’s cannot be granted effective approval.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency or the courts in ways that may significantly affect our business and our products candidates. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of such changes, if any, may be.

**Foreign Regulation of New Drug Compounds**

Approval of a product by comparable regulatory authorities may be necessary in foreign countries prior to the commencement of marketing of the product in those countries, whether or not FDA approval has been obtained. The approval procedure varies among countries and can involve requirements for additional testing. The time required may differ from that required for FDA approval. Although there are some procedures for unified filings for some European countries with the sponsorship of the country which first granted marketing approval, in general each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

In Europe, marketing authorizations may be submitted at a centralized, a decentralized or a national level. The centralized procedure is mandatory for the approval of biotechnology products and provides for the grant of a single marketing authorization which is valid in all European Union member states. As of January 1995, a mutual recognition procedure is available at the request of the applicant for all medicinal products which are not subject to the centralized procedure. We will choose the appropriate route of European regulatory filing to accomplish the most rapid regulatory approvals. However, our chosen regulatory strategy may not secure regulatory approvals on a timely basis or at all.

**Hazardous Materials**

Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material.

**Reimbursement**

In both the United States and foreign markets, our ability to successfully commercialize BiDil and any future products successfully depends in part on the extent to which reimbursement for the costs of such products will be available from government health administration authorities, private health insurers and other third-party payors. Significant uncertainty exists as to the reimbursement status of newly-approved health care products, products used for indications not approved by the FDA and products which have competitors for their approved indications. If we are unable to achieve preferential reimbursement treatment for BiDil, or any of our other product candidates, from government and other third-party payors, our ability to sell our products may be limited or our ability to establish acceptable pricing schemes for our products may be impaired, thereby reducing our revenue.
Scientific Advisors

Scientific Advisory Board

We seek advice from a number of leading scientists and physicians on scientific and medical matters. In 2005 our scientific advisory board was chaired by our founder and member of our board of directors, Joseph Loscalzo, M.D., Ph.D. The board met to assess:

- our research and development programs;
- the design and implementation of our clinical programs;
- our patent and publication strategies;
- market opportunities from a clinical perspective;
- new technologies relevant to our research and development programs; and
- specific scientific and technical issues relevant to our business.

The members of our 2005 scientific advisory board were:

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<th>Name</th>
<th>Position/Institutional Affiliation</th>
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<tr>
<td>Joseph Loscalzo, M.D., Ph.D.</td>
<td>Chairman, Department of Medicine; Physician in Chief, Brigham and Women’s Hospital; member, NitroMed board of directors</td>
</tr>
<tr>
<td>Jay N. Cohn, M.D.</td>
<td>Professor of Medicine, Cardiovascular Division, University of Minnesota Medical School</td>
</tr>
<tr>
<td>Martin Feelisch, Ph.D.</td>
<td>Professor of Medicine, Boston University School of Medicine</td>
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<tr>
<td>John D. Folts, Ph.D.</td>
<td>Director, Coronary Thrombosis Research and Prevention Laboratory, Department of Medicine, University of Wisconsin-Madison and Professor of Medicine and Nutritional Science, University of Wisconsin School of Medicine</td>
</tr>
<tr>
<td>Robert F. Furchgott, Ph.D.</td>
<td>Professor of Pharmacology, Medical University of South Carolina and Nobel Laureate for his work on nitric oxide</td>
</tr>
<tr>
<td>Michael A. Marletta, Ph.D.</td>
<td>Professor of Biochemistry and Molecular Biology, University of California, Berkeley</td>
</tr>
<tr>
<td>Kevin McIntyre, M.D., J.D.</td>
<td>Associate Clinical Professor of Medicine, Harvard Medical School</td>
</tr>
<tr>
<td>Ínigo Saenz de Tejada, M.D.</td>
<td>President, Fundación para la Investigación y el Desarrollo en Andrología, Madrid, Spain</td>
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In December 2005, our scientific advisory board was replaced by our technical review committee.

Technical Review Committee

Since the beginning of fiscal year 2006, we have sought advice for our drug research and development efforts from a technical review committee which is chaired by our founder and member of our board of directors, Joseph Loscalzo, M.D., Ph.D. The technical review committee meets regularly to assess the same research and development matters addressed by our former scientific advisory board.
The current members of our technical review committee are:

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<tbody>
<tr>
<td>Joseph Loscalzo, M.D., Ph.D.</td>
<td>Chairman, Department of Medicine; Physician-in-Chief, Brigham &amp; Women’s Hospital; member, NitroMed board of directors</td>
</tr>
<tr>
<td>Frank L. Douglas, M.D., Ph.D.</td>
<td>Executive Director, Massachusetts Institute of Technology Center for Biomedical Innovation, Professor of the Practice; member, NitroMed board of directors</td>
</tr>
<tr>
<td>Zola Horovitz, Ph.D.</td>
<td>Consultant; formerly member of management at Bristol-Myers Squibb; member, NitroMed board of directors</td>
</tr>
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Employees

As of December 31, 2005, we had 96 full-time employees, 30 of whom were engaged in sales and marketing, 45 of whom were engaged in research and development and 21 of whom were engaged in management, administration and finance. Of our employees, 25 hold M.D. or Ph.D. degrees. Our success depends in part on our ability to recruit and retain talented and trained scientific personnel and senior management. We have been successful to date in obtaining and retaining such personnel, but may not be successful in the future. None of our employees are represented by a labor union or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

Product Liability Insurance

The administration of our products to humans, whether in clinical trials or after marketing approvals are obtained and the product is in use commercially, may expose us to liability claims. These claims might be made by customers, including corporate partners, clinical trial subjects, patients, pharmaceutical companies or others. We maintain product liability insurance coverage for claims arising from the use of our products, whether in clinical trials or approved commercial usage. However, coverage is becoming increasingly expensive, and our insurance may not provide sufficient coverage to fully protect us against liability. If we are unable to maintain sufficient levels of insurance due to increased costs or if our insurance does not provide sufficient coverage against liability claims, a finding of liability could deplete our resources and reduce the assets available for our daily operations.

Significant Customers

Mckesson, Cardinal Health and AmerisourceBergen accounted for approximately 44%, 21% and 14% of our product sales, and Boston Scientific accounted for 100% of our research and development revenues in fiscal 2005. No other company accounted for more than 10% of our total revenues in fiscal 2005. Merck accounted for 90% and 96% of our total research and development revenues in fiscal 2004 and 2003 respectively. Another company accounted for the remainder of our revenues in 2004 and 2003.

Research and Development

We have dedicated a significant portion of our resources to research and development as a method of producing new products, improving existing products and growing our revenues. We estimate that approximately 48% to 51% of our employees' time has been devoted to research and development for each of the last three fiscal years. We incurred research and development expenses of $31.9 million, $28.0 million, and $18.9 million in fiscal 2005, 2004 and 2003, respectively. We anticipate that a significant portion our operating expenses will continue to be related to research and development activities in fiscal 2006.
Raw Materials

We order bulk materials from the same suppliers that were used for the clinical trial batches of BiDil: hydralazine hydrochloride from Flavine International, Inc., the U.S. representative of Sumitomo Corp., and isosorbide dinitrate from Dottikon ES Holding AG, and have them delivered directly to Schwarz Pharma for manufacturing. Sumitomo is currently the only supplier of hydralazine hydrochloride worldwide. We do not have any agreement with Sumitomo regarding the supply of hydralazine hydrochloride.

Subsequent Event

In January 2006, we completed a direct offering of shares of our common stock previously registered under our effective shelf registration statement, which was filed with the Securities and Exchange Commission (SEC) in August 2005. Pursuant to this offering, we sold approximately 6.1 million shares of our common stock to selected institutional investors at a price of $10.25 per share. Proceeds to us from this registered direct offering, net of offering expenses and placement agency fees, totaled $58.6 million. The net proceeds of the financing will be used for general corporate purposes, including the continued commercial launch of BiDil.

Available Information

Our internet website address is http://www.nitromed.com. Through our website, we make available, free of charge, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendments to those reports, proxy and registration statements, and all of our insider Section 16 reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. These SEC reports can be accessed through the “Investors” section of our website. The information found on our website is not part of this or any other report we file with, or furnish to, the SEC.

For additional information regarding our segment reporting, please refer to Note 2 of Notes to Financial Statements included in Part II, Item 8 “Financial Statements and Supplementary Data” of this annual report on Form 10-K.

ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors, in addition to other information included in this annual report, in evaluating NitroMed and our business. If any of the following risks occur, our business, financial condition and operating results could be materially adversely affected.

Risks Relating to our Business

Our business is substantially dependent on the commercial success of BiDil, and if sales of BiDil do not increase our business will be materially harmed and our stock price will decline.

On June 23, 2005, the FDA approved BiDil for the treatment of heart failure in self-identified black patients as an adjunct to current standard therapy. We launched BiDil in July 2005 and therefore have only recently begun to receive revenue from sales of BiDil. BiDil is currently our only commercial product, and we expect that it will account for all of our product sales and substantially all of our total revenues for the next several years. We face a number of significant risks relating to our ability to successfully commercialize BiDil, including risks relating to: our ability to successfully secure preferable reimbursement treatment from government and third-party insurers for BiDil; our ability to effectively and efficiently transition our contract field sales force to NitroMed and our ability to continue to increase the productivity of our sales force; our ability to effectively develop and/or contract for adequate marketing and manufacturing capabilities; our ability to gain market acceptance of BiDil as safe, effective and medically necessary; our ability to maintain the necessary patent protection, licenses and regulatory
approvals required to market and sell BiDil; the availability of substantial cash to fund our BiDil commercialization plans; competitive factors, including the possibility of physicians prescribing the two lower cost generic drugs that compose BiDil itself as a substitute for BiDil, and adverse effects on pricing or reimbursement resulting from the possibility of this generic substitution; and the various other factors discussed in detail throughout this section titled “Risk Factors.” In order for us to successfully commercialize BiDil, our sales of BiDil must increase significantly from their current levels. If we fail to significantly increase BiDil sales, our near-term ability to generate product revenue, our reputation and our ability to raise additional capital will be materially impaired, and the value of an investment in our stock will decline.

If we do not successfully market and sell BiDil or our other product candidates, either directly or through third parties, our future revenue will be limited.

We currently have limited sales, marketing and distribution experience. We have launched BiDil in the United States ourselves, using a contract sales force. We transitioned to the use of a smaller sales force during the first quarter of 2006, and we intend to internalize this sales force by the third quarter of 2006. This transition could adversely affect our marketing of BiDil, and any adverse effect on BiDil sales will depress the value of our stock. In the future, we may also seek to market other products ourselves which are not already subject to marketing agreements and where we believe the target physician market can be effectively reached by the sales force we have established. In order to develop our internal sales force or to contract for sales and marketing capabilities, we will have to invest significant amounts of money and management resources. For BiDil and any other product candidates for which we decide to perform the sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

• we may not be able to effectively or efficiently transition our contract sales force to NitroMed or to attract, build and retain a significant and qualified marketing or sales force;

• the cost of establishing a marketing and sales force may not be justifiable in light of the revenues generated by any particular product or combination of products; and

• our direct sales and marketing efforts may not be successful.

For potential future products with larger target physician markets, we plan to rely significantly on sales, marketing and distribution arrangements with third parties. We may not be able to successfully enter into sales, marketing and/or distribution agreements with third parties in the future, on terms that are favorable to us, if at all. In addition, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues for any products for which we rely on third-party sales, marketing and distribution support will depend heavily on the success of the efforts of these third parties.

Physicians, payors and patients may not be receptive to BiDil or our other product candidates, if approved, which could prevent us from achieving and maintaining profitability.

We currently market BiDil only in the United States. Key participants in the U.S. pharmaceutical marketplace, such as physicians, payors and patients, may not accept a product intended to improve therapeutic results based on ethnicity. As a result, it may be more difficult for us to convince the medical community, third-party payors and patients to accept and use BiDil. Our business is substantially dependent on market acceptance of BiDil.

Other factors that we believe will materially affect market acceptance of BiDil include:

• the availability of favorable government and third-party payor reimbursement;

• the timing of our receipt of marketing approval, if any, for next-generation BiDil products, such as BiDil XR and BiDil Combination products, or for any expansion of our current label for BiDil, such as extended product dating or inclusion of new data;
• the success of our promotional programs;

• the timing of our receipt of any marketing approvals outside the U.S., the terms of any non-U.S.
approval (including labeling requirements and/or limitations), and the countries in which approvals
are obtained, if any;

• the safety, efficacy and ease of administration of BiDil; and

• the ability to produce BiDil at a competitive price.

We will require substantial additional cash to fund our operating plan, including commercializing BiDil,
and, if additional capital is not available, we may need to limit, scale back or cease our operations.

We have used and will continue to require substantial funds to sell, market and manufacture BiDil,
which was commercially launched in July 2005, to conduct research and development, including pre-
clinical testing and clinical trials of our product candidates, and to market and manufacture any future
products that are approved for commercial sale. In particular, we expect that we will incur significant
expenses during 2006 and beyond relating to manufacturing, sales and marketing of BiDil. Moreover, we
may incur significant additional expenditures to conduct clinical testing of our proprietary nitric
oxide-enhancing cardiovascular agent and pre-clinical testing of our early-stage development programs.
Because the successful commercialization of BiDil, and the timing of when we might receive significant
revenue from BiDil, if at all, is uncertain, and because the successful development of any other product
candidates is uncertain, we are unable to estimate the actual funds we will require to commercialize BiDil
and to complete research and development of our product candidates. We believe that our existing cash,
cash equivalents and marketable securities, together with the proceeds from our recent offering, will be
sufficient to fund our current operating plan, including increased operating expenses in support of the
launch and commercialization of BiDil, for at least the next 21 months.

However, our future capital requirements, and the period in which we expect our current cash to
support our operations, may vary from what we expect due to a number of factors, including the following:

• the cost of successfully commercializing BiDil;

• the timing, receipt and amount of revenue from sales of BiDil;

• the timing and costs of obtaining regulatory approvals, if any, for our other product candidates;

• the timing, receipt and amount of milestone and other payments, if any, from collaborators;

• the timing, receipt and amount of sales and royalties, if any, from our product candidates;

• the resources required to successfully complete our clinical trials, if any;

• continued progress in our research and development programs, as well as the magnitude of these
programs;

• the effect of competing technological and market developments;

• the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;

• the costs related to acquiring and/or in-licensing new technologies and/or products or product
candidates; and

• our ability to establish and maintain additional collaborative arrangements.

We may be required to seek additional funding in the future and may do so through collaborative
arrangements and/or public or private financings. Additional financing may not be available to us on
acceptable terms, or at all. In addition, the terms of the financing may adversely affect the holdings or the
rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further
dilution to our then-existing stockholders will result. If we are unable to obtain funding on a timely basis,
we may be required to significantly curtail our marketing efforts for BiDil or one or more of our research
or development programs. We also could be required to seek funds through arrangements with
collaborators or others that may require us to relinquish rights to some of our technologies, product
candidates or products which we would otherwise pursue on our own.

**Poor performance by our contract sales organization or difficulties arising in our planned transition to an
internal sales force could prevent us from achieving the significant growth we need to achieve in BiDil
revenues.**

We have an agreement with Publicis, a contract sales organization, pursuant to which, on our behalf,
Publicis has employed and trained a specialty sales force currently consisting of 144 sales representatives,
to sell BiDil to our target prescriber markets. Under separate agreements, Publicis has recruited, hired and
trained seven account executives and one national director, who are dedicated to NitroMed on a non-
exclusive basis, who assist us in gaining formulary access for BiDil and has hired six medical science liaisons
to report into our medical affairs group. Our near-term revenue for BiDil will depend heavily upon the
efforts and success of Publicis. If Publicis does not devote the resources, time and training required to
establish, manage and maintain an effective and qualified sales force, our ability to achieve revenue from
sales of BiDil will be harmed.

We intend to transition the contract sales representatives to NitroMed by the third quarter of 2006.
We may not be able to effectively or efficiently complete this transition. Any failure to transition our
current contract sales representatives, or election by us not to transition certain of these representatives, to
NitroMed, will result in the need to recruit and train new sales representatives to cover our revised sales
territories. We may not be able to successfully recruit and train new sales representatives, and the efforts to
do so will result in additional costs and expenses related to our sales efforts. In addition, we have recently
elected to reduce the number of sales territories in which we have sales representation. Any failure to
adequately cover our current sales territories, or to cover through alternative marketing efforts the
territories in which we have elected not to have sales representation, may result in reduced sales
productivity and loss of revenue related to BiDil.

**Because we have a history of losses and our future profitability is uncertain, our common stock is a highly
speculative investment.**

We have experienced significant operating losses since our inception in 1992. For the year ended
December 31, 2005, we had a net loss of $105.9 million. As of December 31, 2005, we had an accumulated
deficit of $242.5 million. We expect that we will continue to incur substantial losses and that our
cumulative losses will increase as our research, development and commercialization efforts expand. We
expect that the losses that we incur will fluctuate from quarter to quarter and that these fluctuations may
be substantial. We received approval for our first product, BiDil, from the FDA on June 23, 2005, and
launched commercial sales of BiDil in July 2005. All of our other product candidates, with the exception of
NMI-3377 for which we expect to file an IND in the second quarter of 2006, are in research or pre-clinical
development and will require significant additional testing prior to submission of any regulatory
applications and, as such, are not expected to be commercially available for many years, if at all.

A large portion of our expenses is fixed, including expenses related to facilities, equipment and
personnel. We have spent significant amounts to launch BiDil, and we expect to incur significant operating
expenses in connection with our ongoing commercialization activities related to BiDil. We have also spent
significant amounts to fund research, development and commercialization of our product candidates and
to enhance our core technologies. Although we currently estimate that our operating expenses will
decrease during fiscal year 2006, we will still need to generate significant revenue to achieve profitability.
We are currently unable to estimate the level of revenues that we will realize from the commercialization of BiDil or any of our other product candidates. We are therefore unable to estimate when we will achieve profitability, if at all. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

Our BiDil product revenues have been and will continue to be subject to considerable variation due to volatility in prescription volume, the manner in which we account for product sales considering product returns rates, level of purchases by individual customers and other matters related to the commercialization of this product. We have experienced and are likely to continue to experience significant revenue deferrals and product returns, as well as additional charges and expenses associated with stocking incentives, other promotional incentives, and other matters related to the launch and commercialization of this product. Significant inventory adjustments may also occur due to the 12-month shelf life of BiDil, sales forecast variances, or other factors. Any deferrals, returns or adjustments that negatively impact revenue, or our failure, for this or any other reason, to generate significant near-term revenue growth, could depress our stock price and adversely affect our ability to raise capital.

The availability of lower priced generic substitutes for BiDil may adversely affect our sales of BiDil and the pricing or reimbursement we are able to obtain for BiDil.

BiDil is a fixed-dosed combination of two generic drugs, which are approved and separately marketed, in dosages similar to those we include in BiDil, at prices substantially below the prices we are charging for BiDil. While neither of these two generic drugs is approved for the treatment of heart failure, as a practical matter it may be impossible for us to prevent physicians from prescribing a combination of these two, lower cost generic drugs as a substitute for prescribing BiDil. If substantial numbers of physicians prescribe the combination of these two generic drugs, rather than BiDil, we could fail to achieve the sales of BiDil necessary for successful commercialization which would severely limit our ability to generate revenue from the sales of BiDil. Our ability to generate revenue could also be limited if potential large purchasers of BiDil such as hospitals or health maintenance organizations require the substitution of these generic drugs for BiDil, or if state formularies or other government agencies or private payors that approve reimbursement for drugs require such substitution, or if the availability of these generic drugs reduces the price or reimbursement amounts we are able to achieve for BiDil.

We may not have the technology internally to successfully develop BiDil XR and we may not be able to acquire such technology on favorable terms, if at all.

Although we intend to pursue the development of an extended release formulation of BiDil, called BiDil XR, to be taken either once or twice a day, we do not currently have the technology internally to pursue this development on our own. The technology underlying extended release formulations of pharmaceutical products is highly proprietary and would take years and the expenditure of significant amounts of capital to develop by us. If we are unable to find extended release technology from a third party which is compatible for use with BiDil, we would be prevented from pursuing the development of BiDil XR. Even if we are able to identify compatible extended release technology, we may not be able to acquire rights to such technology on favorable terms, if at all. In addition, even if we are successful in acquiring such rights, we may be required to forfeit certain rights to our BiDil XR product to the owner of such technology, thereby reducing our future potential revenue from commercialization of this product.
If the third-party manufacturer of BiDil encounters delays or difficulties in production, we may not be able to meet demand for the product, and we may lose potential revenue.

We do not manufacture BiDil and have no plans to do so. We have engaged Schwarz Pharma Manufacturing, under a five-year exclusive manufacture and supply agreement solely for the three times daily immediate release dosage formulation of BiDil. Under the supply agreement, we have the right to engage a backup manufacturer but do not currently have any backup manufacturing agreement in place. The terms of the supply agreement provide that it may be terminated by either us or Schwarz Pharma under specified circumstances, including a material breach of the supply agreement by either party, the occurrence of a payment default by us, our material impairment of the manufacturing licenses we have granted to Schwarz Pharma or a failure of Schwarz Pharma to supply conforming products. In addition, either party may terminate the supply agreement in the event the FDA takes any action, the result of which is to permanently prohibit the manufacture, sale or use of the product. If we are unable to maintain a commercially reasonable manufacturing agreement for the production of BiDil with Schwarz Pharma, we may not be able to successfully commercialize BiDil and our stock price may decline.

Furthermore, Schwarz Pharma may encounter difficulties in production. These problems may include, but are not limited to:

- difficulties with production costs and yields;
- quality control and assurance;
- difficulties obtaining ingredients for our products;
- shortages of qualified personnel;
- compliance with strictly enforced federal, state and foreign regulations; and
- lack of capital funding.

The number of third-party manufacturers with the manufacturing and regulatory expertise and facilities necessary to manufacture finished products for us on a commercial scale is limited, and it would take a significant amount of time to arrange, qualify, and receive necessary regulatory approval for alternative arrangements. We may not be able to contract for manufacturing on acceptable terms, if at all.

Any of these factors could increase our costs and result in our inability to effectively commercialize BiDil. Furthermore, if Schwarz Pharma or any other third-party manufacturer of BiDil fails to deliver the required commercial quantities of finished product on a timely basis and at commercially reasonable prices, we may be unable to meet the demand for our product, and we may lose potential revenues.

**The development and commercialization of our product candidates may be terminated or delayed, and the cost of development and commercialization may increase, if third parties on whom we rely to manufacture our products do not fulfill their obligations.**

We do not manufacture any of our product candidates and have no current plans to develop any capacity to do so in the future. In order to continue to develop product candidates, apply for regulatory approvals and commercialize our products, we plan to rely on third parties for the production of clinical and commercial quantities of our product candidates. We may not be able to secure a third-party manufacturer for our product candidates on commercially favorable terms, if at all. In addition, contract manufacturers are subject to ongoing periodic, unannounced inspection by the FDA and corresponding state and foreign agencies or their designees to ensure strict compliance with current Good Manufacturing Practices, or cGMP, and other governmental regulations and corresponding foreign standards. The cGMP requirements govern quality control of the manufacturing process and documentation of policies and procedures. Other than through contract, we do not have control over compliance by our contract manufacturers with these regulations and standards. Our present or future contract manufacturers may not
be able to comply with cGMPs and other FDA requirements or similar regulatory requirements outside the United States. Failure of our contract manufacturers to comply with applicable regulations could result in sanctions being imposed on us in some cases, including fines, injunctions, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect our business. We will depend upon these third parties to perform their obligations in a timely manner and in accordance with applicable laws and regulations. If we fail to secure a third-party manufacturer on commercially favorable terms, or to the extent that third-party manufacturers with whom we contract fail to perform their obligations in accordance with applicable laws and regulations, we may be adversely affected in a number of ways, including:

- we may not be able to initiate or continue clinical trials of our product candidates, including BiDil XR and BiDil Combination products;
- we may be delayed in submitting applications for regulatory approvals for our product candidates, including BiDil XR and BiDil Combination products;
- we may be required to cease distribution and/or recall some or all batches of our products; and
- we may not be able to meet commercial demands for our products or achieve profitability.

We rely on a single source supplier for one of the two active ingredients in BiDil, and the loss of this supplier could prevent us from selling BiDil, which would materially harm our business.

We rely on Sumitomo Corp. for our supply of hydralazine hydrochloride, one of the two active ingredients in BiDil. Sumitomo is currently the only supplier of hydralazine hydrochloride worldwide. We do not have any agreement with Sumitomo regarding the supply of hydralazine hydrochloride. If Sumitomo stops manufacturing or is unable to manufacture hydralazine hydrochloride, or if we are unable to procure hydralazine hydrochloride from Sumitomo on commercially favorable terms, we may be unable to continue to sell BiDil on commercially viable terms, if at all. Furthermore, because Sumitomo is currently the sole supplier of hydralazine hydrochloride, Sumitomo has unilateral control over the price of hydralazine hydrochloride. Any increase in the price for hydralazine hydrochloride may reduce our gross margins and adversely affect our ability to achieve profitability.

If our partners and we do not obtain and maintain the regulatory approvals required to market and sell our product candidates, then our business will be unsuccessful, and the market price of our stock will substantially decline.

Our partners and we will not be able to market any of our product candidates in the United States, Europe or in any other country without marketing approval from the FDA or equivalent foreign regulatory agency. The process of obtaining FDA approval of pharmaceutical products is costly and time consuming. Any new pharmaceutical product must undergo rigorous preclinical and clinical testing and an extensive regulatory approval process mandated by the FDA. Such regulatory review includes the determination of manufacturing capability and product performance. The approval process is affected by such factors as:

- the severity of the disease;
- the quality of the regulatory submission;
- the clinical efficacy and safety;
- the strength of the chemistry and manufacturing control of the process;
- the manufacturing facility compliance;
- the availability of alternative treatments;
• the risks and benefits demonstrated in clinical trials; and
• the patent status and marketing exclusivity rights of certain innovative products.

The regulatory process to obtain market approval for a new drug takes many years and requires expenditures of substantial resources. We have had only limited experience in preparing applications and obtaining regulatory approvals.

There can be no assurance that our pharmaceutical products currently in development, or those product candidates acquired or in-licensed by us, will be approved by the FDA. In addition, there can be no assurance that all necessary approvals will be granted for future product candidates or that FDA review or actions will not involve delays caused by the FDA’s request for additional information or testing that could adversely affect the time to market and sale of these product candidates.

If we do not receive required regulatory approval or clearance to market any of our product candidates, we will not be able to develop and commercialize these product candidates, which will affect our ability to achieve profitability and may cause the market price of our common stock to substantially decline.

Even if we obtain regulatory approvals, our marketed products, including BiDil, will be subject to ongoing regulatory review. If we fail to comply with continuing United States and foreign regulations, we could lose our approvals to market our products and our business would be seriously harmed.

Even after approval, any products we develop will be subject to ongoing regulatory review and restrictions, including the review of clinical results which are reported after our products are made commercially available, and restrictions on the indications for which we can market the product. The FDA can propose to withdraw our approval if new clinical data or experience shows that a product is not safe for use under the approved conditions of use. The FDA or we may need to send important information about our products to healthcare providers. The marketing claims we are permitted to make in labeling or advertising regarding our marketed products are limited to those specified in any FDA approval. For example, because BiDil is specifically approved for labeling for self-identified black patients, we may not promote BiDil for use in other patient populations. For our prescription drugs, we must submit copies of our advertisements and promotional labeling, including, for example, professional journal advertisements, website pages, professional direct mailers, direct-to-consumer advertisements, convention booth panels and handouts, to the FDA at the time of initial publication or dissemination. If the FDA believes these materials or statements made by sales representatives or other Company officials promote our products for unapproved indications, the FDA could allege that our promotional activities misbrand our products. Specifically, the FDA could issue an untitled letter or warning letter, which requests, among other things, that we cease such promotional activities, including disseminating the advertisements and promotional labeling, and that we issue corrective advertisements and labeling, including sending letters to healthcare providers. The FDA also could take enforcement action including seizure of allegedly misbranded product, injunction or criminal prosecution against the Company and its officers or employees. If we repeatedly or deliberately failed to submit such advertisements and labeling to the agency, the FDA could withdraw our approvals. The FDA also monitors manufacturers’ support of continuing medical education, or CME, programs where the programs involve the manufacturers’ or a competitor’s products to ensure that manufacturers do not influence the CME content as a means of promoting their products for off label uses.

In addition, the manufacturer and manufacturing facilities we use to produce any of our product candidates will be subject to periodic review and inspection by the FDA. We will be required to report any serious and unexpected adverse experiences and certain quality problems with our products and make other periodic reports to the FDA. The discovery of any previously unknown problems with the product, manufacturer or facility may result in restrictions on the product or manufacturer or facility, including
withdrawal of the product from the market. Certain changes to an approved product, including the way it is manufactured or promoted, often require prior FDA approval before the product as modified may be marketed. If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, untitled letters, warning letters, civil penalties, suspension or withdrawal of regulatory approvals, product recalls and seizures, injunctions, operating restrictions and/or criminal prosecutions and penalties.

**If we, our third-party manufacturers or our service providers fail to comply with applicable laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to market and sell our products and harm our reputation.**

If we or our third-party manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to fewer acceptances of our products by the market. These enforcement actions include:

- product seizures;
- voluntary or mandatory recalls;
- patient or physician notifications, including letters to healthcare professionals and corrective advertising;
- withdrawal of product approvals;
- restrictions on, or prohibitions against, marketing our products;
- fines;
- restrictions on importation of our products;
- injunctions;
- debarments;
- civil and criminal penalties; and
- suspension of review of, or refusal to approve, pending applications.

**The application of our nitric oxide technology is unproven in humans and, as a result, we may not be able to successfully develop and commercialize any products based upon this technology.**

A component of our strategy is to seek to improve existing medicines with our proprietary nitric oxide technology, such as any future BiDil Combination product. Our product candidates include nitric oxide enhancements of existing drugs. Thus, we are modifying compounds whose chemical and pharmacological profiles are well-documented and understood. However, many of our potential product candidates are new molecules with chemical and pharmacological profiles that differ from that of the existing drugs. These compounds may not demonstrate in patients the chemical and pharmacological properties shown in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. In addition, it is possible that existing drugs or newly-discovered drugs may not benefit from the application of our nitric oxide technology. If we are not able to successfully develop and commercialize drugs based upon our technology, we will not generate revenue based on these drugs, and the value of our stock will decline.

**If our clinical trials for any product candidates we advance into clinical testing are not successful, we may not be able to successfully develop and commercialize these product candidates.**

In order to obtain regulatory approvals for the commercial sale of our product candidates, our collaborators or we will be required to complete extensive clinical trials in humans to demonstrate the
safety and efficacy of our product candidates. We may not be able to obtain authority from the FDA or other regulatory agencies to commence or complete these clinical trials. If permitted, such clinical testing may not prove that our product candidates are sufficiently safe and effective to permit us to obtain marketing approvals from regulatory authorities. Moreover, positive results demonstrated in pre-clinical studies and clinical trials that we complete may not be indicative of results obtained in future clinical trials. Furthermore, we, one of our collaborators, institutional review boards or regulatory agencies may suspend clinical trials at any time if it is believed that the patients participating in such trials are being exposed to unacceptable health risks. Adverse or inconclusive clinical trial results concerning any of our product candidates could require us to conduct additional clinical trials, result in increased costs and significantly delay the filing for marketing approval for those product candidates with the FDA, result in a filing for a narrower indication than was originally sought or result in a decision to discontinue development of those product candidates.

The successful completion of our clinical trials will depend on, among other things, the rate of patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the nature of the clinical protocol, the availability of alternative treatments, the proximity of patients to clinical sites and the eligibility criteria for the study. We may be unable to enroll the number of patients we need to complete a trial on a timely basis. Moreover, delays in planned patient enrollment for clinical trials may cause us to incur increased costs and delay commercialization.

We have relied on academic institutions or clinical research organizations to supervise or monitor some or all aspects of our African American Heart Failure Trial (A-HeFT), and we expect to rely on academic institutions and clinical research organizations for other product candidates we advance into clinical testing. In addition, we may need to rely on third parties for technology to support the development of our product candidates. Accordingly, we have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own.

As a result of these factors, we, or third parties on whom we rely, may not successfully begin or complete our clinical trials in the time periods we have forecasted, if at all. Moreover, if we incur costs and delays in our programs or if we do not successfully develop and commercialize our products, our future revenues may be materially impaired.

Our failure to successfully acquire, develop and market additional drug candidates or approved drugs would impair our ability to grow.

As part of our strategy, we intend to acquire, develop and market additional products and product candidates for cardiovascular and metabolic diseases. The success of this strategy depends upon our ability to identify, select and acquire appropriate pharmaceutical product candidates and products.

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

Proposing, negotiating and implementing an economically viable acquisition of a product or product candidate is a lengthy and complex process. Other companies, including those with substantially greater financial, marketing and sales resources, may compete with us for the acquisition of product candidates and approved products. We may not be able to acquire the rights to additional product candidates and approved products on terms that we find acceptable, if at all.
The expiration of the research term under our collaboration agreement with Boston Scientific has resulted in the loss of potential royalty-based revenue from the collaboration and may indicate that the development of nitric oxide-enhancing stents is not viable.

In November 2001, we entered into a research, development and license agreement with Boston Scientific pursuant to which we granted Boston Scientific an exclusive worldwide license to develop and commercialize certain of our nitric oxide-enhancing compounds for use with their stents or specialty catheters in the area of restenosis. In December 2003, we extended the research collaboration to develop nitric oxide-enhancing paclitaxel-coated stents until December 31, 2005. The research term of this agreement expired on December 31, 2005, although certain rights extend beyond this term. If we are not able to continue the development of the technology developed under this agreement, we may lose any investment made in the development of, and any potential revenue that may have resulted from, the development, sale or licensing of, nitric oxide-enhancing stents.

The termination of our collaboration agreement with Merck, resulting from Merck’s decision to withdraw its COX-2 inhibitor, Vioxx, from worldwide markets, has resulted in the loss of potential milestone and royalty-based revenue from the collaboration and may indicate that the development of nitric oxide-enhancing COX-2 inhibitors is not viable.

In December 2002, we entered into an exclusive, worldwide research, collaboration and licensing agreement with Merck pursuant to which we granted Merck marketing and sales rights to our technology for nitric oxide-enhancing COX-2 inhibitors. On September 30, 2004, Merck halted the phase II trial of our lead candidate in nitric oxide-enhancing COX-2 inhibitors. We and Merck terminated our collaboration agreement during November 2004, which will result in the loss of any potential milestone or royalty revenue from the sale of products that may have resulted from the collaboration as well as any research and development funding that we may have received beyond the end of the initial research term in December 2005. In April 2005, the FDA imposed several restrictions on the labeling and sale of non-steroidal anti-inflammatory drugs, including COX-2 inhibitors. If the FDA imposes additional regulatory burdens for the approval of new COX-2 inhibitors, if COX-2 inhibitors continue to pose safety concerns, or if the market for COX-2 inhibitors contracts, then we may lose any investment made in the development of, and any potential revenue that may have resulted from, the development, sale or licensing of nitric oxide-enhancing COX-2 inhibitors.

Any future collaborative arrangements that we seek to enter into with third parties may not be scientifically or commercially successful.

Factors that may affect the success of our future collaborations include the following:

• our future collaborators may be pursuing alternative technologies or developing alternative product candidates, either on their own or in collaboration with others, that may be competitive with the product candidate on which they will be collaborating with us and which could affect their commitment to our future collaboration;

• future reductions in marketing or sales efforts or a discontinuation of marketing or sales of our products by our collaborators would reduce our revenues which would be based on a percentage of net sales by the collaborator;

• our future collaborators may terminate their collaborations with us, which could make it difficult for us to attract new collaborators or adversely affect how we are perceived in the business and financial communities; and

• our future collaborators may pursue higher-priority programs or change the focus of their development programs, which could affect the collaborators’ commitment to us.
If the estimates we make and the assumptions on which we rely in preparing our financial statements prove inaccurate, our actual results may vary significantly.

Our financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges taken by us and related disclosure. Such estimates and judgments include revenue recognition, the carrying value of our accounts receivables, inventory and assets, our estimates of accrued expenses and our estimates of the fair value of equity instruments granted or sold by us. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. However, these estimates and judgments, or the assumptions underlying them, may prove to be incorrect. Accordingly, our actual financial results may vary significantly from the estimates contained in our financial statements. For a further discussion of the estimates and judgments that we make and the critical accounting policies that affect these estimates and judgments, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations - Critical Accounting Policies and Estimates” above.

Risks Relating to our Intellectual Property Rights

Our patent protection for BiDil, which is a combination of two generic drugs, is limited, and we may be subject to generic substitution or competition and resulting pricing pressure.

We have no composition of matter patent covering BiDil, our product for the treatment of heart failure in self-identified black patients as an adjunct to current standard therapy. BiDil is a fixed-dose combination of two generic drugs, isosorbide dinitrate and hydralazine hydrochloride, which are approved and separately marketed, in dosages similar to those we include in BiDil, for indications other than heart failure, at prices below the prices we are charging for BiDil. We have three issued method-of-use patents, one of which covers the use of the combination of isosorbide dinitrate and hydralazine hydrochloride to reduce the incidence of mortality associated with chronic congestive heart failure, expiring in 2007, and the others covering the treatment of heart failure in black patients, expiring in 2020. As a practical matter, we may not be able to enforce these method-of-use patents to prevent physicians from prescribing isosorbide dinitrate and hydralazine hydrochloride separately for the treatment of heart failure in black patients, even though neither drug is approved for such use. We also may not be able to enforce these method-of-use patents to prevent hospitals and pharmacies from supplying such patients with these generic drugs separately in lieu of BiDil.

Other factors may also adversely affect our patent protection for BiDil. If we are successful in marketing BiDil, manufacturers of generic drugs will have an incentive to challenge our patent position. The combination therapy of isosorbide dinitrate and hydralazine hydrochloride for use in heart failure was developed through lengthy, publicly-sponsored clinical trials conducted during the 1980s, prior to the filing of the patent application that resulted in the 2007 patent. The U.S. Patent and Trademark Office, or U.S. patent office, considered published reports on these clinical trials and concluded that they did not constitute prior art that would prevent the issuance of the 2007 patent. The U.S. patent office also considered the question of whether the 2007 patent constituted prior art with respect to the 2020 patents, and determined that the claims of the 2020 patents were non-obvious and patentable. A court considering the validity of the 2007 or 2020 patents with respect to questions of prior art might be presented with other alleged prior art or might reach conclusions different from those reached by the U.S. patent office. If the 2007 or 2020 patents were to be invalidated or if physicians were to prescribe isosorbide dinitrate and hydralazine hydrochloride separately for heart failure in black patients, our BiDil revenue could be significantly reduced, we could fail to recover the cost of developing BiDil and BiDil might not be a viable commercial product.
If we are not able to obtain and enforce patent protection for our discoveries, our ability to develop and commercialize our product candidates will be harmed, and we may not be able to operate our business profitably.

Our success depends, in part, on our ability to protect proprietary methods and technologies that we develop under the patent and other intellectual property laws of the United States and other countries, in order to prevent others from using our inventions and proprietary information. Because certain United States patent applications are confidential until patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date which will not be filed in foreign countries, third parties may have filed patent applications for technology covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over patent applications of others.

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. Despite our efforts to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary. The mere issuance of a patent does not guarantee that it is valid or enforceable, so even if we obtain patents, they may not be valid or enforceable against third parties.

The issued patents and patent applications for our product candidates and nitric oxide technology include claims with respect to both the composition of specific products or compounds and specific methods of using these products or compounds in therapeutic areas. In some cases, like BiDil, our only patent protection is with respect to the method of using a product or compound, and we do not have patent claims covering the underlying composition of the product or compound. Method-of-use patents may provide less protection for our product candidates and products because it may be more difficult to prove direct infringement against a pharmaceutical manufacturer or distributor once they have gained approval for an alternative indication. In addition, if any other company gains FDA approval for an indication separate from the one we are pursuing and markets a product that we expect to market under the protection of a method-of-use patent, physicians will be able to prescribe that product for use in the indication for which we have obtained approval, even though the product is not approved for such indication. As a practical matter, we may not be able to enforce our method-of-use patents against physicians prescribing products for such off-label use. Off-label use and any resulting off-label sales could make it more difficult to obtain the price we would otherwise wish to achieve for, or to successfully commercialize, our products. In addition, in those situations where we have only method-of-use patent coverage for a product candidate, it may be more difficult to find a pharmaceutical company partner to license or support development of our product candidate.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards which the U.S. patent office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims allowed in any patents issued to us or to others.

We also rely on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.
If we become involved in patent litigation or other proceedings to enforce our patent rights, we would incur substantial costs and expenses, substantial liability for damages and/or be required to stop our product development and commercialization efforts.

A third party may sue us for infringing on its patent rights. Likewise, we may need to resort to litigation to enforce a patent issued to us or to determine the scope and validity of third-party proprietary rights. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management’s efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, our strategy of providing nitric oxide-enhancing versions of existing products could lead to more patent litigation as the markets for these existing products are very large and competitive. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

For example, we have filed an opposition in the European Patent Office, or EPO, to revoke NicOx S.A.’s European Patent No. 904 110, which we refer to as EP ’110. This patent is directed to the use of organic compounds containing a nitrate group or inorganic compounds containing a nitric oxide group to reduce the toxicity caused by certain drugs, including non-steroidal anti-inflammatory drugs, or NSAID’s. The basis for our opposition, in part, is that the claims in EP ’110 are anticipated and therefore invalid if they are construed to cover a single compound chemically linked to a nitrate moiety. While we believe that the claims in EP ’110 will be invalidated, or be narrowed, we cannot predict with certainty the outcome of the opposition. If the EPO finds that there are valid claims in EP ’110 that cover compounds chemically linked to nitrates, we may be adversely affected in our ability to market our product candidates for reducing gastrointestinal toxicity without first obtaining a license from NicOx, which may not be available on favorable terms, if at all.

If any parties are able to successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties’ patent rights. In addition to any damages we might have to pay, a court could require us to stop the infringing activity or obtain a license on unfavorable terms. Moreover, any legal action against us or our partners claiming damages and seeking to enjoin commercial activities relating to the affected products and processes could, in addition to subjecting us to potential liability for damages, require us or our partners to obtain a license in order to continue to manufacture or market the affected products and processes. Any license required under any patent may not be made available on commercially-acceptable terms, if at all. In addition, some licenses may be non-exclusive, and therefore our competitors may have access to the same technology licensed to us. If we fail to obtain a required license or are unable to design around a patent, we may be unable to effectively market some of our technology and product candidates, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations.

We in-license a significant portion of our principal proprietary technologies, and if we fail to comply with our obligations under any of the related agreements, we could lose license rights that are necessary to commercializing BiDil and developing our other product candidates.

We are a party to a number of licenses that give us rights to third-party intellectual property that are necessary for our business. In particular, we have obtained the exclusive right to develop and commercialize BiDil pursuant to a license agreement with Dr. Jay N. Cohn and some of our intellectual property rights relating to nitric oxide compounds have been obtained pursuant to license agreements with the Brigham and Women’s Hospital and Boston University. We expect to enter into additional licenses in the future. These licenses impose various development, commercialization, funding, royalty, diligence, and other obligations on us. If we breach these obligations, the licensor may have the right to terminate the
license or render the license non-exclusive, which would result in us being unable to develop, manufacture and sell products that are covered by the licensed technology.

**Risks Relating to our Industry**

*If the government or third-party payors do not reimburse patients for BiDil or any of our product candidates that are approved for marketing, or do not reimburse such products at favorable levels, they might not be used or purchased, and our revenues and profits will be adversely affected.*

Our revenues and profits depend heavily upon the availability of coverage and favorable reimbursement for the use of BiDil and any of our other product candidates that may be approved for marketing, from third-party healthcare and state and federal government payors, both in the United States and in foreign markets. Reimbursement by a third party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Since reimbursement approval for a product is required from third-party and government payors in order for patients to be reimbursed for the cost of a product, seeking this approval, particularly when seeking approval for a preferred form of reimbursement over other competitive products, is a time-consuming and costly process. Third-party payors may require cost-benefit analysis data from us in order to demonstrate the cost-effectiveness of any product we might bring to market. For any individual third-party payor, we may not be able to provide data sufficient to gain reimbursement on a similar or preferred basis to competitive products or at all. Once reimbursement at an agreed level is approved by a third-party payor, we may lose that reimbursement entirely, or we may lose the similar or better reimbursement we receive compared to competitive products. As reimbursement is often approved for a period of time, this risk is greater at the end of the time period, if any, for which the reimbursement was approved. In addition, legislative or regulatory efforts to control or reduce healthcare costs or reform government healthcare programs could result in lower prices or rejection of our products. Changes in coverage and reimbursement policies or healthcare cost containment initiatives that limit or restrict reimbursement for our products may cause our revenue to decline. Any failure by us to obtain reimbursement for our products, or to secure a preferred form of reimbursement that reduces costs to patients, may negatively impact market acceptance of our products and adversely affect our ability to generate revenues from sales.

Most private insurers, and the majority of Medicare Part D plans, cover BiDil at the Tier III level. We may not be able to obtain preferential reimbursement treatment for BiDil from many private insurers. Any failure by us to secure such preferential reimbursement treatment would have a substantially negative effect on sales of BiDil. In addition, although some Medicare Part D plans are currently providing reimbursement for BiDil at Tier II levels, the number of overall plans providing this preferential reimbursement is small. Moreover, because Medicare Part D was only implemented on January 1, 2006, the Medicare Part D plans are still actively in the process of enrolling participants. We cannot know if any of the plans on which we are currently listed will have a significant number of African American participants, if any at all. We also cannot know if BiDil will continue to be listed on any of these plans at a preferential reimbursement level, if at all. Accordingly, we cannot assess the impact that the current listing of BiDil on any given plan will have on our future revenues, if any. If the plans on which BiDil is currently listed do not enroll a significant number of African American participants, we will not benefit from these listings. In addition, if BiDil is not listed on any plans that do succeed in enrolling African American participants, or if BiDil does not receive preferable reimbursement treatment on such plans, market
acceptance of BiDil could be negatively impacted and our ability to generate revenues from sales significantly impaired.

We could be negatively impacted by the application or enforcement of federal and state fraud and abuse laws, including anti-kickback laws and other federal and state anti-referral laws.

We are subject to various federal and state laws pertaining to healthcare fraud and abuse, including anti-kickback laws and physician self-referral laws. Violations of these laws are punishable by criminal and civil sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state healthcare programs, including the Medicare, Medicaid and Veterans Administration health programs. Because of the far-reaching nature of these laws, we may be required to alter or discontinue one or more of our practices to be in compliance with these laws. Healthcare fraud and abuse regulations are complex, and even minor irregularities can potentially give rise to claims that a statute or prohibition has been violated. Any violations of these laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our business, financial condition and results of operations. If there is a change in law, regulation or administrative or judicial interpretations, we may have to change or discontinue our business practices or our existing business practices could be challenged as unlawful, which could have a material adverse effect on our business, financial condition and results of operations. In addition, we could become subject to false claims litigation under federal statutes, which can lead to treble damages based on the reimbursements by federal healthcare programs, civil money penalties (including penalties levied on a per false claim basis), restitution, criminal fines and imprisonment, and exclusion from participation in Medicare, Medicaid and other federal and state healthcare programs. These false claims statutes include the False Claims Act, which allows any person to bring suit on behalf of the federal government alleging the submission of false or fraudulent claims, or causing to present such false or fraudulent claims, under federal programs or contracts claims or other violations of the statute and to share in any amounts paid by the entity to the government in fines or settlement. These suits against biotechnology companies have increased significantly in recent years and have increased the risk that a healthcare company will have to defend a false claim action, pay fines or restitution, or be excluded from the Medicare, Medicaid or other federal and state healthcare programs as a result of an investigation arising out of such action. We cannot assure you that we will not become subject to such litigation or, if we are not successful in defending against such actions, that such actions will not have a material adverse effect on our business, financial condition and results of operations. In addition, we cannot assure you that the costs of defending claims or allegations under the False Claims Act will not have a material adverse effect on our business, financial condition and results of operations.

We face significant competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The pharmaceutical industry is highly competitive and characterized by rapid and significant technological change. Our principal competitors in the markets we have targeted, including cardiovascular disease, are large, multinational pharmaceutical companies that have substantially greater financial and other resources than we do and are conducting extensive research and development activities on technologies and product candidates similar to or competitive with ours. Many of our competitors are more experienced than we are in pharmaceutical development and commercialization, obtaining regulatory approvals and product marketing and manufacturing. As a result, they may:

- develop and commercialize products that render our products obsolete or non-competitive or that block or delay approval of our product candidates as a result of patent or non-patent exclusivity;
- develop product candidates and market products that are less expensive or more effective than our products;
• commercialize competing products before we or our partners can launch any products developed from our product candidates;

• initiate or withstand substantial price competition more successfully than we can;

• have greater success in recruiting skilled scientific workers from the limited pool of available talent; and

• more effectively negotiate third-party licenses and strategic relationships; and take advantage of product acquisition or other opportunities more readily than we can.

There are a number of companies currently marketing and selling products to treat heart failure in the general population that will compete with BiDil. These include GlaxoSmithKline, plc, which currently markets Coreg®, Merck & Co., Inc., which currently markets Vasotec® and Astra Zeneca, plc, which currently markets Toprol XL®.

We also face competition from other pharmaceutical companies seeking to develop drugs using nitric oxide technology. For example, we are aware of at least seven companies working in the area of nitric oxide based therapeutics. These companies are: Angiogenix Inc., GB Therapeutics, NicOx S.A., OxoN Medica, RenoPharm, Vasopharm BIOTECH GmbH and Nitrox LLC.

We may be exposed to product liability claims and may not be able to obtain or maintain adequate product liability insurance.

Our business exposes us to the risk of product liability claims that is inherent in the manufacturing, testing, and marketing of human therapeutic products. Our clinical trial liability and commercial product liability insurance is subject to deductibles and coverage limitations. We may not be able to obtain or maintain insurance on acceptable terms, or at all. Moreover, any insurance that we do obtain may not provide adequate protection against potential liabilities, and our capital resources could be depleted as a result.

Risks Relating to our Common Stock

The price of our common stock is likely to continue to be volatile in the future.

The stock market has from time to time experienced significant price and volume fluctuations that may be unrelated to the operating performance of particular companies. In particular, the market price of our common stock, like that of the securities of other biopharmaceutical companies, has been and may continue to be highly volatile. During the period from January 1, 2003 to January 1, 2006, our stock price has ranged from a low of $5.70 per share (on July 16, 2004) to a high of $27.99 per share (on February 2, 2005). The following factors, among others, may affect the price of our common stock:

• fluctuations in our financial results, including with respect to sales of BiDil;

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

• governmental regulations and regulatory developments in both the U.S. and foreign countries affecting us or our competitors;

• announcements of actual or potential medical results relating to products under development by us or our competitors’ products;

• disputes relating to patents or other proprietary rights affecting us or our competitors;

• public concern as to the safety of products developed by us or other biotechnology and pharmaceutical companies;

• general market conditions;
• fluctuations in price and volume in the stock market in general, or in the trading of the stock of biopharmaceutical and biotechnology companies in particular, that are unrelated to our operating performance;

• issuances of securities in equity, debt or other financings;

• sales of common stock by existing stockholders; and

• the perception that such issuances or sales could occur.

**Insiders have substantial control over us and could delay or prevent a change in corporate control.**

As of February 15, 2006, our directors, executive officers and principal stockholders, together with their affiliates, owned, in the aggregate, approximately 40% of our outstanding common stock. As a result, these stockholders, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, if acting together, will have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

• delaying, deferring or preventing a change in control of our company;

• impeding a merger, consolidation, takeover or other business combination involving our company; or

• discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company.

**Provisions in our charter documents and under Delaware law may prevent or frustrate attempts by stockholders to change current management and hinder efforts to acquire a controlling interest in our company.**

Provisions of our restated certificate of incorporation and bylaws may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions may prevent or frustrate attempts by stockholders to replace or remove our current management. These provisions include:

• a prohibition on stockholder action through written consent;

• a requirement that special meetings of stockholders be called only by a majority of the board of directors, the chairman of the board or the chief executive officer;

• advance notice requirements for stockholder proposals and nominations;

• limitations on the ability of stockholders to amend, alter or repeal our certificate of incorporation or bylaws; and

• the authority of the board of directors to issue preferred stock with such terms as the board of directors may determine.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally defined as a person or entity which together with its affiliates owns or within the last three years has owned 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Section 203 may discourage, delay or prevent a change in control of our company.
Substantially all of our outstanding common stock may be sold into the market at any time. This could cause the market price of our common stock to drop significantly.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of February 23, 2006, there were 36,632,342 shares of common stock. Substantially all of these shares may also be resold in the public market at any time. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

We may incur significant costs and suffer management distraction and reputational damage from class action litigation and regulatory or government investigations and actions due to trading in our common stock.

Our stock price has been, and is likely to continue to be, volatile. When the market price of a company’s stock is volatile, holders of that company’s stock may bring securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit was without merit, we could incur substantial costs defending the lawsuit.

On July 20, 2004, the Market Regulation Department of the NASD advised us that it initiated a review of trading activity in our common stock surrounding our July 19, 2004 announcement that we had halted our phase III clinical trial of BiDil due to the significant survival benefit seen with BiDil. The NASD is reviewing, among other things, information on relationships between our officers, directors and service providers and individuals and institutions that may have traded in our common stock prior to the July 19, 2004 announcement. We have cooperated with this review and have identified certain persons on the list provided to us by the NASD as having a relationship with our chief executive officer and others at NitroMed. We have established a special committee of our board of directors to oversee our response to this review.

The SEC or other securities regulators may investigate trading activity of insiders and others around events that result in stock price volatility, such as our July 19, 2004 announcement, and we may incur substantial costs in connection with any such government investigation or related action. A stockholder lawsuit, SEC or other investigation or action could also damage our reputation or that of our officers or directors and divert their time and attention away from our management.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

**ITEM 2. PROPERTIES**

We lease a facility that contains approximately 52,000 square feet of laboratory and office space in Lexington, Massachusetts. The lease has a term ending in 2014. We believe that our current facility is adequate for our needs for the foreseeable future, and that, should it be needed, suitable additional space will be available to accommodate expansion of our operations on commercially reasonable terms.

**ITEM 3. LEGAL PROCEEDINGS**

We are currently not a party to any material legal proceedings.

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

No matters were submitted to a vote of security holders of our company, through solicitations of proxies or otherwise, during the quarter ended December 31, 2005.
PART II

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

(a) Market Price of and Dividends on NitroMed’s Common Stock and Related Stockholder Matters; Recent Sales of Unregistered Securities.

Market Price and Dividends

Our common stock is traded on the NASDAQ National Market under the symbol “NTMD”. The following table sets forth the high and low sale prices per share of our common stock as reported on the NASDAQ National Market for the periods indicated.

<table>
<thead>
<tr>
<th>Fiscal year ended December 31, 2005</th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>First quarter</td>
<td>$27.99</td>
<td>$16.54</td>
</tr>
<tr>
<td>Second quarter</td>
<td>$21.09</td>
<td>$13.80</td>
</tr>
<tr>
<td>Third quarter</td>
<td>$24.45</td>
<td>$17.10</td>
</tr>
<tr>
<td>Fourth quarter</td>
<td>$22.61</td>
<td>$13.24</td>
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</table>

<table>
<thead>
<tr>
<th>Fiscal year ended December 31, 2004</th>
<th>High</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>First quarter</td>
<td>$ 9.65</td>
<td>$ 6.90</td>
</tr>
<tr>
<td>Second quarter</td>
<td>$ 8.15</td>
<td>$ 5.75</td>
</tr>
<tr>
<td>Third quarter</td>
<td>$25.78</td>
<td>$ 5.70</td>
</tr>
<tr>
<td>Fourth quarter</td>
<td>$27.30</td>
<td>$19.14</td>
</tr>
</tbody>
</table>

On February 23, 2006, the reported last sale price of our common stock on the NASDAQ National Market was $11.80 per share, and we had approximately 56 holders of record of our common stock.

We have never paid or declared any cash dividends on our common stock. We currently intend to retain earnings, if any, to finance the growth and development of our business, and we do not expect to pay any cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors.

Recent Sales of Unregistered Securities

On June 28, 2005, we borrowed (i) $10.0 million from Oxford Finance Corporation (Oxford) and (ii) $10.0 million from General Electric Capital Corporation (GECC) pursuant to the terms of promissory notes made by us with both Oxford and GECC, respectively. The notes bear interest at a fixed rate of 9.95% per annum and are payable in 36 consecutive monthly installments of principal and accrued interest, beginning July 1, 2005. We issued these promissory notes to Oxford and GECC in reliance on the exemption provided by Section 4(2) of the Securities Act of 1933, as amended, which we refer to as the Securities Act. The notes are secured by a security interest in all our personal property and fixtures with the exception of any intellectual property or products acquired, whether by purchase, license or otherwise, on or after the execution of the notes. The agreements that we entered into with each of Oxford and GECC in connection with the notes also contain a material adverse change clause with both Oxford and GECC. Under this clause, if Oxford or GECC reasonably determine that our ability to repay the notes has been materially impaired, we would be considered in default. As of December 31, 2005, we were in compliance with this clause.
(b) Use of Proceeds from Registered Securities

On December 20, 2004, we completed a follow-on public offering of our common stock at a price to the public of $24.46 per share. We sold an aggregate of 3,579,476 shares of our common stock resulting in gross proceeds of $87.6 million. The offer and sale of all the shares in the follow-on public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-120280), which was declared effective by the SEC on December 7, 2004. Deutsche Bank Securities Inc., J.P. Morgan Securities Inc., Pacific Growth Equities and Bear, Sterns & Co. Inc. were the managing underwriters of the follow-on public offering. In connection with the offering we paid $5.3 million in underwriting discounts and commissions and incurred $0.5 million in other offering expenses. As part of the initial public offering, we granted these underwriters an over-allotment option to purchase up to an additional 431,581 shares of our common stock from us. The underwriters exercised a portion of the over-allotment option. There were no selling stockholders in the offering.

None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours. After deducting the underwriting discounts and commissions and offering expenses, we received net proceeds from the offering of $81.8 million.

On November 10, 2003, we completed an initial public offering of 6,000,000 shares of our common stock at a price to the public of $11.00 per share. The offer and sale of all of the shares in the initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-108104), which was declared effective by the SEC on November 5, 2003. Deutsche Bank Securities Inc., J.P. Morgan Securities Inc. and Pacific Growth Equities were the managing underwriters of the initial public offering. The offering commenced on November 5, 2003 and did not terminate until after the sale of all of the securities registered in the Registration Statement. As part of the initial public offering, we granted these underwriters an over-allotment option to purchase up to an additional 900,000 shares of our common stock from us. The underwriters did not exercise the over-allotment option. There were no selling stockholders in the offering.

The aggregate price of the initial public offering amount registered on our behalf was $66.0 million. In connection with the offering, we paid $4.6 million in underwriting discounts and commissions to the underwriters and incurred an estimated $1.3 million in other offering expenses. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10 percent or more of our common stock or to any affiliates of ours. After deducting the underwriting discounts and commissions and offering expenses, we received net proceeds from the offering of $60.1 million.

ITEM 6. SELECTED FINANCIAL DATA

You should read carefully the financial statements included in this report, including the notes to the financial statements and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The selected financial data in this section are not intended to replace the financial statements.

We derived the statement of operations data for the years ended December 31, 2005, 2004 and 2003 and the balance sheet data as of December 31, 2005 and 2004 from our audited financial statements, which are included elsewhere in this report. We derived the statement of operations data for the years ended December 31, 2002 and 2001 and the balance sheet data as of December 31, 2003, 2002 and 2001 from our audited financial statements which are not included herein. Historical results are not necessarily indicative of future results. See the notes to the financial statements for an explanation of the method used to determine the number of shares used in computing basic and diluted net loss per common share.
ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

We are an emerging pharmaceutical company with substantial expertise and intellectual property in nitric oxide-based drug development. Our goal is to become a leading, multi-product pharmaceutical company by developing innovative nitric oxide-based products and by building on our BiDil development experience and commercialization infrastructure to identify and market additional products for cardiovascular and metabolic diseases. We have devoted substantially all of our efforts towards the research and development of our product candidates and the commercialization of our currently marketed product, BiDil. Since our inception, we have mainly funded our operations through the sale of equity securities, debt financings, license fees, research and development funding and milestone payments from our collaborative partners. We have never been profitable and have incurred an accumulated deficit of $242.5 million as of December 31, 2005.
In June 2005, the FDA approved our product, BiDil, for the treatment of heart failure in self-identified black patients as an adjunct to current standard therapies. BiDil is an orally administered fixed-dose combination of isosorbide dinitrate and hydralazine hydrochloride. We commercially launched BiDil in July 2005 and generated product sales of $4.5 million during the year ended December 31, 2005. We market BiDil to primary care physicians and cardiologists who treat African Americans with heart failure. Our sales and marketing organization is comprised internally of a senior vice president of sales and marketing, a vice president of sales, a vice president of marketing, three regional sales directors and fifteen district sales managers. In addition, we have an agreement with Publicis Selling Solutions pursuant to which, on our behalf, Publicis has employed and trained a specialty sales force currently consisting of 144 sales representatives to sell BiDil to our target prescriber markets. We have also engaged Schwarz Pharma under a five-year exclusive manufacturing and supply agreement exclusively for the three times daily immediate release dosage formulation of BiDil.

We are also applying our nitric oxide technology to develop novel pharmaceuticals, as well as safer and more effective versions of existing drugs, to target significant diseases that are characterized by a deficiency in nitric oxide and to treat underserved patient populations. Our nitric oxide-development strategy involves the internal development of proprietary nitric oxide-enhancing product candidates, such as BiDil, the co-development of nitric oxide-enhancing drugs with partners and the out-licensing of our nitric oxide-enhancing technology in exchange for potential milestone payments and royalties on sales.

We expect that research, development and commercialization expenses relating to our products and product candidates and to enhancing our core technologies will continue to fluctuate in the near-term and may vary significantly from our current estimates. Our operating expenses related to our research and development efforts and our sales, general and administrative costs for the year ended December 31, 2005, total $105.9 million. We currently estimate that our operating expenses for fiscal year 2006 will range between $95.0 million and $110.0 million, excluding cost of product sales and expenses related to the adoption of Statement of Financial Accounting Standards (“SFAS”) No. 123R, Share-Based Payment. We believe that our existing cash, cash equivalents and marketable securities, together with the proceeds from our recent equity offering in January 2006, which generated net proceeds to the Company of $58.6 million, will be sufficient to fund our current operating plan, including operating expenses in support of the launch and commercialization of BiDil, for at least the next 21 months.

In the near-term, a key driver of our success will be our ability to successfully launch, commercialize and achieve market penetration of BiDil. We will need to generate significant revenues to achieve profitability. At the present time we are unable to estimate the level of revenues that we will realize from sales of BiDil or from the other products that we may successfully develop and commercialize. We are therefore unable to estimate when we will achieve profitability, if at all.

Financial Operations Overview

Revenue. Our first commercial product, BiDil, was launched in July 2005, and generated product sales of $4.5 million for the year ended December 31, 2005. Prior to the launch of BiDil, all of our revenue had been derived from license fees, research and development payments and milestone payments that we received from our corporate collaborators. In future years, we will seek to generate revenue from a combination of product sales, license fees, milestone and royalty payments in connection with collaborative or strategic relationships, as well as royalties resulting from the license of our intellectual property. We expect that any collaborative revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of research and development, milestone and other payments received under our collaborative or strategic relationships and related continuing obligations, as well as the timing and amount of revenue we recognize for the sale of our products, to the extent any are successfully commercialized.
Research and Development. Research and development expense consists of expenses incurred in identifying, developing and testing product candidates. These expenses consist primarily of salaries and related expenses for personnel, fees paid to professional service providers for independent monitoring and analysis of our clinical trials, costs of contract research and manufacturing, costs of facilities and BiDil medical support costs.

The following summarizes our primary research and development programs. We have not provided program costs because prior to 2000 we did not track and accumulate cost information by research program.

- **BiDil.** From May 2001 to July 2004, we enrolled 1,050 patients at 169 clinical sites in the United States in our phase III clinical trial for BiDil. We halted the trial in July 2004 due to a significant survival benefit in the preliminary data for patients taking BiDil. The FDA approved BiDil on June 23, 2005, and we launched BiDil in July 2005. The total cost for the BiDil A-HeFT trial was approximately $43.0 million.

- **BiDil Life Cycle Management: BiDil XR and BiDil Combination.** The current formulation of BiDil is an immediate-release tablet that must be taken three times daily. We are currently pursuing the development of an extended release formulation of BiDil, BiDil XR, that could be taken either once or twice a day, depending on the particular formulation we pursue. We are also engaging in research and development efforts to develop BiDil Combination products which would combine BiDil with existing, marketed medicines, such as ACE inhibitors, beta blockers, or aldosterone receptor blockers.

- **Cardiovascular Portfolio.** We are utilizing our nitric oxide expertise and proprietary position to develop product candidates for a variety of additional medical conditions. As part of this effort, we recently announced that we expect to file an Investigational New Drug Application (IND) for NMI 3377, a proprietary nitric oxide-enhancing cardiovascular agent, in the second quarter of 2006. We have retained all commercial rights to this product candidate. Because these programs are in pre-clinical development, the successful development of products based upon these programs is highly uncertain. As such, we are not able to estimate the cost to complete research and development, nor are we able to estimate the timing of bringing product candidates to market and, therefore, when material cash inflows from product sales, milestones and royalties could commence.

- **Nitric Oxide-Enhancing Product Candidates.** We are using our know-how and expertise in nitric oxide to develop new chemical entities, or drugs, that are nitric oxide-enhancing versions of existing medicines in the areas of cardiovascular medicine, acute renal failure and other areas. These studies are at a pre-clinical stage of testing, and it remains speculative whether the addition of nitric oxide will result in an improved clinical profile of these medicines. The many uncertainties involved with the development of successful new products will exist until a new product candidate successfully passes all preclinical safety testing as well as clinical evaluation. A new and novel nitric oxide-enhancing medicine will take several years and involve a significant and largely unknown sum of expenditures. The success of achieving a new nitric oxide-enhancing medicine is important as it is needed to fill our pipeline. Failure to produce and successfully commercialize a new product in a timely fashion may have a material adverse effect on our business, financial position and results of operations.

- **Nitric Oxide Stents.** We formerly had a research agreement with Boston Scientific to develop cardiovascular stents enhanced with a bio-compatible polymer that is capable of releasing nitric oxide. The research program under this agreement focused on pre-clinical development. In accordance with the terms of our agreement with Boston Scientific, the research term expired in December 2005. We expect that additional expenditures will be required in the area of nitric oxide stents development, if we should choose to pursue this area either alone or together with another collaborative partner to conduct pre-clinical testing and, if such pre-clinical testing is successful, to
apply for and conduct clinical trials. Because our former program was in pre-clinical development, the successful development of products based upon this program is highly uncertain. As such, we are unable to estimate the cost to complete any future research and development, nor are we able to estimate the timing of bringing any product candidates to market and, therefore, when material cash inflows from milestones and royalties could commence. Our failure, or any future partner’s failure, to commercialize products based upon this program on a timely basis could have a material adverse effect on our business, financial position and results of operations.

- **Nitric Oxide-Enhancing COX-2 Inhibitors.** From December 2002 until November 2004, we had a collaboration with Merck Frosst Canada & Co., a wholly-owned subsidiary of Merck & Co., or Merck, to screen proprietary nitric oxide-enhanced COX-2 inhibitors in advance of clinical testing as analgesic and anti-inflammatory agents and in other specified disease areas. These agents are intended to be second-generation COX-2 inhibitors. On September 30, 2004, Merck halted the phase II trial of our lead candidate in nitric oxide-enhancing COX-2 inhibitors. In November 2004, we agreed with Merck to terminate the collaboration agreement. We retain all rights to our technology in the field of nitric oxide-enhancing COX-2 inhibitors and may seek collaborations with other potential partners to utilize the full value, if any, of this technology in the development of new analgesic and anti-inflammatory agents. Significant additional expenditures will be required to conduct pre-clinical testing and to apply for, and conduct, clinical trials. Because these agents are in pre-clinical development, their successful development is highly uncertain. As such, we are not able to estimate the cost to complete the research and development phase, nor are we able to estimate the timing of bringing potential candidates to market and, therefore, when material cash inflows from milestones and royalties could commence. Our failure, or any future partner’s failure, to commercialize these product candidates under development on a timely basis could have a material adverse effect on our business, financial condition and results of operations.

**Sales, General and Administrative.** Consists primarily of salaries and other related costs for personnel in sales and marketing, executive, finance, investor relations, accounting, business development and human resource functions. Other costs include facility costs not otherwise included in research and development expense; costs for public relations, advertising and promotion services; professional fees for legal and accounting services; and costs related to our third party contract sales agreement with Publicis Selling Solutions, Inc., or Publicis.

**Non-Operating Income.** Includes interest earned on our cash, cash equivalents and marketable securities, and interest expense associated with our long-term debt.

**Boston Scientific Collaboration.** In November 2001, we entered into a research, development and license agreement with Boston Scientific in the field of restenosis. We granted Boston Scientific an exclusive worldwide license to develop and commercialize nitric oxide-enhancing cardiovascular stents. We also granted to Boston Scientific a right of first refusal to obtain an exclusive license under our nitric oxide technologies to commercialize products for restenosis, which right of first refusal is for a period of three years after the end of the research term. In December 2003, we agreed to extend the agreement to continue the research and development collaboration through December 2005. Boston Scientific made an up-front license payment of $1.5 million to us in 2001, and made an additional payment of $3.0 million in December 2003 in connection with the extension of the research and development collaboration. In the event that specified research, development and commercialization milestones were achieved, Boston Scientific would have been obligated to make milestone payments to us. In addition, Boston Scientific also would have been obligated to pay royalties to us on the sale of any products resulting from the collaboration. Boston Scientific made a $3.5 million equity investment in our stock in 2001. In August 2003, in connection with a private placement, Boston Scientific made an additional $500,000 equity investment in our stock. The research term of the Boston Scientific agreement expired on December 31, 2005, although certain rights extend beyond this term. We intend to evaluate the continued development of this technology and in the future may seek collaboration with other potential partners.
Merck Collaboration. From December 2002 until November 2004, we were party to an exclusive, worldwide research, collaboration and licensing agreement that granted Merck marketing and sales rights for nitric oxide-enhancing COX-2 inhibitors. The research portion of the agreement was for three years. In 2003, we received an upfront non-refundable license payment of $10.0 million and two payments, each of $5.0 million, for achieving the first two milestones. The license fee revenue and the revenue from the first $5.0 million milestone payment were being recognized ratably over the contractual term of the research and development program, which was expected to end on December 31, 2005. The revenue from the second $5.0 million payment was recognized in the fourth quarter of 2003, the period in which Merck achieved the milestone. On September 30, 2004, Merck halted the phase II trial of our lead candidate in nitric oxide-enhancing COX-2 inhibitors. This lead nitric oxide candidate is composed of a derivative of rofecoxib. Rofecoxib is the active ingredient in Vioxx, a COX-2 inhibitor which Merck voluntarily withdrew from worldwide markets on September 30, 2004. In November 2004, we agreed with Merck to terminate the collaboration agreement. Merck paid us a lump sum of $1.8 million in 2004, representing the full amount of the research funding that was owed to us for 2005. We will not receive any commercialization milestones or royalty payments from Merck. As a result of the termination of this agreement, we accelerated the recognition of deferred license revenue of $5.3 million in the fourth quarter of 2004, and we recognized the lump sum payment of $1.8 million as revenue in the fourth quarter of 2004.

Results of Operations

Years Ended December 31, 2005, 2004 and 2003

Revenue. Total revenue for the year ended December 31, 2005 was $6.0 million, compared to $16.5 million in 2004 and $12.8 million in 2003.

Product sales were $4.5 million for the year ended December 31, 2005 due to the commercial launch of BiDil in July 2005. There were no product sales for the years ended December 31, 2004, and 2003.

Research and development revenues were $1.6 million for the year ended December 31, 2005, compared to $16.5 million for 2004 and $12.8 million for 2003. The $14.9 million, or 90% decrease in revenue in 2005 compared to 2004, is primarily due to the termination of the Merck agreement in November 2004. For the year ended December 31, 2004, research and development revenues totaled $16.5 million, a 29% or $3.7 million increase in revenue in 2004 compared to 2003. This increase is primarily attributable to our collaboration agreement with Merck, which was terminated in November 2004. In 2004 we recognized $14.9 million in revenue under this agreement, which included all amounts previously deferred. Due to the termination of this collaboration agreement, we no longer have any future performance obligations, and accordingly, we recognized previously deferred license revenue of $5.3 million. In addition, we recognized $1.8 million that was originally scheduled to be paid to us during 2005 for research and development funding, but was instead paid to us in 2004 when the agreement was terminated. We also recognized an additional $1.2 million in revenue in 2004 over 2003 relating to the December 2003 extension of our agreement with Boston Scientific. The research term of this agreement with Boston Scientific expired on December 31, 2005 in accordance with its terms, and we do not expect to receive any additional payments under this agreement.

Cost of Product Sales. Cost of product sales increased to $8.0 million in 2005 from $0 in 2004 due to the launch of BiDil in July 2005. Included in cost of product sales is an inventory impairment charge of $5.6 million related to short dated commercial trade and patient sample inventory, and a $1.5 million charge for contractual purchase commitments. The charges are due to the Company’s current estimate of inventory requirements based on its sales forecast.

Research and Development. Research and development expense for the year ended December 31, 2005 was $31.9 million, compared to $28.0 million in 2004 and $18.9 million in 2003. The $3.9 million, or 14% increase in research and development expenses in 2005 compared with 2004 is primarily the result of
increased clinical and medical expenses which support the commercial launch of BiDil in the areas of continuing medical education, clinical advisory boards, medical services fees, publications and other various contracted services totaling $13.2 million. We also incurred increased research and development expenses in 2005 of $2.6 million related to product development projects. Offsetting the increased medical support and research expenses in 2005 is a decrease of $10.2 million in clinical trial expenses as a result of the completion of the A-HeFT trial, in 2004, a decrease in drug manufacturing expense of $1.1 million and a decrease in compensation expense of $0.6 million. The $9.1 million, or 48% increase in research and development expenses in 2004 compared with 2003 is primarily the result of an additional $2.8 million of expenses associated with the BiDil trial, including costs associated with the halt of the A-HeFT trial, commencement of the open label A-HeFT trial (X-A-HeFT), and the preparation and filing of an amended NDA with the FDA. We also incurred increased research and development expenses in 2004 of $2.0 million related to compensation-related expenses due to additional headcount and non-cash stock-based compensation related expense; $1.2 million related to preparation of contract manufacturing capabilities relating to the potential BiDil product line; $1.0 million pertaining to milestone payments under a collaboration and license agreement for BiDil; and increased outside consulting costs of $0.8 million.

The following table summarizes the primary components of our research and development expense for our principal research and development programs for the fiscal years ended December 31, 2005, 2004 and 2003.

<table>
<thead>
<tr>
<th>Research and Development Program</th>
<th>2005</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>BiDil</td>
<td>$19,052,000</td>
<td>$20,000,000</td>
<td>$11,751,000</td>
</tr>
<tr>
<td>Nitric oxide-enhancing cardiovascular compounds</td>
<td>6,073,000</td>
<td>500,000</td>
<td>—</td>
</tr>
<tr>
<td>Nitric oxide-enhancing COX-2 inhibitors</td>
<td>—</td>
<td>2,500,000</td>
<td>2,358,000</td>
</tr>
<tr>
<td>Nitric oxide stents</td>
<td>2,279,000</td>
<td>2,500,000</td>
<td>1,447,000</td>
</tr>
<tr>
<td>Other</td>
<td>4,526,000</td>
<td>2,495,000</td>
<td>3,351,000</td>
</tr>
<tr>
<td>Total research and development expense</td>
<td>$31,930,000</td>
<td>$27,995,000</td>
<td>$18,907,000</td>
</tr>
</tbody>
</table>

Sales, General and Administrative. Sales, general and administrative expense for the year ended December 31, 2005 was $74.0 million, compared to $19.6 million in 2004 and $3.1 million in 2003. The $54.4 million, or 278% increase in sales, general and administrative expenses in 2005 compared to 2004 was primarily due to an increase of $25.6 million for the implementation of our contract sales force under our agreement with Publicis, $4.0 million for the hiring of sales and marketing management personnel, and $20.9 million for advertising and promotional services and public relations. We also incurred higher general and administrative expense in 2005 due to increased costs of $1.1 million associated with the accrual of business development expenses pertaining to the approval process for BiDil; $1.8 million pertaining to additional legal and consulting expenses; $0.4 million related to the hiring of executive management and additional administrative personnel. Sales, general and administrative expense for the year ended December 31, 2004 was $19.6 million, compared to $3.1 million in 2003. The $16.5 million, or 529% increase in sales, general and administrative expenses in 2004 compared to 2003 was primarily due to $10.2 million for the preparation for the potential launch of BiDil, including costs relating to the payment of contract sales personnel; hiring of sales and marketing management personnel; public relations services; and advertising and promotion services. We also incurred higher general and administrative expense in 2004 due to increased costs of $1.9 million associated with business development and milestone payment expenses pertaining to the approval process for BiDil; $1.2 million pertaining to additional legal and consulting expenses; $1.0 million related to the hiring of executive management and additional administrative personnel; an increase in insurance costs of $0.7 million due to operating as a public company; and higher infrastructure related expenses of $0.7 million, including moving to a new facility.
Non-Operating Income. Non-operating income increased to $2.0 million in 2005 compared to $1.4 million in 2004 and $0.5 million in 2003. The $0.6 million, or 51% increase in non-operating income in 2005 compared to 2004 was primarily related to higher interest income due to higher average investment balances and higher interest rates in 2005, offset by interest expense related to long—term debt. The $0.9 million, or 184% increase in non-operating income in 2004 compared to 2003 was primarily related to higher average fund balances available for investment and higher interest rates due to investing in longer maturity securities.

Liquidity and Capital Resources

We have financed our operations since inception through the sale of equity, debt and payments from collaborative partners for licenses, research and development and achievement of milestones. As of December 31, 2005, we have received net proceeds of $263.2 million from the issuance of equity securities and debt instruments, primarily as the result of the sale of $99.1 million of our redeemable convertible preferred stock; net proceeds of $60.1 million from our initial public offering in November 2003; net proceeds of $81.8 million from our follow-on public offering in December 2004, and $20 million in debt financing in June 2005, which is described below. At December 31, 2005, we had $61.5 million in cash, cash equivalents and marketable securities, and in January 2006, we raised an additional $58.6 million in net proceeds from an equity financing from the sale of 6.1 million shares of our common stock.

In January 2006, we completed a direct offering of shares of our common stock previously registered under our effective shelf registration statement, which was filed with the Securities and Exchange Commission, or the SEC, in August 2005. Pursuant to this offering, we sold approximately 6.1 million shares of our common stock to selected institutional investors at a price of $10.25 per share. Proceeds to us from this offering, net of offering expenses and placement agency fees, totaled approximately $58.6 million.

On June 28, 2005, we borrowed (i) $10.0 million from Oxford Finance Corporation (Oxford) and (ii) $10.0 million from General Electric Capital Corporation (GECC) pursuant to the terms of promissory notes made by us with both Oxford and GECC, respectively. The notes bear interest at a fixed rate of 9.95% per annum and are payable in 36 consecutive monthly installments of principal and accrued interest, beginning July 1, 2005. The notes are secured by a security interest in all our personal property and fixtures with the exception of any intellectual property or products acquired, whether by purchase, license or otherwise, on or after the execution of the notes. The agreements that we entered into with each of Oxford and GECC in connection with the notes also contain a material adverse change clause with both Oxford and GECC. Under this clause, if Oxford or GECC reasonably determine that our ability to repay the notes has been materially impaired, we would be considered in default. As of December 31, 2005, we were in compliance with this clause. As of December 31, 2005 we had paid aggregate principal in the amount of $3.1 million.

During the year ended December 31, 2005, operating activities used cash of $98.2 million primarily due to a net loss of $105.9 million, and increases in accounts receivable of $4.1 million and inventories of $3.2 million due to launching BiDil, capitalizing inventory, and shipping product. These cash flow decreases are offset by adjustments for non-cash charges for stock-based compensation and depreciation and amortization of $1.4 million, an increase in accounts payable and accrued expenses of $12.3 million, and an increase in deferred revenue of $1.9 million.

During the year ended December 31, 2005, investing activities provided cash of $55.4 million due to the net sales of marketable securities of $56.3 million, offset by the purchases of computer and lab equipment of $0.9 million due to an increase in personnel. We expect to invest $1.5 million to $2.5 million for capital expenditures in 2006, principally related to the purchase of laboratory equipment and computer equipment to support headcount growth.
During the year ended December 31, 2005, financing activities provided cash of $18.1 million due to proceeds from $20.0 million in long-term debt and $1.2 million from the issuance of common stock under our employee stock plans, offset by $3.1 million in principal payments on long-term debt.

The following table summarizes our contractual obligations at December 31, 2005 and the effects such obligations are expected to have on our liquidity and cash flows in future periods.

### Payments Due by Period

<table>
<thead>
<tr>
<th>Contractual Obligations</th>
<th>Total</th>
<th>Less than one year</th>
<th>1-3 years</th>
<th>3-5 years</th>
<th>More than five years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating lease obligation</td>
<td>$13,879,000</td>
<td>$1,425,000</td>
<td>$3,010,000</td>
<td>$3,254,000</td>
<td>$6,190,000</td>
</tr>
<tr>
<td>Long-term debt</td>
<td>19,187,000</td>
<td>7,675,000</td>
<td>11,512,000</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Purchase Obligations (1)</td>
<td>28,603,000</td>
<td>26,637,000</td>
<td>1,966,000</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total contractual cash obligations</td>
<td>$61,669,000</td>
<td>$35,737,000</td>
<td>$16,488,000</td>
<td>$3,254,000</td>
<td>$6,190,000</td>
</tr>
</tbody>
</table>

(1) In November 2004, as amended in May 2005, we entered into an agreement with Publicis, a contract sales organization, pursuant to which, on our behalf, Publicis has employed and trained a specialty sales force currently consisting of approximately 144 sales representatives to sell BiDil to our target prescriber markets. The agreement is for a current term of 24 months beginning on January 31, 2005, with our option to continue the agreement beyond this term. Year one costs recorded in 2005 were $29.8 million, excluding one-time start-up costs, and year two costs under the agreement are projected at approximately $24.3 million. We have the right to terminate this agreement upon 90 days written notice to Publicis. If we had terminated this agreement during the period between January 31, 2005 and January 30, 2006, we would have been required to pay a termination fee in the amount of $1.0 million. If we terminate during the period between January 31, 2006 and July 31, 2006, the termination fee will be $750,000. If we terminate the agreement after July 31, 2006, Publicis is not eligible for a termination fee. Other purchase obligations are $2.4 million in purchase commitments to Schwarz Pharma for manufacture of finished goods in the first and second quarter of 2006.

We believe that our existing cash, cash equivalents and marketable securities, including the net proceeds received from the sale of 6.1 million shares of our common stock in January 2006, will be sufficient to fund our planned operations, including increases in spending for the launch and commercialization of BiDil and our current development programs, for at least 21 months from the date of this report. However, we may require significant additional funds earlier than we currently expect to continue to support the commercial launch of BiDil, and to obtain regulatory approvals necessary to develop and launch our other product candidates.

We may seek additional funding through collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates, or products which we would otherwise pursue on our own.

Even if we are able to raise additional funds in a timely manner, our future capital requirements may vary from what we expect and will depend on many factors, including the following:

- the costs of launching and commercializing BiDil;
- the magnitude of product sales of BiDil;
• the timing, receipt, and amount of milestone and other payments, if any, from potential collaborators;
• the timing, receipt, and amount of sales and royalties, if any, from our potential product candidates;
• the resources required to successfully complete our clinical trials;
• the time and costs involved in obtaining regulatory approvals;
• continued progress in our research and development programs, as well as the magnitude of these programs;
• the cost of manufacturing, marketing and sales activities;
• the costs involved in preparing, filing, prosecuting, maintaining, and enforcing patent claims;
• the cost of obtaining and maintaining licenses to use patented technologies; and
• our ability to establish and maintain additional collaborative arrangements.

Application of Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, inventory, accrued expenses and the factors used to determine the fair value of our stock options. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect our more significant judgments and estimates used in the preparation of our consolidated financial statements.

Revenue. Our principal source of revenue is the sale of BiDil, which began shipping in July of 2005. Other sources of revenue to date include license fees, research and development payments and milestone payments that we have received from our corporate collaborators.

Product Sales/Deferred Revenue. We follow the provisions of Staff Accounting Bulletin No. 104, Revenue Recognition and recognize revenue from product sales upon delivery of product to wholesalers or pharmacies, when persuasive evidence of an arrangement exists, the fee is fixed or determinable, title to product and associated risk of loss has passed to the wholesaler and collect-ability of the related receivable is reasonably assured. All revenues from product sales are recorded net of applicable allowances for sales returns, rebates, and discounts. For arrangements where the risk of loss has not passed to wholesalers or pharmacies, we defer the recognition of revenue by recording deferred revenue until such time that risk of loss has passed. In addition, we evaluate our level of shipments to wholesalers and pharmacies on a quarterly basis compared to the estimated level of inventory in the channel, remaining shelf-life of the product shipped and quarterly forecasted sales. As a result of this evaluation, we deferred $2.1 million of revenue from December shipments and recorded this amount in deferred revenue as of December 31, 2005. Also, the cost of BiDil associated with amounts recorded as deferred revenue are recorded in inventory until such time as risk of loss has passed.
**Sales Returns, Allowances, Rebates and Discounts.** Our product sales are subject to returns, allowances, rebates and discounts that are customary in the pharmaceutical industry.

A large portion of our product sales are made to pharmaceutical wholesalers for further distribution through pharmacies to patients, who are consumers of the product. All revenues from product sales are recorded net of applicable allowances for sales returns, wholesaler allowances, rebates and cash and contract discounts. We determine our provisions for sales returns, allowances, rebates and discounts based primarily on estimates and on contractual terms. In developing a reasonable estimate for the reserve for product returns, we considered the factors in paragraph 8 of SFAS 48, *Revenue Recognition When a Right of Return Exists*. Although we have not yet developed our own history of product returns because of the recent launch of BiDil, we believe we can develop a reasonable estimate of returns. BiDil is a heart failure drug that is similar to other drugs in the marketplace which have similar channels of distribution, similar shelf lives and similar return rights. We were able to verify through discussions with other pharmaceutical firms that promote and sell these other drugs that our initial estimate of returns is reasonable in relation to product launch. We will continue to monitor actual returns as we gain more sales experience with BiDil.

**Product Returns.** Consistent with industry practice, we offer contractual return rights that allow customers to return product only during the period that is three months prior to, and twelve months after product expiration. Commercial product shipped during 2005 had a shelf-life of twelve months from date of manufacture with expiration dates ranging from April 2006 to August 2006. Factors that are considered in our estimate of future product returns include an analysis of the amount of product in the wholesaler and pharmacy channels, discussions with key wholesalers and other customers regarding inventory levels and shipment trends, review of consumer consumption data as reported by Source Projected Launchtrac, Wolters Kluwer Health, return rates for similar pharmaceutical products that are sold in the same distribution channel, the remaining time to expiration of our product and our forecast of future sales of our product. At December 31, 2005, our product return reserve was $98,000. This reserve is evaluated on a quarterly basis, assessing each of the factors described above, and adjusted accordingly. Based on the factors noted above, we believe our estimate of product returns is reasonable, and changes, if any, from this estimate would not have a material impact to our financial statements.

**Initial Trade Shipments Incentive.** During July of 2005, we offered certain product stocking incentives to a number of wholesalers and pharmacy customers. These incentives included units with guaranteed sales provisions and extended payment terms. As a result of these provisions, we concluded that these sales were essentially consignment sales as the risk of loss of these units has not passed to the customer. Accordingly, we have deferred all revenue related to these units until such time as the unit is provided to a patient with a prescription. As of December 31, 2005, the remaining balance of deferred revenue related to these units is $1.2 million.

**Cash Incentives.** During the third quarter of 2005, we offered certain additional incentives to a number of pharmacy customers. These cash incentives included placement and advertising assistance in the amount of $328,000. We recorded this amount as a reduction to revenue during the year ended December 31, 2005.

**Sample Voucher Program.** Beginning in the third quarter of 2005, we initiated a sample voucher program whereby we offered an incentive to patients in the form of a free 30-day trial (approximately 100 tablets) of BiDil. We have accounted for this program in accordance with Emerging Issues Task Force Issue No. 01-09, *Accounting for Consideration Given by a Vendor to a Customer* (EITF No. 01-09). These initial sample vouchers had an expiration date of September 30, 2005 at which time we reduced revenue for the actual amount of reimbursement claims received for the vouchers distributed during the third quarter of 2005. This program was repeated during the fourth quarter with sample vouchers that had an expiration date of December 31, 2005, at which time we reduced revenue for the actual amount of reimbursement claims received for the vouchers distributed during the fourth quarter of 2005. As a result
of this program, we recorded a reduction to revenue of $786,000 for the year ended December 31, 2005. We expect to continue to offer sample voucher incentives in future periods.

**Sales Discounts, Rebates and Allowances.** Sales discounts, rebates and allowances result primarily from sales under contract with wholesalers, healthcare providers, Medicaid programs and other governmental agencies. We estimate rebates and contractual allowances, cash and contract discounts and other rebates by considering the following factors: current contract prices and terms, estimated customer and wholesaler inventory levels and current average rebate rates. For the year end December 31, 2005, we recorded cash discounts, rebates and other allowances of $125,000.

**Collaboration Revenue.** We record revenue on an accrual basis as it is earned and when amounts are considered collectible. Revenues received in advance of performance obligations or in cases where we have a continuing obligation to perform services, are deferred and recognized over the contractual or estimated performance period. Revenues from milestone payments that represent the culmination of a separate earnings process are recorded when the milestone is achieved. Contract revenues are recorded as the services are performed. When we are required to defer revenue, the period over which such revenue should be recognized is subject to estimates by management and may change over the course of the collaborative agreement. In future periods, we expect revenues derived from collaboration agreements will continue to decrease as a percentage of total revenue, and product revenues will continue to increase based on anticipated increased volume of prescriptions of BiDil.

**Inventories.** We review our estimates of the net realizable value of our inventories at each reporting period. Our estimate of the net realizable value of our inventories is subject to judgment and estimation. The actual net realizable value of our inventories could vary significantly from our estimates and could have a material effect on our financial condition and results of operations in any reporting period. BiDil currently has a twelve month shelf life. On a quarterly basis, we analyze our current inventory levels and future irrevocable inventory purchase commitments and write down inventory that has become un-saleable, inventory that has a cost basis in excess of its expected net realizable value and irrevocable inventory purchase commitments that are in excess of expected future inventory requirements based on our sales forecasts. Expired inventory will be disposed of, and the related costs will be written off. For the year ended December 31, 2005, we recorded an inventory impairment charge of $5.6 million to cost of sales related to commercial trade and patient sample inventory, and a $1.5 million charge to cost of sales for contractual purchase commitments.

**Accrued Expenses.** As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements. Examples of estimated expenses for which we accrue include contract service fees such as amounts paid to clinical monitors, data management organizations and investigators in conjunction with clinical trials, fees paid to contract manufacturers for the production of finished goods, marketing and medical support fees, such as advisory boards, and publications, marketing service fees and professional service fees, such as lawyers and accountants. In connection with such service fees, our estimates are most affected by our understanding of the status and timing of services provided relative to the actual levels of services incurred by such service providers. The majority of our service providers invoice us monthly in arrears for services performed. In the event that we do not identify certain costs, which have begun to be incurred, or we over or under-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high. The date on which certain services commence, the level of services performed on or before a given date and the cost of such services are often determined based on subjective judgments. We make these judgments based upon the facts and circumstances known to us in accordance with generally accepted accounting principles.
**Stock-Based Compensation.** We have elected to follow Accounting Principle Board, or APB, Opinion No. 25, *Accounting for Stock Issued to Employees*, or APB 25, and related interpretations, in accounting for our stock-based compensation plans, rather than the alternative fair value method provided for under Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation*, or SFAS 123. In 2003 and 2002, certain grants of stock options were made at exercise prices less than the fair value of our common stock and, as a result, we recorded deferred stock compensation expense. In the notes to our financial statements, we provide pro forma disclosures in accordance with SFAS 123. We account for transactions in which services are received from non-employees in exchange for equity instruments based on the fair value of such services received or of the equity instruments issued, whichever is more reliably measured, in accordance with SFAS 123 and the Emerging Issues Task Force, or EITF, Issue 96-18, *Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, or EITF 96-18.

Accounting for equity instruments granted or sold by us under APB 25, SFAS 123 and EITF 96-18 requires fair value estimates of the equity instrument granted or sold. If our estimates of the fair value of these equity instruments are too high or too low, our expenses may be over or under stated. For equity instruments granted or sold in exchange for the receipt of goods or services, we estimate the fair value of the equity instruments based upon consideration of factors which we deem to be relevant at that time. Because shares of our common stock were not publicly traded prior to the commencement of our public offering on November 5, 2003, market factors historically considered in valuing stock and stock option grants include comparative values of public companies discounted for the risk and limited liquidity provided for in the shares we are issuing, pricing of private sales of our redeemable convertible preferred stock, prior valuations of stock grants and the effect of events that have occurred between the time of such grants, economic trends, and the comparative rights and preferences of the security being granted compared to the rights and preferences of our other outstanding equity.

Prior to our initial public offering, the fair value of our common stock was determined by our board of directors contemporaneously with the grant. In the absence of a public trading market for our common stock, our board of directors considered numerous objective and subjective factors in determining the fair value of our common stock. At the time of option grants and other stock issuances, our board of directors considered the liquidation preferences, dividend rights, voting control and anti-dilution protection attributable to our then-outstanding redeemable convertible preferred stock, the status of private and public financial markets, valuations of comparable private and public companies, the likelihood of achieving a liquidity event such as an initial public offering, our existing financial resources, our anticipated continuing operating losses and increased spending levels required to complete our clinical trials, dilution to common stockholders from anticipated future financings and a general assessment of future business risks.

**Inflation**

We believe the effects of inflation generally do not have a material adverse impact on our operations or financial condition.

**Off-Balance Sheet Arrangements**

We do not have any material off-balance sheet arrangements.

**Recently Issued Accounting Pronouncement**

Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, or APB 25, and amends SFAS No. 95, *Statement of Cash Flows*. Generally, the approach in SFAS 123R is similar to the approach described in SFAS 123. However, SFAS 123R requires all share-based payments to employees, including grants of employee stock options, to be recognized in the income statement based on their fair values at the date of grant. Pro forma disclosure is no longer an alternative. SFAS 123R must be adopted in fiscal periods beginning after June 15, 2005. We will adopt SFAS 123R on January 1, 2006, the commencement of our first quarter of fiscal 2006.

SFAS 123R permits companies to adopt its requirements using one of two methods. A “modified prospective” method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS 123 for all awards granted to employees prior to the effective date of SFAS 123R that remain unvested on the effective date. A “modified retrospective” method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS 123 for purposes of pro forma disclosures for either (a) all prior periods presented or (b) prior interim periods of the year of adoption. The Company anticipates adopting the “modified prospective” method.

As permitted by SFAS 123, we currently account for share-based payments to employees using APB 25’s intrinsic value method and, as such, generally recognize no compensation cost for employee stock options. Accordingly, the adoption of SFAS 123R’s fair value method may have a significant impact on our result of operations, although it will have no impact on our overall financial position. The impact of adoption of SFAS 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, had we adopted SFAS 123R in prior periods, the impact of that standard would have approximated the impact of SFAS 123 as described in the disclosure of pro forma net loss and net loss per share in Note 2 to our financial statements. We are currently evaluating the impact of the adoption of SFAS 123R on our financial position and results of operations, including the valuation methods and support for the assumptions that underlie the valuation of the awards.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

We are exposed to market risk related to changes in interest rates. Our current investment policy is to maintain an investment portfolio consisting mainly of U.S. money market and high-grade corporate and U.S. government-related securities, directly or through managed funds, with maturities of two years or less. Our cash is deposited in and invested through highly rated financial institutions in North America. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 10% from levels at December 31, 2005, we estimate that the fair value of our investment portfolio would decline by an immaterial amount. We have the ability to hold our fixed income investments until maturity, and therefore we do not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.
ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
NitroMed, Inc.

We have audited the accompanying balance sheets of NitroMed, Inc. as of December 31, 2005 and 2004, and the related statements of operations, redeemable convertible preferred stock and stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of NitroMed, Inc. at December 31, 2005 and 2004, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of NitroMed, Inc.’s internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 28, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2006
NITROMED, INC.
BALANCE SHEETS
(in thousands, except par value amounts)

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2005</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASSETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>$11,091</td>
<td>$35,882</td>
</tr>
<tr>
<td>Marketable securities</td>
<td>50,450</td>
<td>106,485</td>
</tr>
<tr>
<td>Accounts receivable</td>
<td>4,078</td>
<td>—</td>
</tr>
<tr>
<td>Inventories</td>
<td>3,247</td>
<td>—</td>
</tr>
<tr>
<td>Prepaid expenses and other current assets</td>
<td>3,860</td>
<td>3,216</td>
</tr>
<tr>
<td>Total current assets</td>
<td>72,726</td>
<td>145,583</td>
</tr>
<tr>
<td>Property and equipment, net</td>
<td>2,992</td>
<td>2,963</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>803</td>
<td>811</td>
</tr>
<tr>
<td>Total assets</td>
<td>$76,521</td>
<td>$149,357</td>
</tr>
</tbody>
</table>

| **LIABILITIES AND STOCKHOLDERS’ EQUITY** |                   |      |
| Current Liabilities:           |                   |      |
| Accounts payable               | $11,810           | $2,662 |
| Accrued expenses               | 11,269            | 8,091 |
| Deferred revenue               | 3,451             | 1,592 |
| Current portion of long-term debt | 6,272       | —     |
| Total current liabilities      | 32,802            | 12,345 |
| Long-term debt                 | 10,653            | —     |

Commitments and contingencies

Stockholders’ equity:
Preferred stock, $0.01 par value; 5,000 shares authorized; no shares issued or outstanding | — | — |
Common stock, $.01 par value; authorized 65,000 shares; issued and outstanding 30,512 shares and 30,124 shares as of December 31, 2005 and 2004, respectively | 305 | 301 |
Additional paid-in capital         | 276,510           | 275,727 |
Deferred stock compensation       | (1,208)           | (2,095) |
Accumulated deficit               | (242,471)         | (136,619) |
Accumulated other comprehensive loss | (70)             | (302) |
Total stockholders’ equity        | 33,066            | 137,012 |
Total liabilities and stockholders’ equity | $76,521 | $149,357 |

The accompanying notes are an integral part of the financial statements.
## Nitromed, Inc.
### Statements of Operations
(in thousands, except per share amounts)

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenues:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Products sales</td>
<td>$4,455</td>
<td>$—</td>
<td>$—</td>
</tr>
<tr>
<td>Research and development</td>
<td>1,592</td>
<td>16,458</td>
<td>12,775</td>
</tr>
<tr>
<td><strong>Total revenues:</strong></td>
<td>6,047</td>
<td>16,458</td>
<td>12,775</td>
</tr>
<tr>
<td><strong>Cost and operating expenses:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of product sales</td>
<td>8,009</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Research and development</td>
<td>31,930</td>
<td>27,995</td>
<td>18,907</td>
</tr>
<tr>
<td>Sales, general and administrative</td>
<td>74,006</td>
<td>19,591</td>
<td>3,114</td>
</tr>
<tr>
<td><strong>Total cost and operating expenses:</strong></td>
<td>113,945</td>
<td>47,586</td>
<td>22,021</td>
</tr>
<tr>
<td><strong>Loss from operations:</strong></td>
<td>(107,898)</td>
<td>(31,128)</td>
<td>(9,246)</td>
</tr>
<tr>
<td><strong>Non-operating income:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interest expense</td>
<td>(930)</td>
<td>(1)</td>
<td>(4)</td>
</tr>
<tr>
<td>Interest income</td>
<td>2,976</td>
<td>1,336</td>
<td>399</td>
</tr>
<tr>
<td>Rental and other income</td>
<td>—</td>
<td>20</td>
<td>82</td>
</tr>
<tr>
<td><strong>Net loss:</strong></td>
<td>2,046</td>
<td>1,355</td>
<td>477</td>
</tr>
</tbody>
</table>

**Deemed dividends related to beneficial conversion feature of redeemable convertible preferred stock:** — — (19,357)

**Dividends and accretion to redemption value of redeemable convertible preferred stock:** — — (2,794)

**Net loss attributable to common stockholders:** $(105,852) $(29,773) $(30,920)

**Basic and diluted net loss attributable to common stockholders per common share:** $ (3.49) $ (1.14) $ (6.95)

**Shares used in computing basic and diluted net loss attributable to common stockholders per common share:** 30,355 26,152 4,447

The accompanying notes are an integral part of the financial statements.
NITROMED, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except per share amounts)

<table>
<thead>
<tr>
<th>Redeemable Convertible Preferred Stock</th>
<th>Common Stock</th>
<th>Additional Paid-in Capital</th>
<th>Deferred Stock Compensation</th>
<th>Accumulated Deficit</th>
<th>Accumulated Other Comprehensive Income (Loss)</th>
<th>Total Stockholders' Equity (Deficit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Par Value</td>
<td>Capital</td>
<td>(527)</td>
<td>$75,926</td>
</tr>
<tr>
<td>Balance at December 31, 2002</td>
<td>30,770</td>
<td>2,884</td>
<td>$8</td>
<td>$8</td>
<td>$985</td>
<td>$985</td>
</tr>
<tr>
<td>Exercise of stock options</td>
<td>217</td>
<td>2</td>
<td>131</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deferred stock compensation expense</td>
<td>3,317</td>
<td>(3,317)</td>
<td>—</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amortization of deferred stock</td>
<td></td>
<td>325</td>
<td>(325)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compensation expense associated with</td>
<td></td>
<td>37</td>
<td>(37)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>options issued to non-employees and</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>performance options issued to</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>employees</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accretion of Series E dividends</td>
<td>2,469</td>
<td></td>
<td>(2,469)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accretion of preferred stock to</td>
<td>325</td>
<td></td>
<td>(325)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>redemption value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beneficial conversion feature of Series</td>
<td>19,320</td>
<td></td>
<td>(19,320)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beneficial conversion feature of Series</td>
<td>37</td>
<td></td>
<td>(37)</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Issuance of Series E preferred stock</td>
<td>2,776</td>
<td>19,900</td>
<td>$7.20</td>
<td>19,900</td>
<td></td>
<td></td>
</tr>
<tr>
<td>per share for cash (net of issuance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>costs of $100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Issuance of common stock from initial</td>
<td>6,000</td>
<td>60</td>
<td>60,012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>public offering (&quot;IPO&quot;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(net of issuance costs of $5,928)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conversion of preferred stock to</td>
<td>(33,546)</td>
<td>18,399</td>
<td>105,394</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>common stock at IPO</td>
<td></td>
<td>184</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrealized gains on cash equivalents</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and marketable securities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balance at December 31, 2003</td>
<td>—</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of the financial statements.
### NITROMED, INC.

**STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)**

(in thousands, except per share amounts)

<table>
<thead>
<tr>
<th>Redeemable Convertible Preferred Stock</th>
<th>Common Stock</th>
<th>Additional Paid-in Capital</th>
<th>Deferred Stock Compensation</th>
<th>Accumulated Deficit</th>
<th>Accumulated Other Comprehensive Income (Loss)</th>
<th>Total Stockholders' Equity (Deficit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Par Value</td>
<td>Shares</td>
<td>Amount</td>
<td></td>
<td></td>
<td>Shares</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>--------------</td>
<td>---------------------------</td>
<td>-----------------------------</td>
<td>---------------------</td>
<td>---------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Exercise of stock options</td>
<td>676</td>
<td>7</td>
<td>871</td>
<td>$(3,240)</td>
<td></td>
<td>878</td>
</tr>
<tr>
<td>Exercise of warrants</td>
<td>237</td>
<td>2</td>
<td>(2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amortization of deferred stock compensation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compensation expense associated with options issued to non-employees and performance options issued to employees</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Issuance of stock under employee stock purchase plan</td>
<td>30</td>
<td>—</td>
<td>155</td>
<td></td>
<td></td>
<td>1,540</td>
</tr>
<tr>
<td>Issuance of common stock from public offering (net of issuance costs of $5,796)</td>
<td>3,580</td>
<td>36</td>
<td>81,722</td>
<td>(163)</td>
<td>163</td>
<td>81,758</td>
</tr>
<tr>
<td>Cancellation of compensatory stock options</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrealized losses on marketable securities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(29,773)</td>
</tr>
<tr>
<td>Comprehensive loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(29,773)</td>
</tr>
<tr>
<td>Balance at December 31, 2004</td>
<td>—</td>
<td>$301</td>
<td>$275,727</td>
<td>$(2,095)</td>
<td>$(136,619)</td>
<td>$137,012</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of the financial statements.
<table>
<thead>
<tr>
<th>Redeemable Convertible Preferred Stock</th>
<th>Common Stock</th>
<th>Additional Paid-in Capital</th>
<th>Deferred Stock Compensation</th>
<th>Accumulated Deficit</th>
<th>Accumulated Other Comprehensive Income (Loss)</th>
<th>Total Stockholders' Equity (Deficit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shares</td>
<td>Amount</td>
<td>Shares</td>
<td>Par Value</td>
<td>$</td>
<td>(2,095)</td>
<td>$(136,619)</td>
</tr>
<tr>
<td>30,124</td>
<td>301</td>
<td>339</td>
<td>3</td>
<td>653</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>887</td>
</tr>
<tr>
<td>30,512</td>
<td>305</td>
<td>37</td>
<td>1</td>
<td>523</td>
<td>(394)</td>
<td></td>
</tr>
<tr>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>232</td>
<td>105,852</td>
</tr>
<tr>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1,208)</td>
<td>(242,471)</td>
</tr>
</tbody>
</table>

The accompanying notes are an integral part of the financial statements.
NITROMED, INC.

STATEMENTS OF CASH FLOWS

(in thousands)

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2005</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash flows from operating activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(105,852)</td>
<td>$(29,773)</td>
<td>$(8,769)</td>
</tr>
<tr>
<td>Adjustments to reconcile net loss to net cash (used in) provided by operating activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depreciation and amortization</td>
<td>896</td>
<td>421</td>
<td>251</td>
</tr>
<tr>
<td>Stock-based compensation expense</td>
<td>493</td>
<td>2,522</td>
<td>907</td>
</tr>
<tr>
<td>Changes in operating assets and liabilities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounts receivable</td>
<td>(4,078)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Inventories</td>
<td>(3,247)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Prepaid expenses and other current assets</td>
<td>(644)</td>
<td>(1,920)</td>
<td>8,971</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>1,859</td>
<td>(12,858)</td>
<td>3,825</td>
</tr>
<tr>
<td>Accounts payable and accrued expenses</td>
<td>12,326</td>
<td>7,854</td>
<td>627</td>
</tr>
<tr>
<td>Net cash (used in) provided by operating activities</td>
<td>(98,247)</td>
<td>(33,754)</td>
<td>5,812</td>
</tr>
<tr>
<td>Cash flows from investing activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purchases of property and equipment</td>
<td>(925)</td>
<td>(2,698)</td>
<td>(655)</td>
</tr>
<tr>
<td>Purchases of marketable securities</td>
<td>(126,159)</td>
<td>(131,410)</td>
<td>(37,562)</td>
</tr>
<tr>
<td>Sales of marketable securities</td>
<td>182,426</td>
<td>54,072</td>
<td>14,796</td>
</tr>
<tr>
<td>Restricted cash</td>
<td>8</td>
<td>(711)</td>
<td>—</td>
</tr>
<tr>
<td>Net cash provided by (used in) investing activities</td>
<td>55,350</td>
<td>(80,747)</td>
<td>(23,421)</td>
</tr>
<tr>
<td>Cash flows from financing activities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proceeds from long-term debt</td>
<td>20,000</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Principal payments on long-term debt</td>
<td>(3,075)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Net proceeds from sale of common stock in public offering</td>
<td>—</td>
<td>81,758</td>
<td>60,072</td>
</tr>
<tr>
<td>Proceeds from employee stock plans</td>
<td>1,181</td>
<td>1,033</td>
<td>133</td>
</tr>
<tr>
<td>Principal payments on notes payable</td>
<td>—</td>
<td>(22)</td>
<td>(42)</td>
</tr>
<tr>
<td>Net proceeds from sale of redeemable convertible preferred stock</td>
<td>—</td>
<td>—</td>
<td>19,900</td>
</tr>
<tr>
<td>Net cash provided by financing activities</td>
<td>18,106</td>
<td>82,769</td>
<td>80,063</td>
</tr>
<tr>
<td>Net (decrease) increase in cash and cash equivalents</td>
<td>(24,791)</td>
<td>(31,732)</td>
<td>62,454</td>
</tr>
<tr>
<td>Cash and cash equivalents, beginning balance</td>
<td>35,882</td>
<td>67,614</td>
<td>5,160</td>
</tr>
<tr>
<td>Cash and cash equivalents, ending balance</td>
<td>$11,091</td>
<td>$35,882</td>
<td>$67,614</td>
</tr>
</tbody>
</table>

Supplemental disclosure:

Cash paid during the year for interest | $790 | $1 | $4

The accompanying notes are an integral part of the financial statements.
1. The Company

NitroMed, Inc. (the “Company”) is an emerging pharmaceutical company focused on the research, development and commercialization of proprietary pharmaceuticals based on the therapeutic benefits of nitric oxide. In June 2005, the U.S. Food and Drug Administration (FDA) approved the Company’s product, BiDil, for the treatment of heart failure in self-identified black patients. BiDil is an orally administered fixed-dose combination of isosorbide dinitrate and hydralazine hydrochloride. The Company commercially launched BiDil in July 2005 and generated product sales of $4.5 million during the year ended December 31, 2005. The Company’s goal is to become a leading, multi-product pharmaceutical company by developing additional innovative nitric oxide products and by building on the Company’s BiDil development experience and commercialization infrastructure to identify and market additional products for cardiovascular and metabolic diseases. The Company is applying its nitric oxide technology to develop novel pharmaceuticals, as well as safer and more effective versions of existing drugs, to target significant diseases that are characterized by a deficiency in nitric oxide and to treat underserved patient populations. The Company’s nitric oxide-development strategy involves the internal development of proprietary nitric oxide-enhancing product candidates, such as BiDil, the co-development of nitric oxide-enhancing drugs with partners and the out-licensing of our nitric oxide-enhancing technology in exchange for potential milestone payments and royalties on sales.

On January 25, 2006, the Company completed a registered direct public offering of shares of its common stock previously registered under an effective shelf registration statement, which was filed with the Securities and Exchange Commission in August 2005. Pursuant to this offering, the Company sold approximately 6.1 million shares of its common stock to selected institutional investors at a price of $10.25 per share. Proceeds to the Company from this registered direct offering, net of offering expenses and placement agency fees, totaled $58.6 million.

2. Summary of Significant Accounting Policies

Cash Equivalents and Marketable Securities

Cash equivalents are short-term, highly liquid investments with maturities of three months or less at the time of acquisition. Investments with maturities in excess of three months at the time of acquisition are classified as marketable securities and designated as available-for-sale. Cash equivalents consist of institutional money market funds. Available-for-sale securities are carried at fair market value, as reported by the custodian, and unrealized gains and losses are reported as a separate component of accumulated other comprehensive income within stockholders’ equity. Realized gains and losses were not material for the years ended December 31, 2005, 2004 and 2003.

Fair Value of Financial Instruments

Financial instruments mainly consist of cash and cash equivalents, marketable securities and long-term debt. The carrying amounts of these cash and cash equivalents, and marketable securities approximate their fair values. The fair value of long-term debt is $13.3 million.

Research and Development Expenses

Research and development expenses primarily consist of salaries and related expenses for personnel, fees paid to consultants and outside service providers, materials used in clinical trials and research and development, and medical support costs related to the launch and commercialization of BiDil.
2. Summary of Significant Accounting Policies (Continued)

Company charges research and development expenses, including costs associated with acquiring patents, to operations as incurred.

The Company enters into contracts with professional service providers to conduct clinical trials and related services. These professional service providers render services over an extended period of time, generally one to three years. Typically, the Company enters into two types of vendor contracts, patient-based or time-based. Under a patient-based contract, the Company first determines an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients, the cost assigned to each patient based on a patient’s number of visits and the total dollar value of the contract. The Company then records expense based upon the total number of patients enrolled during the period and the status of each patient. Under a time based contract, using critical factors contained within the contract such as the stated duration of the contract and the timing of services provided, the Company records the contractual expense for each service provided ratably over the period during which the Company estimates the service will be performed. On a monthly basis, the Company reviews both the timetable of services to be rendered and the timing of services actually received based on regular communications with its vendors in order to gauge the reasonableness of its estimates. Based upon this review, revisions may be made to the forecasted timetable or the extent of services performed, or both, in order to reflect the Company’s most current estimate of the contract.

Revenue Recognition

The Company’s principal source of revenue is the sale of BiDil (isosorbide dinitrate/hydralazine hydrochloride), the Company’s product for the treatment of heart failure in self-identified black patients as an adjunct to current standard therapies. BiDil was launched and began shipping in the third quarter of 2005. Other sources of revenue include collaboration revenue, which has generally been recognized ratably over the research and development collaboration term. The Company expects that revenues derived from its collaboration agreements will continue to decrease as a percentage of total revenue in future periods, and product revenues will continue to increase based on anticipated increased volume of prescriptions of BiDil.

Product Sales/Deferred Revenue.

The Company follows the provisions of Staff Accounting Bulletin No. 104, Revenue Recognition and recognizes revenue from product sales upon delivery of product to wholesalers or pharmacies, when persuasive evidence of an arrangement exists, the fee is fixed or determinable, title to product and associated risk of loss has passed to the wholesaler and collectability of the related receivable is reasonably assured. All revenues from product sales are recorded net of applicable allowances for sales returns, rebates, and discounts. For arrangements where the risk of loss has not passed to wholesalers or pharmacies, the Company defers the recognition of revenue by recording deferred revenue until such time that risk of loss has passed. In addition, the Company evaluates its level of shipments to wholesalers and pharmacies on a quarterly basis compared to the estimated level of inventory in the channel, remaining shelf-life of the product shipped and quarterly forecasted sales. As a result of this evaluation, the Company deferred $2.1 million of revenue from December shipments and recorded this amount in deferred revenue as of December 31, 2005. The cost of BiDil associated with amounts recorded as deferred revenue are recorded in inventory until such time as risk of loss has passed.
2. Summary of Significant Accounting Policies (Continued)

Sales Returns, Allowances, Rebates and Discounts. The Company’s product sales are subject to returns, allowances, rebates and discounts that are customary in the pharmaceutical industry.

A large portion of the Company’s product sales are made to pharmaceutical wholesalers for further distribution through pharmacies to patients, who are consumers of the product. All revenues from product sales are recorded net of applicable allowances for sales returns, wholesaler allowances, rebates and cash and contract discounts. The Company determines provisions for sales returns, allowances, rebates and discounts based primarily on estimates and on contractual terms. In developing a reasonable estimate for the reserve for product returns, the Company considered the factors in paragraph 8 of Statement of Financial Accounting Standards (SFAS) No. 48, Revenue Recognition When a Right of Return Exists. Although the Company has not yet developed its own history of product returns because of the recent launch of BiDil, the Company believes it can develop a reasonable estimate of returns. BiDil is a heart failure drug that is similar to other drugs in the marketplace which have similar channels of distribution, similar shelf lives and similar return rights. The Company was able to verify through discussions with other pharmaceutical firms that promote and sell these other drugs that the Company’s initial estimate of returns is reasonable in relation to product launch. The Company will continue to monitor actual returns as the Company gains more sales experience with BiDil.

Product Returns. Consistent with industry practice, the Company offers contractual return rights that allow customers to return product only during the period that is three months prior to, and twelve months after product expiration. Commercial product shipped during 2005 had a shelf-life of twelve months from date of manufacture with expiration dates ranging from April 2006 to August 2006. Factors that are considered in the Company’s estimate of future product returns include an analysis of the amount of product in the wholesaler and pharmacy channels, discussions with key wholesalers and other customers regarding inventory levels and shipment trends, review of consumer consumption data as reported by Source Projected Launchtrac, Wolters Kluwer Health, return rates for similar pharmaceutical products that are sold in the same distribution channel the remaining time to expiration of the Company’s product and the Company’s forecast of future sales of the product. At December 31, 2005, the Company’s product return reserve was $98,000. This reserve is evaluated on a quarterly basis, assessing each of the factors described above, and adjusted accordingly. Based on the factors noted above, the Company believes its estimate of product returns is reasonable, and changes, if any, from this estimate would not have a material impact to the Company’s financial statements.

Initial Trade Shipments Incentive. During July of 2005, the Company offered certain product stocking incentives to a number of wholesalers and pharmacy customers. These incentives included units with guaranteed sales provisions and extended payment terms. As a result of these provisions, the Company concluded that these sales were essentially consignment sales as the risk of loss of these units has not passed to the customer. Accordingly, the Company deferred all revenue related to these units until such time as the unit is provided to a patient with a prescription. As of December 31, 2005, the remaining balance of deferred revenue related to these units is $1.2 million.

Cash Incentives. During the third quarter of 2005, the Company offered certain additional incentives to a number of pharmacy customers. These cash incentives included placement and advertising assistance in the amount of $328,000. The Company recorded this amount as a reduction to revenue for the year ended December 31, 2005.
2. Summary of Significant Accounting Policies (Continued)

Sample Voucher Program. Beginning in the third quarter of 2005, the Company initiated a sample voucher program whereby the Company offered an incentive to patients in the form of a free 30-day trial (approximately 100 tablets) of BiDil. The Company accounted for this program in accordance with Emerging Issues Task Force Issue No. 01-09, Accounting for Consideration Given by a Vendor to a Customer (EITF No. 01-09). These initial sample vouchers had an expiration date of September 30, 2005 at which time the Company reduced revenue for the actual amount of reimbursement claims received for the vouchers distributed during the third quarter of 2005. This program was repeated during the fourth quarter with sample vouchers that had an expiration date of December 31, 2005, at which time the Company reduced revenue for the actual amount of reimbursement claims received for the vouchers distributed during the fourth quarter of 2005. As a result of this program, the Company recorded a reduction to revenue of $786,000 for the year ended December 31, 2005. The Company expects to continue to offer sample voucher incentives in future periods.

Sales Discounts, Rebates and Allowances. Sales discounts, rebates and contractual allowances result primarily from sales under contract with healthcare providers, wholesalers, Medicaid programs and other governmental agencies. The Company estimates rebates and contractual allowances, cash and contract discounts and other rebates by considering the following factors: current contract prices and terms, estimated customer and wholesaler inventory levels and current average rebate rates. For the year end December 31, 2005, the Company recorded cash discounts, rebates and other allowances of $125,000.

Collaboration Revenue. The Company records collaboration revenue on an accrual basis as it is earned and when amounts are considered collectible. Revenues received in advance of performance obligations or in cases where the Company has a continuing obligation to perform services are deferred and recognized over the contractual or estimated performance period. Revenues from milestone payments that represent the culmination of a separate earnings process are recorded when the milestone is achieved. Contract revenues are recorded as the services are performed. When the Company is required to defer revenue, the period over which such revenue should be recognized is subject to estimates by management and may change over the course of the collaborative agreement. In future periods, the Company expects revenues derived from collaboration agreements will continue to decrease as a percentage of total revenue in future periods and product revenues will continue to increase based on anticipated increased volume of prescriptions of BiDil.

Accounts Receivable

Accounts receivable consists of amounts due from wholesalers and pharmacies for the purchase of BiDil. Ongoing evaluations of customers are performed and collateral is generally not required. As of December 31, 2005, the Company has not reserved any amount for bad debts related to the sale of BiDil. The Company continuously reviews all customer accounts to determine if an allowance for uncollectible accounts is necessary. The Company currently provides substantially all of its distributors with payment terms of up to 30 days on purchases of BiDil. Amounts past due from customers are determined based on contractual payment terms. Through December 31, 2005, payments have generally been made in a timely manner.
2. Summary of Significant Accounting Policies (Continued)

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over their estimated useful lives, which range between three to five years. Leasehold improvements are amortized based upon the lesser of the term of the lease or the useful life of the asset. The Company reviews its property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable and recognizes an impairment loss when the estimated undiscounted cash flows are less than the carrying value of the asset. The asset is written down to its fair value determined by either a quoted market price or by a discounted cash flow technique, whichever is more appropriate under the circumstances.

Inventories

Inventories are stated at the lower of cost or market, with cost determined on a first-in, first-out basis. Inventories consisted of the following:

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2005</th>
<th>December 31, 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw materials</td>
<td>$2,599</td>
<td>$—</td>
</tr>
<tr>
<td>Finished goods</td>
<td>481</td>
<td>—</td>
</tr>
<tr>
<td>Consigned inventory</td>
<td>167</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$3,247</strong></td>
<td><strong>$—</strong></td>
</tr>
</tbody>
</table>

During the year ended December 31, 2005, the Company purchased and capitalized inventories to be used for commercial trade sales and samples related to the July 2005 product launch of BiDil. BiDil currently has a twelve month shelf life.

On a quarterly basis, the Company analyzes its current inventory levels and future irrevocable inventory purchase commitments and writes down inventory that has become un-saleable, inventory that has a cost basis in excess of its expected net realizable value and future irrevocable inventory purchase commitments that are in excess of expected future product sales. Expired inventory is disposed of, and the related costs are written off. For the year ended December 31, 2005, the Company recorded an inventory impairment charge of $5.6 million to cost of sales related to commercial trade and patient sample inventory product, and a $1.5 million charge to cost of sales for contractual purchase commitments in excess of expected future inventory requirements based on the Company’s sales forecast.

Net Loss Per Share

Basic net loss per share is computed by dividing net loss available to common stockholders by the weighted average number of shares of common stock outstanding during the period. Diluted net loss per share is computed by dividing net loss available to common stockholders by the weighted average number of shares of common stock and the dilutive potential common stock equivalents then outstanding. Potential common stock equivalents consist of stock options, warrants and redeemable convertible preferred stock. Since the Company has a net loss for all periods presented, the effect of all potentially dilutive securities is antidilutive. Accordingly, basic and diluted net loss per share is the same.
2. Summary of Significant Accounting Policies (Continued)

The following table sets forth the computation of basic and diluted net loss per share for the respective periods:

<table>
<thead>
<tr>
<th>Year Ended December 31,</th>
<th>2005</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic and Diluted:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net loss</td>
<td>$(105,852)</td>
<td>$(29,773)</td>
<td>$(8,769)</td>
</tr>
<tr>
<td>Deemed dividends related to beneficial conversion feature of redeemable convertible preferred stock</td>
<td>—</td>
<td>—</td>
<td>(19,357)</td>
</tr>
<tr>
<td>Dividends and accretion to redemption value of redeemable convertible preferred stock prior to conversion</td>
<td>—</td>
<td>—</td>
<td>(2,794)</td>
</tr>
<tr>
<td>Net loss attributable to common stockholders</td>
<td>$(105,852)</td>
<td>$(29,773)</td>
<td>$(30,920)</td>
</tr>
<tr>
<td>Weighted average common shares used to compute net loss per share</td>
<td>30,355</td>
<td>26,152</td>
<td>4,447</td>
</tr>
<tr>
<td>Basic and diluted net loss per share</td>
<td>$(3.49)</td>
<td>$(1.14)</td>
<td>$(6.95)</td>
</tr>
</tbody>
</table>

Options to purchase 3,819,676, 3,246,631 and 2,898,584 shares of common stock for the years ended December 31, 2005, 2004 and 2003, respectively, and warrants to purchase 1,319, 13,861 and 275,096 shares of common stock for the years ended December 31, 2005, 2004 and 2003, respectively, have been excluded from the computation of net loss per share as their effects would have been antidilutive.

**Single Source Suppliers**

The Company currently obtains one of the key active pharmaceutical ingredients for its commercial requirements for BiDil from a single source. The disruption or termination of the supply of the commercial requirement for BiDil or a significant increase in the cost of the key active pharmaceutical ingredient from this single source could have a material adverse effect on the Company’s business, financial position and results of operations.

**Concentration of Credit Risk**

SFAS No. 105, Disclosure of Information about Financial Instruments with Off-Balance-Sheet Risk and Financial Instruments with Concentrations of Credit Risk, requires disclosure of any significant off-balance-sheet and credit risk concentrations. Financial instruments that potentially subject the Company to concentration of credit risk consists principally of marketable securities and trade accounts receivable. The Company has no off-balance-sheet or concentrations of credit risk such as foreign exchange contracts, options contracts or other foreign hedging arrangements. The Company maintains its cash and cash equivalents and marketable securities balances with several nonaffiliated institutions.
2. Summary of Significant Accounting Policies (Continued)

The following table summarizes the number of trade customers that individually comprise greater than 10% of total revenues and their respective percentage of the Company’s total product revenues. This table excludes revenues from collaboration agreements from which the Company recognized revenue in 2005, 2004 and 2003 from solely two collaborative partners:

<table>
<thead>
<tr>
<th>Number of Significant Customers</th>
<th>Percentage of Total Product Revenues by Customer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Year ended December 31, 2005.</td>
<td>3</td>
</tr>
</tbody>
</table>

The following table summarizes the number of customers that individually comprise greater than 10% of total accounts receivable and their respective percentage of the Company’s total accounts receivable:

<table>
<thead>
<tr>
<th>Number of Significant Customers</th>
<th>Percentage of Total Accounts Revenues by Customer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>As of December 31, 2005. .</td>
<td>2</td>
</tr>
</tbody>
</table>

Advertising Costs

All advertising costs are expensed as incurred. Advertising expenses were $20.1 million and $2.0 million for the years ended December 31, 2005 and 2004, respectively. There were no advertising costs for the year ended December 31, 2003.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Such estimates relate to allowances for accounts receivable and customer returns rates, the net realizable value of inventory, useful lives of fixed assets, and accrued liabilities. Actual results could differ from those estimates, and such differences may be material to the financial statements.

Stock-Based Compensation

The Company has elected to account for its stock-based compensation plans under the intrinsic value method pursuant to Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB 25), and related Interpretations, rather than the alternative fair value accounting provided under SFAS No. 123, Accounting for Stock-Based Compensation (SFAS 123). In accordance with EITF 96-18, Accounting for Equity Instruments that are Issued to Other than Employees for Acquiring, or in Connection with Selling Goods or Services (EITF 96-18), the Company records compensation expense equal to the fair value of the option granted to non-employees over the vesting period, which is generally the period of service.
2. Summary of Significant Accounting Policies (Continued)

SFAS 123 requires pro forma information regarding net loss and net loss per share as if the Company had accounted for its stock-based awards to employees under the fair value method of SFAS 123. The fair value of the Company’s stock options used to compute pro forma net loss is the estimated fair value at the grant date using the Black-Scholes option-pricing model with the following weighted-average assumptions:

<table>
<thead>
<tr>
<th></th>
<th>December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2005</td>
</tr>
<tr>
<td>Risk-free interest rate</td>
<td>4.0%</td>
</tr>
<tr>
<td>Expected volatility</td>
<td>73%</td>
</tr>
<tr>
<td>Expected lives</td>
<td>6 years</td>
</tr>
<tr>
<td>Expected dividend</td>
<td>—</td>
</tr>
</tbody>
</table>

The per-share, weighted-average grant date fair value of options granted during the years ended December 31, 2005, 2004 and 2003 was $11.51, $9.66 and $6.49, respectively.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized over the option vesting period. Had compensation expense for the Company’s stock-based compensation plans been determined based on the fair value at the grant dates for awards under those plans consistent with the method of SFAS 123, the Company’s net loss and net loss per share would have been as follows:

<table>
<thead>
<tr>
<th>Years Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
</tr>
<tr>
<td>Net loss attributable to common stockholders as reported .</td>
</tr>
<tr>
<td>Add: Stock-based employee compensation expense included in reported net loss</td>
</tr>
<tr>
<td>Deduct: Stock-based employee compensation expense determined under fair value based method .</td>
</tr>
<tr>
<td>Pro forma net loss</td>
</tr>
</tbody>
</table>

Basic and diluted net loss per share:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>As reported</td>
<td>$(3.49)</td>
</tr>
<tr>
<td>Pro forma</td>
<td>$(3.66)</td>
</tr>
</tbody>
</table>

Accumulated Other Comprehensive Income (Loss)

The Company presents comprehensive income (loss) in accordance with SFAS No. 130, Reporting Comprehensive Income. Accumulated other comprehensive income is comprised entirely of unrealized gains and losses on available-for-sale marketable securities.

Income Taxes

Deferred tax assets and liabilities are determined based on differences between the financial reporting and income tax basis of assets and liabilities, as well as net operating loss carryforwards and tax credits, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to reflect the uncertainty associated with their ultimate realization.
2. Summary of Significant Accounting Policies (Continued)

Segment Information

During the three years ended December 31, 2005, 2004 and 2003, the Company operated in one reportable business segment, developing nitric oxide enhancing medicines, under the management approach of SFAS No. 131, Disclosures about Segments of an Enterprise and Related Information.

New Accounting Standard

On December 16, 2004, the Financial Accounting Standards Board issued SFAS No. 123 (revised 2004) (SFAS 123R), Share-Based Payment, which is a revision of SFAS No. 123, Accounting for Stock-Based Compensation. SFAS 123R supersedes APB 25 and amends SFAS No. 95, Statement of Cash Flows. Generally, the approach in SFAS 123R is similar to the approach described in SFAS 123. However, SFAS 123R requires all share-based payments to employees, including grants of employee stock options, to be recognized in the income statement based on their fair values at the date of grant. Pro forma disclosure is no longer an alternative. The Company will adopt SFAS 123R on January 1, 2006, the commencement of its first quarter of fiscal 2006.

SFAS 123R permits companies to adopt its requirements using one of two methods. A “modified prospective” method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS 123 for all awards granted to employees prior to the effective date of SFAS 123R that remain unvested on the effective date. A “modified retrospective” method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS 123 for purposes of pro forma disclosures for either (a) all prior periods presented or (b) prior interim periods of the year of adoption. The Company anticipates adopting the “modified prospective” method.

As permitted by SFAS 123, the Company currently accounts for share-based payments to employees using APB 25’s intrinsic value method and, as such, generally recognizes no compensation cost for employee stock options. Accordingly, the adoption of SFAS 123R’s fair value method may have a significant impact on the Company’s result of operations, although it will have no impact on the Company’s overall financial position. The impact of adoption of SFAS 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, had the Company adopted SFAS 123R in prior periods, the impact of that standard would have approximated the impact of SFAS 123 as described in the disclosure of pro forma net loss and net loss per share in Note 2 to these financial statements. The Company is currently evaluating the impact of the adoption of SFAS 123R on its financial position and results of operations, including the valuation methods and support for the assumptions that underlie the valuation of the awards.
3. Cash Equivalents and Marketable Securities

The following is a summary of the fair market value of available-for-sale money market funds and marketable securities the Company held at December 31, 2005 and 2004:

<table>
<thead>
<tr>
<th>December 31, 2005</th>
<th>Amortized Cost</th>
<th>Gross Unrealized Gains</th>
<th>Gross Unrealized Losses</th>
<th>Estimated Fair Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and money market funds</td>
<td>$11,091</td>
<td>$—</td>
<td>$—</td>
<td>$11,091</td>
</tr>
<tr>
<td>U.S. Government agencies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one year or less</td>
<td>$ 7,750</td>
<td>$—</td>
<td>$(20)</td>
<td>$ 7,730</td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>1,000</td>
<td>—</td>
<td>(17)</td>
<td>983</td>
</tr>
<tr>
<td>Taxable auction securities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>32,725</td>
<td>—</td>
<td>—</td>
<td>32,725</td>
</tr>
<tr>
<td>Corporate notes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one year or less</td>
<td>9,045</td>
<td>—</td>
<td>(33)</td>
<td>9,012</td>
</tr>
<tr>
<td>Total marketable securities</td>
<td>$50,520</td>
<td>$—</td>
<td>$(70)</td>
<td>$50,450</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>December 31, 2004</th>
<th>Amortized Cost</th>
<th>Gross Unrealized Gains</th>
<th>Gross Unrealized Losses</th>
<th>Estimated Fair Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash and money market funds</td>
<td>$ 35,882</td>
<td>$—</td>
<td>$—</td>
<td>$ 35,882</td>
</tr>
<tr>
<td>Commercial paper</td>
<td>$ 11,962</td>
<td>$—</td>
<td>$—</td>
<td>$ 11,962</td>
</tr>
<tr>
<td>U.S. Government agencies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one year or less</td>
<td>5,905</td>
<td>—</td>
<td>(28)</td>
<td>5,877</td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>7,759</td>
<td>—</td>
<td>(82)</td>
<td>7,677</td>
</tr>
<tr>
<td>Asset-backed securities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>8,243</td>
<td>—</td>
<td>(31)</td>
<td>8,212</td>
</tr>
<tr>
<td>Taxable auction securities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>50,200</td>
<td>—</td>
<td>—</td>
<td>50,200</td>
</tr>
<tr>
<td>Corporate notes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due in one year or less</td>
<td>9,384</td>
<td>—</td>
<td>(38)</td>
<td>9,346</td>
</tr>
<tr>
<td>Due in one to three years</td>
<td>13,334</td>
<td>—</td>
<td>(123)</td>
<td>13,211</td>
</tr>
<tr>
<td>Total marketable securities</td>
<td>$106,787</td>
<td>$—</td>
<td>$(302)</td>
<td>$106,485</td>
</tr>
</tbody>
</table>

4. Property and Equipment

Property and equipment consist of the following:

| Laboratory furniture, fixtures and equipment | $3,033 | $2,538 |
| Office furniture, fixtures and equipment     | 1,514  | 1,144  |
| Leasehold improvements                        | 422    | 362    |
| Less accumulated depreciation and amortization| (1,977) | (1,081) |
| Total                                         | $2,992 | $2,963 |
5. Accrued Expenses

Accrued expenses consist of the following:

<table>
<thead>
<tr>
<th></th>
<th>December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2005</td>
</tr>
<tr>
<td>Clinical trial and related costs</td>
<td>$1,250</td>
</tr>
<tr>
<td>Sales and marketing</td>
<td>3,596</td>
</tr>
<tr>
<td>Compensation, and related benefits</td>
<td>1,446</td>
</tr>
<tr>
<td>Contracted purchase commitments</td>
<td>1,468</td>
</tr>
<tr>
<td>Other</td>
<td>3,509</td>
</tr>
<tr>
<td>Total</td>
<td>$11,269</td>
</tr>
</tbody>
</table>

6. Long-Term Debt

On June 28, 2005, the Company borrowed (i) $10.0 million from Oxford Finance Corporation (“Oxford”), and (ii) $10.0 million from General Electric Capital Corporation (“GECC”) pursuant to the terms of Promissory Notes (“the Notes”). The Notes bear interest at a fixed rate of 9.95% per annum and are payable in 36 consecutive monthly installments of principal and accrued interest, beginning on July 1, 2005. Also on June 28, 2005, the Company entered into Master Security Agreements with both Oxford and GECC (“the Agreements”). Under terms of these Agreements, the Company granted to both Oxford and GECC a security interest in and against all of the property of the Company and in and against all additions, attachments, accessories and accessions to such property, all substitutions, replacements or exchanges, and all insurance and/or other proceeds (“the Collateral”). The Collateral comprises all of the Company’s personal property and fixtures including, but not limited to, all inventory, equipment, fixtures, accounts, deposit accounts, documents, investment property, instruments, general intangibles, chattel paper and any and all proceeds (but excluding intellectual property). The Collateral does not include any intellectual property or products (or interests in any intellectual property or products (including any royalties)) acquired, whether by purchase, license or otherwise, on or after the execution of the Agreements (collectively, “New Property”), nor do the Agreements limit any indebtedness secured by any New Property provided that debt or non-cash equity (e.g., stock) is used to acquire New Property. In the event that the Company uses cash to purchase New Property, Oxford’s and GECC’s existing liens will extend to such New Property. The Agreements also contain a Material Adverse Change clause with both Oxford and GECC. Under this clause, if Oxford or GECC reasonably determine that the Company’s ability to repay the Notes has been materially impaired, the Company would be considered in default. As of December 31, 2005 the Company was in compliance with this clause.
6. Long-Term Debt (Continued)

The following schedule sets forth the principal payments due as of December 31, 2005:

<table>
<thead>
<tr>
<th>Year</th>
<th>Principal Payments (in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>$6,272</td>
</tr>
<tr>
<td>2007</td>
<td>6,925</td>
</tr>
<tr>
<td>2008</td>
<td>3,728</td>
</tr>
<tr>
<td>Total</td>
<td>$16,925</td>
</tr>
</tbody>
</table>

7. Redeemable Convertible Preferred Stock and Stockholders’ Equity (Deficit)

Stockholders’ Equity (Deficit)

Public Offerings

On November 10, 2003, the Company completed its initial public offering and sold 6,000,000 shares of common stock for $11.00 per share for net proceeds of $60.1 million. In connection with the initial public offering all of the outstanding shares of the Company’s redeemable convertible preferred stock (Series A, B, C, D, E and F), including accrued but unpaid Series E dividends of $6.4 million, converted into 18,398,496 shares of the Company’s common stock based upon the conversion ratios then applicable.

On December 20, 2004, the Company completed a follow-on public offering of its common stock at a price of $24.46 per share. The Company sold an aggregate of 3,579,476 shares of its common stock resulting in gross proceeds of $87.6 million. In connection with the offering, the Company paid $5.3 million in underwriting discounts and commissions and incurred $0.5 million in other offering expenses. After deducting the underwriting discounts and commissions and offering expenses, the Company received net proceeds from the offering of $81.8 million.

Private Offerings

On August 1, 2003, the Company completed the sale of 2,776,347 shares of Series E redeemable convertible preferred stock for net proceeds of $19.9 million. Those shares automatically converted to common stock upon the closing of the Company’s initial public offering of common stock on November 10, 2003. Those shares contained a beneficial conversion feature based on the fair value of the common stock into which the shares were convertible. In accordance with EITF 98-5, Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios, the value of such beneficial conversion feature of $8.3 million was recognized as a deemed dividend in the three month period ended September 30, 2003.

The Series F conversion ratio provided for additional shares of common stock when the Company issued equity securities, as defined, for consideration of less than $14 per share, the purchase price of Series F. As a result of the above sale of these Series E shares, the Series F conversion ratio was increased from 1:1 to 1:1.073364. The adjustment to the Series F conversion ratio is a beneficial conversion feature. In accordance
7. Redeemable Convertible Preferred Stock and Stockholders’ Equity (Deficit) (Continued)

with EITF 00-27, Application of Issue 98-5 to Certain Convertible Instruments, the value of such beneficial conversion feature of $37,000 was recognized as a deemed dividend in the three month period ended September 30, 2003.

Subsequent to the August 2003 sale of the Series E shares, the Series E stockholders and the Company agreed to increase the Series E conversion ratio from 1:1 to 1:1.1526 in consideration of the Series E stockholders waiving their rights to certain anti-dilution provisions. The adjustment to the conversion ratio, which was contingent on the initial public offering, was a beneficial conversion feature. In accordance with EITF 00-27, the value of the Series E beneficial conversion feature of $11.0 million was recognized as a deemed dividend in the period of issuance, which occurred in the fourth quarter of 2003 as a result of the initial public offering. In addition, the conversion of the Series E shares in the initial public offering caused the accrued but unpaid Series E dividends of $6.4 million to become payable through the issuance of 513,033 shares of common stock at the time of the initial public offering.

Stock Purchase Warrants

At December 31, 2005 and 2004, there were stock purchase warrants outstanding to purchase 1,319 and 13,861 shares of common stock, respectively, at exercise prices between $.01 and $.08 per share, which expire through 2007.

Stock Option Plans

The Company's Restated 1993 Equity Incentive Plan (the “1993 plan”) provided for the grant of incentive stock options, nonstatutory stock options and restricted stock awards to purchase up to 2,288,200 shares of common stock. Officers, employees, directors, consultants and advisors of the Company were eligible to be granted options under the 1993 plan at a price not less than 100% (110% in the case of incentive stock options granted to 10% or greater stockholders) of the fair market value of such stock, as determined by the Board of Directors, at the time the option is granted. In May 2003, the Company's stockholders approved the 2003 Stock Incentive Plan (the “2003 Plan”), under which 800,000 shares of common stock were authorized for issuance. In October 2003, the stockholders of the Company approved an amended and restated plan which provided, among other things, for an increase of shares authorized for issuance under the 2003 Plan to 2,500,000. In May 2005, the stockholders of the Company approved an amended plan which provided for an increase of shares authorized for issuance under the 2003 Plan to 3,600,000, and the adoption of a “evergreen provision” that allows for an annual increase in the number of shares of the Company's common stock available for issuance under the 2003 Plan. The evergreen provision provides for an annual increase to be added on the first day of each fiscal year of the Company during the period beginning in fiscal year 2006 and ending on the second day of fiscal year 2013, such increase to be equal to the lesser of (i) 1,400,000 shares of the Company's common stock, (ii) 4% of the outstanding shares on that date or (iii) an amount determined by the Company's board of directors.

While the Company may grant options to employees, which become exercisable at different times or within different periods, the Company generally has granted options to employees that are exercisable in annual installments of 25% each on the first four anniversary dates of the grant.
7. Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit) (Continued)

Information with respect to activity under the 1993 and 2003 Plans is as follows:

<table>
<thead>
<tr>
<th>Stock Option Activity</th>
<th>Number of Options</th>
<th>Weighted-Average Exercise Price Per Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance at December 31, 2002</td>
<td>2,141</td>
<td>$ 1.19</td>
</tr>
<tr>
<td>Options granted</td>
<td>978</td>
<td>5.30</td>
</tr>
<tr>
<td>Options canceled</td>
<td>(3)</td>
<td>1.95</td>
</tr>
<tr>
<td>Options exercised</td>
<td>(217)</td>
<td>0.61</td>
</tr>
<tr>
<td>Balance at December 31, 2003</td>
<td>2,899</td>
<td>2.62</td>
</tr>
<tr>
<td>Options granted</td>
<td>1,129</td>
<td>13.94</td>
</tr>
<tr>
<td>Options canceled</td>
<td>(105)</td>
<td>6.86</td>
</tr>
<tr>
<td>Options exercised</td>
<td>(676)</td>
<td>1.30</td>
</tr>
<tr>
<td>Balance at December 31, 2004</td>
<td>3,247</td>
<td>6.70</td>
</tr>
<tr>
<td>Options granted</td>
<td>984</td>
<td>16.43</td>
</tr>
<tr>
<td>Options canceled</td>
<td>(72)</td>
<td>19.50</td>
</tr>
<tr>
<td>Options exercised</td>
<td>(339)</td>
<td>1.94</td>
</tr>
<tr>
<td>Balance at December 31, 2005</td>
<td>3,820</td>
<td>$ 9.39</td>
</tr>
</tbody>
</table>

The following table summarizes information about options outstanding at December 31, 2005:

<table>
<thead>
<tr>
<th>Range of Exercise Prices</th>
<th>Number of Shares</th>
<th>Weighted-Average Exercise Price</th>
<th>Weighted-Average Remaining Contractual Life (In years)</th>
<th>Number of Shares</th>
<th>Weighted-Average Exercise Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0.08-$2.65</td>
<td>1,360</td>
<td>$ 1.48</td>
<td>4.5</td>
<td>1,074</td>
<td>$ 1.56</td>
</tr>
<tr>
<td>$5.31-$7.96</td>
<td>459</td>
<td>7.09</td>
<td>8.4</td>
<td>114</td>
<td>7.09</td>
</tr>
<tr>
<td>$7.97-$10.62</td>
<td>565</td>
<td>8.52</td>
<td>8.0</td>
<td>241</td>
<td>8.32</td>
</tr>
<tr>
<td>$13.27-$15.92</td>
<td>601</td>
<td>15.00</td>
<td>9.4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>$15.93-$18.58</td>
<td>154</td>
<td>16.62</td>
<td>9.5</td>
<td>1</td>
<td>18.17</td>
</tr>
<tr>
<td>$18.59-$21.23</td>
<td>430</td>
<td>19.29</td>
<td>9.0</td>
<td>66</td>
<td>19.17</td>
</tr>
<tr>
<td>$21.24-$23.88</td>
<td>144</td>
<td>22.74</td>
<td>8.8</td>
<td>31</td>
<td>22.99</td>
</tr>
<tr>
<td>$23.89-$26.54</td>
<td>107</td>
<td>24.69</td>
<td>8.9</td>
<td>25</td>
<td>24.60</td>
</tr>
</tbody>
</table>

Options to purchase 1,277,266 and 1,526,761 shares of common stock were exercisable at December 31, 2004 and 2003, respectively. At December 31, 2005, there were 700,891 options available for future grant in the 2003 Plan and no options available for future grant under the 1993 Plan.

During 1999 and 2000, the Company granted performance-based options to purchase 75,100 and 100,000 shares of common stock, respectively, with an exercise price of $1.30 to certain employees, which allow for acceleration of the vesting period upon the occurrence of certain defined events. Of the 100,000 options granted in 2002, 5,000 options were forfeited in 2002. Based on the terms of the arrangements, the awards are required to be accounted for as variable, and compensation expense is measured as the
7. Redeemable Convertible Preferred Stock and Stockholders’ Equity (Deficit) (Continued)

difference between the fair market value of the Company's common stock at the reporting period date and the exercise price of the award. Compensation expense is recognized over the vesting period. The Company recognized a reversal of stock based compensation expense of ($261,000) for the year ended December 31, 2005, and an expense of $529,000 and $118,000 for the years ended December 31, 2004 and 2003, respectively.

Since 1999, the Company has granted options to purchase a total of 201,000 shares of common stock to nonemployees at a weighted-average exercise price of $3.50 per share, of which 128,750 remained outstanding at December 31, 2005. The Company has applied the recognition provisions of SFAS 123 and EITF 96-18 related to these stock options and utilized the Black-Scholes option pricing model to determine the fair value of these stock options at each reporting date. In connection with these awards, the Company recognized a reversal of stock based compensation expense of ($133,000) for the year ended December 31, 2005 and an expense of $1,011,000 and $185,000 for the years ended December 31, 2004 and 2003, respectively.

During 2003 and 2002, the Company granted options to purchase 413,250 and 241,000 shares of common stock, respectively, to employees at exercise prices below the fair value of the Company’s common stock. The weighted average exercise price of these options is $2.00 per share. The Company recorded deferred stock compensation expense related to these grants of $3,317,000 and $566,000 for the years ended December 31, 2003 and 2002, respectively. These amounts are being recognized as stock-based compensation expense ratably over the vesting period of four years. Included in the results of operations for the years ended December 31, 2005, 2004 and 2003 is stock based compensation expense of $887,000, $982,000 and $604,000, respectively.

Employee Stock Purchase Plan

On August 18, 2003, the Board of Directors adopted the 2003 Employee Stock Purchase Plan (the “Stock Purchase Plan”), which provides for the sale of up to 75,000 shares of common stock to participating employees. Under the Stock Purchase Plan, eligible employees may purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each six month period during the term of the Stock Purchase Plan. Participation in the offering is limited to 10% of the employee’s compensation or $25,000 in any calendar year. The first offering period began on January 1, 2004. During the years ended December 31, 2005 and 2004, the Company issued 37,358 and 30,342 shares of common stock, respectively, under the Stock Purchase Plan.

At December 31, 2005, there were 7,300 shares available for grant under the Stock Purchase Plan.

8. Operating Lease

The Company leased its previous research facilities under an operating lease that expired on September 30, 2004. Annual rent expense was $532,000 for 2004 and $580,000 for 2003. The Company subleased a portion of its premises and recognized rental income of $82,000 in 2003. The sublease agreement ended in 2003.

On January 30, 2004, the Company executed a lease for 52,000 square feet of laboratory and office space in Lexington, Massachusetts. The rent obligation for the building commenced on August 7, 2004,
8. Operating Lease (Continued)

which was 30 days after the date the Company commenced occupancy of the building. The lease is for a term of ten years with options that permit renewals for additional five-year periods. The Company has the option to terminate the lease at the end of the fifth year for a fee of $4.2 million. The expected minimum rental commitments under the lease agreement are $1,425,000, $1,505,000, $1,505,000, $1,566,000, and $1,688,000 for each year in the five calendar year period ending December 31, 2010, respectively, and $6.2 million in total for the remainder of the lease term. In addition to the minimum lease commitment, the lease agreement requires the Company to pay its pro rata share of property taxes and building operating expenses. Rent expense for 2005 and 2004 under this lease was $1.7 million and $0.6 million, respectively. Under the lease, a security deposit of $800,000 is required to be held in escrow for the life of the lease. This amount has been recorded as restricted cash.

9. License, Manufacturing and Commercialization Agreements

The Company has entered into various research, license and commercialization agreements to support its research and development and commercialization activities.

**Boston Scientific Collaboration.** In November 2001, the Company entered into a research, development and license agreement with Boston Scientific in the field of restenosis. The Company granted Boston Scientific an exclusive worldwide license to develop and commercialize nitric oxide-enhancing cardiovascular stents. The Company also granted to Boston Scientific a right of first refusal to obtain an exclusive license under the Company’s nitric oxide technologies to commercialize products for restenosis, which right of first refusal is for a period of three years after the end of the research term. In December 2003, the Company agreed to extend the agreement to continue the research and development collaboration through December 2005. Boston Scientific made an up-front license payment of $1.5 million to the Company in 2001, and made an additional payment of $3.0 million in December 2003 in connection with the extension of the research and development collaboration. The Company had been recognizing the up-front license payment of $1.5 million and $3.0 million extension fee ratably over the term of the contractual performance obligation. For the years ended December 31, 2005, 2004 and 2003, the Company recognized revenue of $1,592,000, $1,592,000 and $442,000, respectively. In the event that specified research, development and commercialization milestones were achieved, Boston Scientific would have been obligated to make milestone payments to the Company. In addition, Boston Scientific also would have been obligated to pay royalties to the Company on the sale of any products resulting from the collaboration. Boston Scientific made a $3.5 million equity investment in the Company’s stock in 2001. In August 2003, in connection with a private placement, Boston Scientific made an additional $500,000 equity investment the Company’s stock. The research term of the Boston Scientific agreement expired on December 31, 2005, although certain rights extend beyond this term.

**Merck Collaboration.** From December 2002 until November 2004, the Company was party to an exclusive, worldwide research, collaboration and licensing agreement that granted Merck a license to certain existing nitric oxide-enhancing COX-2 technology and any technology pertaining to the license technology developed by the Company under this agreement. The research portion of the agreement was for three years, and the Company was obligated to perform certain research and development activities in consideration of quarterly fees totaling $7.2 million. In consideration of this license in 2003, the Company received an upfront non-refundable license payment of $10.0 million, and two payments, each of
9. License, Manufacturing and Commercialization Agreements (Continued)

$5.0 million, for achieving the first two milestones. The license fee revenue and the revenue from the first $5.0 million milestone payment were being recognized ratably over the contractual term of the research and development program, which was expected to end on December 31, 2005. The revenue from the second $5.0 million payment was recognized in the fourth quarter of 2003, the period in which Merck achieved the milestone. On September 30, 2004, Merck halted the phase II trial of the Company’s lead candidate in nitric oxide-enhancing COX-2 inhibitors. This lead nitric oxide candidate is composed of a derivative of rofecoxib. Rofecoxib is the active ingredient in Vioxx, a COX-2 inhibitor which Merck voluntarily withdrew from worldwide markets on September 30, 2004. In November 2004, the Company agreed with Merck to terminate the collaboration agreement. Merck paid the Company a lump sum of $1.8 million, representing the full amount of the research funding owed to the Company for 2005, however, the Company will not receive any commercialization milestones or royalty payments from Merck. As a result of the termination of this agreement, the Company accelerated the recognition of deferred license revenue of $5.3 million in the fourth quarter of 2004, and the Company recognized the lump sum payment of $1.8 million as revenue in the fourth quarter of 2004. Under this agreement the Company recognized revenue of $14.9 million and $12.3 million for the years ended December 31, 2004 and 2003, respectively.

Dr. Jay N. Cohn. In January 1999, as amended in January 2001 and March 2002, the Company entered into a collaboration and license agreement with Dr. Jay N. Cohn. Under the agreement, Dr. Cohn licensed to the Company an exclusive worldwide royalty-bearing rights to technology and inventions owned or controlled by Dr. Cohn and that relate to BiDil for the treatment of cardiovascular disease. Upon achieving certain developmental events, the Company was required to make milestone payments totaling $1.0 million, which were recorded as a charge to research and development expenses in 2004. Upon commercial sale of BiDil, the Company is required to make royalty payments based on net sales at varying rates depending on sales volume. The royalty terms expires upon the later of the expiration of the patent rights or ten years from the first commercial sale. The agreement imposes upon the Company an obligation to use reasonable best efforts to develop and, upon receipt of regulatory approval, manufacture, market and commercialize products based upon the licensed rights. If the Company fails to meet this obligation, Dr. Cohn has the right to terminate the agreement and the license granted to the Company under the agreement. Dr. Cohn also has the right to terminate the agreement if the Company materially breaches the agreement and fails to remedy the breach within 30 days. The Company has the right to terminate the agreement at any time upon 30 days’ prior written notice. Unless earlier terminated, the agreement continues in perpetuity. Pursuant to the agreement, Dr. Cohn was appointed to the Company’s scientific advisory board (which in 2006 has been replaced by the technical review committee of which Dr. Cohn is not a member), entered into a consulting agreement with the Company and was granted an option to purchase 10,000 shares of the Company’s common stock.
10. Income Taxes

A reconciliation of federal statutory income tax provision to the Company’s actual provision is as follows:

<table>
<thead>
<tr>
<th>Year Ended December 31</th>
<th>2005</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit at federal statutory tax rate</td>
<td>$(35,990)</td>
<td>$(10,123)</td>
<td>$(2,982)</td>
</tr>
<tr>
<td>State taxes, net of federal benefit</td>
<td>(6,637)</td>
<td>(1,867)</td>
<td>(550)</td>
</tr>
<tr>
<td>Non-deductible expenses</td>
<td>254</td>
<td>157</td>
<td>357</td>
</tr>
<tr>
<td>Unbenefited operating losses</td>
<td>42,373</td>
<td>11,833</td>
<td>3,175</td>
</tr>
<tr>
<td>Income tax provision</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

The significant components of the Company’s deferred tax assets are as follows:

<table>
<thead>
<tr>
<th>December 31</th>
<th>2005</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deferred tax assets:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Net operating loss carryforwards</td>
<td>$59,805</td>
<td>$20,724</td>
</tr>
<tr>
<td>Capitalized research costs, net of amortization</td>
<td>24,991</td>
<td>18,908</td>
</tr>
<tr>
<td>Tax credit carryforwards</td>
<td>6,245</td>
<td>5,807</td>
</tr>
<tr>
<td>Deferred revenue</td>
<td>1</td>
<td>641</td>
</tr>
<tr>
<td>Depreciation</td>
<td>(29)</td>
<td>409</td>
</tr>
<tr>
<td>Accrued expenses</td>
<td>991</td>
<td>1,600</td>
</tr>
<tr>
<td>Other</td>
<td>146</td>
<td>31</td>
</tr>
<tr>
<td>Valuation allowance</td>
<td>(92,150)</td>
<td>(48,120)</td>
</tr>
<tr>
<td>Net deferred tax assets</td>
<td>$—</td>
<td>$—</td>
</tr>
</tbody>
</table>

The Company has increased its valuation allowance by $44,030,000 in 2005 to provide a full valuation allowance for deferred tax assets since the realization of these benefits is not considered more likely than not. At December 31, 2005, the Company had unused net operating loss carryforwards of $151,132,000 available to reduce federal taxable income expiring in 2010 through 2025 and $134,291,000 available to reduce state taxable income expiring in 2006 through 2010. The Company also has federal and state research tax credits of $7,279,000 available to offset federal and state income taxes, both of which expire beginning in 2010. The net operating losses and tax credit carryforwards may be subject to the annual limitation provisions of Internal Revenue Code (IRC) Sections 382 and 383. No income tax payments were made in 2005, 2004 or 2003.

11. Commitments and Contingencies

In connection with the Company’s efforts to obtain the approval of BiDil from the FDA, the Company contracted with the law firm of FoxKiser LLC (FoxKiser) for services related to the regulatory approval process for BiDil. The agreement provided for payment of legal consulting fees upon receipt of written FDA approval of BiDil. In addition, the agreement requires the Company to pay royalties to FoxKiser on commercial sales of BiDil. The royalty term ends six months after the date of market introduction of an
11. Commitments and Contingencies (Continued)

FDA-approved generic version of BiDil. During the third quarter of 2005, the Company entered into a separate consulting agreement with FoxKiser following the approval by the FDA of BiDil. During the years ended December 31, 2005 and 2004, the Company recorded charges of $1.6 and $1.9 million, respectively, pertaining to the legal consulting fees related to these agreements. On June 23, 2005, the Company received written FDA approval of BiDil, and in July 2005, the Company paid $2.4 million pursuant to the terms of these agreements.

An academic institution has asserted that patents and patent applications which relate to the nitric oxide stent program may require a license from such institution. It is the opinion of the Company’s management and outside legal counsel that the disputed intellectual property has been validly licensed to, or is validly owned by, the Company. Accordingly, the accompanying financial statements do not include any provision related to this claim.

On July 20, 2004, the Market Regulation Department of the National Association of Securities Dealers, Inc. (“NASD”) advised the Company that it initiated a review of trading activity in the Company’s common stock surrounding the Company’s July 19, 2004, announcement that it had halted its phase III clinical trial of BiDil due to the significant survival benefit seen with BiDil. The NASD is reviewing, among other things, information on relationships between the Company’s officers, directors and service providers and individuals and institutions that may have traded in the Company’s common stock prior to the July 19, 2004 announcement. The Company has cooperated with this review and has identified certain persons on the list provided to the Company by the NASD as having a relationship with the Company’s chief executive officer and others at the Company. The Company has established a special committee of its board of directors to oversee the Company’s response to this review. The Company is presently unable to predict the outcome of this matter or the timing of its resolution.

In November 2004, as amended in May 2005, the Company executed an agreement with Publicis Selling Solutions, Inc. (Publicis), a contract sales organization, pursuant to which, on the Company’s behalf, Publicis has employed and trained a specialty sales force currently consisting of approximately 144 sales representatives to sell BiDil to the Company’s target prescriber markets. The agreement is for a current term of 24 months beginning on January 31, 2005, with the Company’s option to continue the agreement beyond this term. Year one costs recorded in 2005 were $29.8 million, excluding one-time start-up costs, and year two costs under the agreement are projected at approximately $24.3 million. The Company has the right to terminate this agreement upon 90 days written notice to Publicis. If the Company had terminated this agreement during the period between January 31, 2005 and January 30, 2006, the Company would have been required to pay a termination fee in the amount of $1.0 million. If the Company were to terminate during the period between January 31, 2006 and July 31, 2006, the termination fee will be $750,000. If the Company terminates the agreement after July 31, 2006, Publicis is not eligible for a termination fee.

On February 16, 2005, the Company engaged Schwarz Pharma Manufacturing, Inc. (“Schwarz Pharma”) under a five-year exclusive manufacturing and supply agreement solely for the three times daily immediate release dosage formulation of BiDil. Under the supply agreement, the Company has the right to engage a backup manufacturer. In connection with this supply agreement, the Company placed binding purchase orders of $1.1 million and $1.3 million for production of BiDil finished goods during the first and second quarters of 2006, respectively.
12. Retirement Plan

The Company sponsors a 401(k) plan covering substantially all employees. The plan provides for salary deferral contributions by participants of up to 75% of eligible wages not to exceed Federal requirements. Those employees over 50 years old are permitted to contribute an additional amount per Federal limits ($4,000 per year for 2005). In October 2005, the Board of Directors approved an employee match in the form of Company Common Stock equal to 50% of employee contributions, limited to the first 6% of salary contributed to the 401(k) plan. For the year ended December 31, 2005, the Company recorded expenses of $88,000 related to the plan.

13. Related Party Transactions - Boston University

Dr. Joseph Loscalzo, a member of the Company’s board of directors, is the Physician-in-Chief and Chair of the Department of Medicine at Brigham and Women’s Hospital in Boston, Massachusetts. Dr. Loscalzo has served as a consultant to the Company since 1992, as the chair of the Company’s scientific advisory board since 1999 and currently is the chair of the Company’s technical review committee, which replaced the Company’s scientific review board at the beginning of fiscal year 2006. In October 2003, the Company entered into a consulting agreement with Dr. Loscalzo, as amended in April 2004, pursuant to which the Company agreed to pay Dr. Loscalzo an annual retainer of $55,000 for his services. The agreement is for a period of ten years, subject to the Company’s right to terminate the agreement at any time on 30 days’ notice. In 2005 and 2004, the Company paid Dr. Loscalzo an aggregate of $68,000 and $75,000, respectively.

In June 1993, as amended in July 1997, January 1999 and December 2002, the Company entered into a research and license agreement with the Trustees of Boston University (“BU”). Under the agreement, the Company agreed to fund a multi-year research program under Dr. Loscalzo’s direction at BU in the area of nitric oxide-enhancing medicines. The Company’s funding is principally for laboratory equipment and supplies as well as a portion of the salary of Martin Feelish, Ph.D., a professor of medicine at BU and a member of the Company’s scientific advisory board (which was replaced at the beginning of 2006 by the technical review committee of which Dr. Feelish is not a member). The Company has also agreed to provide Dr. Feelish with access to the Company’s research facilities at the BU School of Medicine. Under the agreement, in exchange for the Company’s sponsored research funding, BU has granted the Company exclusive worldwide royalty-bearing rights to technology and inventions owned by BU at the effective time of, or developed in the course of, the sponsored research program. The Company has agreed to pay royalties to BU on all products sold or distributed by the Company or its affiliates that incorporate or utilize inventions, material or information specified in the agreement. In 2005, 2004 and 2003, the Company made payments to BU of $120,000, $221,500 and $265,000, respectively, pursuant to this agreement, excluding the lease payments described below.

In May 2003, the Company entered into an oral agreement with BU pursuant to which the Company leases approximately 1,500 square feet of laboratory space from BU at its Evans Biomedical Research Center in Boston, Massachusetts. The lease has a term of three years, and the Company makes annual rental payments of $60,000 pursuant to the lease. As provided above, the Company has agreed to make this space available to Dr. Feelish of BU. In 2005 and 2004, the Company made payments to BU under this agreement of $60,000.
14. Quarterly Results of Operations (Unaudited)

The following table presents unaudited quarterly financial data of the Company:

<table>
<thead>
<tr>
<th>Year Ended December 31, 2005</th>
<th>First Quarter</th>
<th>Second Quarter</th>
<th>Third Quarter</th>
<th>Fourth Quarter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net revenues</td>
<td>$398</td>
<td>$398</td>
<td>$1,515</td>
<td>$3,736</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(19,589)</td>
<td>$(22,624)</td>
<td>$(32,072)</td>
<td>$(31,567)</td>
</tr>
<tr>
<td>Basic and diluted net loss per share</td>
<td>$(0.65)</td>
<td>$(0.75)</td>
<td>$(1.05)</td>
<td>$(1.04)</td>
</tr>
<tr>
<td>Weighted average common shares used to compute net loss per share</td>
<td>30,234</td>
<td>30,275</td>
<td>30,421</td>
<td>30,486</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year Ended December 31, 2004</th>
<th>First Quarter</th>
<th>Second Quarter</th>
<th>Third Quarter</th>
<th>Fourth Quarter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net revenues</td>
<td>$2,331</td>
<td>$2,331</td>
<td>$2,332</td>
<td>$9,464</td>
</tr>
<tr>
<td>Net loss</td>
<td>$(4,556)</td>
<td>$(4,700)</td>
<td>$(10,801)</td>
<td>$(9,716)</td>
</tr>
<tr>
<td>Basic and diluted net loss per share</td>
<td>$(0.18)</td>
<td>$(0.18)</td>
<td>$(0.41)</td>
<td>$(0.36)</td>
</tr>
<tr>
<td>Weighted average common shares used to compute net loss per share</td>
<td>25,601</td>
<td>25,696</td>
<td>26,187</td>
<td>27,115</td>
</tr>
</tbody>
</table>
ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND
FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

(a) Evaluation of Disclosure Controls and Procedures. Our management, with the participation of our
chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and
procedures as of December 31, 2005. The term “disclosure controls and procedures,” as defined in
Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a
company that are designed to ensure that information required to be disclosed by a company in the reports
that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within
the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include,
without limitation, controls and procedures designed to ensure that information required to be disclosed
by a company in the reports that it files or submits under the Exchange Act is accumulated and
communicated to the company’s management, including its principal executive and principal financial
officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes
that any controls and procedures, no matter how well designed and operated, can provide only reasonable
assurance of achieving their objectives and management necessarily applies its judgment in evaluating the
cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure
controls and procedures as of December 31, 2005, our chief executive officer and chief financial officer
concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable
assurance level.


Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over
financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or
15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the
company’s principal executive and principal financial officers and effected by the company’s board of
directors, management and other personnel, to provide reasonable assurance regarding the reliability of
financial reporting and the preparation of financial statements for external purposes in accordance with
generally accepted accounting principles and includes those policies and procedures that:

• Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the
transactions and dispositions of the assets of the company;
• Provide reasonable assurance that transactions are recorded as necessary to permit preparation of
financial statements in accordance with generally accepted accounting principles, and that receipts
and expenditures of the company are being made only in accordance with authorizations of
management and directors of the company; and
• Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition,
use or disposition of the company’s assets that could have a material effect on the financial
statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect
misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that
controls may become inadequate because of changes in conditions, or that the degree of compliance with
the policies or procedures may deteriorate.
Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2005. In making this assessment, the company's management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on this assessment, our management concluded that, as of December 31, 2005, our internal control over financial reporting is effective based on those criteria.

Our independent auditors have issued an audit report on our assessment of our internal control over financial reporting. This report appears below.
Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
NitroMed, Inc.

We have audited management’s assessment, included in the accompanying Management’s Report on Internal Control Over Financial Reporting, that NitroMed, Inc. maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). NitroMed, Inc.’s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management’s assessment and an opinion on the effectiveness of the company’s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management’s assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company’s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management’s assessment that NitroMed, Inc. maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, NitroMed, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of NitroMed, Inc. as of December 31, 2005 and 2004, and the related statements of operations, redeemable convertible preferred stock and stockholders’ equity (deficit), and cash flows for each of the three years in the period ended December 31, 2005 of NitroMed, Inc. and our report dated February 28, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 28, 2006
(c) **Changes in Internal Controls.**

No change in our internal control over financial reporting occurred during the fiscal year ending December 31, 2005 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

**PART III**

**ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT**

Directors and Executive Officers

Information regarding our directors and executive officers may be found under the captions “Election of Directors” and “Executive Officers” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

Audit Committee

We have a separately-designated standing Audit Committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Additional information regarding the Audit Committee may be found under the captions “Board of Directors Meetings and Committee Meetings” and “Report of the Audit Committee” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

Audit Committee Financial Expert

The Board of Directors has determined that it has at least one “Audit Committee Financial Expert” (as defined by Item 401(h)(2) of Regulation S-K of the Exchange Act) on the Audit Committee of the Board of Directors, Davey S. Scoon. The Board of Directors has further determined that Mr. Scoon is “independent” from management within the meaning of Item 7(d)(3)(iv) of Schedule 14A under the Exchange Act.

**Section 16(a) Beneficial Ownership Reporting Compliance**

Information regarding Section 16(a) Beneficial Ownership Reporting Compliance may be found under the caption “Section 16(a) Beneficial Ownership Reporting Compliance” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

**Code of Business Conduct and Ethics**

We have adopted a code of business conduct and ethics, which applies to all of our officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Our code of business conduct and ethics was filed with the SEC as an exhibit to our annual report on Form 10-K for the fiscal year ended December 31, 2003. In addition, we intend to post on our website, which is located at www.nitromed.com, all disclosures that are required by law or NASDAQ Stock Market listing standards concerning any amendments to, or waivers from, any provision of our code of business conduct and ethics.
ITEM 11. EXECUTIVE COMPENSATION

Information with respect to this item may be found under the captions “Directors’ Compensation,” “Compensation Committee Interlocks and Insider Participation,” “Executive Compensation,” and “Employment Agreements,” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Information with respect to this item may be found under the caption “Security Ownership of Certain Beneficial Owners and Management” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Information with respect to this item may be found under the caption “Certain Relationships and Related Transactions” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information with respect to this item may be found under the caption “Audit Fees” in the Proxy Statement for our 2006 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

PART IV
ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) Financial Statements.

For a list of the financial information included herein, see “Index to Financial Statements” on page 56.

(a)(2) Financial Statement Schedules.

All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or Notes thereto.

(a)(3) Exhibits. The list of Exhibits filed as a part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding such Exhibits, and is incorporated herein by this reference.
SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned.

NITROMED, INC.

Date: February 28, 2006

By: /s/ Michael D. Loberg, Ph.D.
   Michael D. Loberg, Ph.D.
   President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this report has been signed by the following persons in the capacities and on the dates indicated.

<table>
<thead>
<tr>
<th>Signature</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>/s/ Michael D. Loberg, Ph.D.</td>
<td>President and Chief Executive Officer and Director (Principal Executive Officer)</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Lawrence E. Bloch, M.D., J.D.</td>
<td>Chief Financial Officer, Chief Business Officer, Treasurer and Secretary (Principal Financial Officer)</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ James G. Ham, III</td>
<td>Vice President of Finance (Principal Accounting Officer)</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Robert S. Cohen</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Frank L. Douglas, M.D., Ph.D.</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Zola Horovitz, Ph.D.</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Argeris Karabelas, Ph.D.</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Mark Leschly</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ John W. Littlechild</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Joseph Loscalzo, M.D., Ph.D.</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>/s/ Davey S. Scoon</td>
<td>Director</td>
<td>February 28, 2006</td>
</tr>
<tr>
<td>Exhibit No.</td>
<td>Description</td>
<td></td>
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<tr>
<td>------------</td>
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<td></td>
</tr>
<tr>
<td>3.1(1)</td>
<td>Restated Certificate of Incorporation of the Company</td>
<td></td>
</tr>
<tr>
<td>3.2(1)</td>
<td>Amended and Restated Bylaws of the Company</td>
<td></td>
</tr>
<tr>
<td>*10.1(1)</td>
<td>Restated 1993 Equity Incentive Plan</td>
<td></td>
</tr>
<tr>
<td>*10.2(1)</td>
<td>Amended and Restated 2003 Stock Incentive Plan</td>
<td></td>
</tr>
<tr>
<td>*10.3(1)</td>
<td>2003 Employee Stock Purchase Plan</td>
<td></td>
</tr>
<tr>
<td>10.4†(1)</td>
<td>Development and License Agreement between the Company and Boston Scientific Corporation dated November 20, 2001</td>
<td></td>
</tr>
<tr>
<td>10.5†(1)</td>
<td>Research and License Agreement between the Company and Brigham and Women’s Hospital, Inc. dated August 1, 1992, as amended November 22, 1996</td>
<td></td>
</tr>
<tr>
<td>10.7(4)</td>
<td>Amendment No. 1 to Collaboration and License Agreement between the Company and Professor Jay N. Cohn dated August 10, 2000</td>
<td></td>
</tr>
<tr>
<td>10.8†(1)</td>
<td>Research and License Agreement between the Company and Trustees of Boston University dated June 1, 1993, as amended January 1, 1999</td>
<td></td>
</tr>
<tr>
<td>10.9†(1)</td>
<td>Agreement between the Company and FoxKiser dated April 26, 2001</td>
<td></td>
</tr>
<tr>
<td>10.11†(1)</td>
<td>Professional Service Agreement between the Company and MIMC, Inc. dated May 1, 2001, as amended</td>
<td></td>
</tr>
<tr>
<td>10.16(1)</td>
<td>Form of Warrant to purchase shares of the Company’s Common Stock, together with a schedule of warrant holders</td>
<td></td>
</tr>
<tr>
<td>10.17(2)</td>
<td>Lease between the Company and PM Atlantic Lexington, LLC dated January 30, 2004</td>
<td></td>
</tr>
<tr>
<td>10.18(2)</td>
<td>Letter Agreement between the Company, Boston University School of Medicine and Martin Feelisch, Ph.D. dated May 5, 2003</td>
<td></td>
</tr>
<tr>
<td>10.19(4)</td>
<td>Consulting Agreement between the Company and Joseph Loscalzo, M.D., Ph.D. dated October 27, 2003, as amended on April 1, 2004</td>
<td></td>
</tr>
<tr>
<td>10.120†(3)</td>
<td>Professional Detailing Services Agreement between the Company and Publicis Selling Solutions, Inc. dated November 4, 2004</td>
<td></td>
</tr>
<tr>
<td>10.21(3)</td>
<td>Letter Agreement between the Company and Merck Frosst Canada &amp; Co. dated November 8, 2004</td>
<td></td>
</tr>
<tr>
<td>*10.22(4)</td>
<td>Letter Agreement between the Company and James G. Ham, III dated September 3, 2004</td>
<td></td>
</tr>
</tbody>
</table>
*10.23(4) Letter Agreement between the Company and Lawrence E. Bloch dated August 30, 2004
10.24†(4) Supply Agreement between the Company and Schwarz Pharma Manufacturing, Inc. dated as of February 16, 2005
*10.25(4) Letter Agreement between the Company and Mark Pavao dated June 30, 2004
*10.27 Base Salaries of Named Executive Officers of the Company
*10.28 Compensation of Directors of the Company
*10.29(4) Form of Incentive Stock Option Agreement Granted Under Amended and Restated 2003 Stock Incentive Plan
*10.30(4) Form of Nonstatutory Stock Option Agreement Granted Under Amended and Restated 2003 Stock Incentive Plan
14.1(2) Code of Business Conduct and Ethics
21.1 Subsidiaries of the Company
23.1 Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
31.1 Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14 of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2 Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14 of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1 Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2 Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Management contract or compensation plan or arrangement required to be filed as an exhibit pursuant to Item 15(c) of Form 10-K
† Confidential treatment requested as to certain portions, which portions have been filed separately with the Securities and Exchange Commission

(1) Incorporated by reference to the exhibits to the Company’s Registration Statement on Form S-1 (File No. 333-108104)

(2) Incorporated by reference to the exhibits to the Company’s Annual Report on Form 10-K for the year ended December 31, 2003 (File No. 000-50439).

(3) Incorporated by reference to the exhibits to the Company’s Current Report on Form 8-K filed on November 8, 2004 (File No. 000-50439).

(4) Incorporated by reference to the exhibits to the Company’s Annual Report on Form 10-K for the year ended December 31, 2004 (File No. 000-50439)

(5) Incorporated by reference to the exhibits to the Company’s Current Report on Form 8-K filed on November 12, 2005 (File No. 000-50439).
CERTIFICATION

I, Michael D. Loberg, certify that:

1. I have reviewed this annual report on Form 10-K of NitroMed, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of registrant’s board of directors (or persons performing the equivalent functions):
   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and
   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Dated: February 28, 2006

/s/ MICHAEL D. LOBERG, PH.D.
Michael D. Loberg, Ph.D.
Chief Executive Officer and President
(Principal Executive Officer)
CERTIFICATION

I, Lawrence E. Bloch, certify that:

1. I have reviewed this annual report on Form 10-K of NitroMed, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant’s other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c) Evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d) Disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter (the registrant’s fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant’s other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):
   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and
   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Dated: February 28, 2006

/s/ Lawrence E. Bloch, M.D., J.D.
Lawrence E. Bloch, M.D., J.D.
Chief Financial Officer, Chief Business Officer,
Treasurer and Secretary
(Principal Financial Officer)
CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of NitroMed, Inc. (the “Company”) for the fiscal year ended December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, Michael D. Loberg, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 28, 2006 /s/ Michael D. Loberg, Ph.D.
Michael D. Loberg, Ph.D.
Chief Executive Officer and President
CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of NitroMed, Inc. (the “Company”) for the fiscal year ended December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, Lawrence E. Bloch, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 28, 2006

/s/ Lawrence E. Bloch, M.D., J.D.
Lawrence E. Bloch, M.D., J.D.
Chief Financial Officer, Chief Business Officer,
Treasurer and Secretary
MANAGEMENT TEAM

ARGERIS (JERRY) N. KARABELAS, Ph.D.
Chairman and interim Chief Executive Officer

KENNETH M. BATE
Chief Operating Officer and Chief Financial Officer

L. GORDON LETTS, Ph.D.
Chief Scientific Officer and Senior Vice President, Research and Development

MICHAEL L. SABOLINSKI, M.D.
Chief Medical Officer

MARK H. PAVAO
Senior Vice President Sales and Marketing

GERALD W. BRUCE
Vice President Sales

JAMES G. HAM, III
Vice President Finance

WILLIAM “BJ” JONES
Vice President Marketing

LISA KELLY
Vice President Human Resources

JANE A. KRAMER
Vice President Corporate Communications

WELTON O’NEAL, JR., PHARM.D.
Vice President Medical Affairs

BOARD OF DIRECTORS

ARGERIS (JERRY) N. KARABELAS, Ph.D.
Chairman of the Board and interim Chief Executive Officer, NitroMed, Inc.
Partner, Care Capital LLC

JOSEPH LOSCALZO, M.D., Ph.D.
Chairman, Department of Medicine, Physician-in-Chief, Brigham and Women’s Hospital

ROBERT S. COHEN
Consultant

FRANK L. DOUGLAS, M.D., Ph.D.
Executive in Residence at the Sloan School of Management, Massachusetts Institute of Technology

ZOLA HOROVITZ, Ph.D.
Consultant

MARK LESCHLY
Managing Partner, Rho Capital Partners

JOHN W. LITTLECHILD
General Partner, HealthCare Ventures LLC

DAVEY S. SCOON, C.P.A.
Non-Executive Chairman of the Board, Tufts Health Plan

CORPORATE INFORMATION

Corporate Headquarters
NitroMed, Inc.
125 Spring Street
Lexington, MA 02421

Independent Registered Public Accounting Firm
Ernst & Young LLP
200 Clarendon Street
Boston, MA 02116

Legal Counsel
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109

Transfer Agent
American Stock Transfer & Trust Company
40 Wall Street, 46th Floor
New York, NY 10005
(800) 937-5449

Stock Listing
NitroMed’s common stock is traded on the Nasdaq National Market under the symbol NTMD.

Web Site
www.nitromed.com

NitroMed’s Annual Report on Form 10-K, as filed with the Securities and Exchange Commission for the fiscal year ended December 31, 2005, which contains important information about NitroMed, is available free of charge upon written request to:

NitroMed, Inc.
Investor Relations
125 Spring Street
Lexington, MA 02421

FORWARD-LOOKING STATEMENTS

This annual report contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding our expectations concerning market acceptance and potential of BiDil®, our ability to commercialize, market and sell BiDil successfully, including our ability to improve managed care reimbursement, effectively internalize the BiDil sales force and enter into partnering and/or co-promotion programs for BiDil, our plans to formulate and commercialize an extended release formulation of BiDil, as well as other plans and objectives for future operations stated herein. We may, in some cases, use words such as “believe,” “expect,” “anticipate,” “plan,” “estimate” and similar expressions to identify these forward-looking statements.

There are a number of important factors that could cause our actual results to differ materially from those indicated by our forward-looking statements, including: uncertainties related to patient, physician and third-party payor acceptance of BiDil® as a safe and effective therapeutic; our ability to successfully execute on our commercialization, marketing and sales strategies for BiDil, including our ability to obtain preferential reimbursement treatment and, if obtained, its impact, if any, on sales; our ability to effectively and efficiently internalize our contract sales force within the time frame expected, if at all, and our ability to successfully negotiate and enter into partnering or co-promotion opportunities; our ability to successfully develop, obtain regulatory approval for and commercialize new formulations of BiDil; our ability to achieve the cost reductions anticipated by our business strategies, including our research and development restructuring and the planned monetization or out-licensing of non-strategic assets; our ability to obtain the substantial additional funding required to continue our commercialization efforts with respect to BiDil® and other factors discussed in our Annual Report on Form 10-K for the year ended December 31, 2005. We disclaim any intention or obligation to update any forward-looking statements as a result of developments occurring after the date such statement was first made.