BIOCRYST PHARMACEUTICALS INC

FORM 10-K
(Annual Report)

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Industry	Biotechnology & Drugs
Sector	Healthcare
Fiscal Year	12/20

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

FORM 10-K

☒ **Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
For the fiscal year ended December 31, 2005

OR

☐ **Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934.**

For the transition period from _____ to _____.

Commission File Number 000-23186

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

DELAWARE	**62-1413174**
(State of other jurisdiction of incorporation or organization)	**(I.R.S. employer identification no.)**

2190 Parkway Lake Drive; Birmingham, Alabama 35244
(Address of principal executive offices)

(205) 444-4600
(Registrant's telephone number, including area code)

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

Title of each class	**Name of each exchange on which registered**
None	**None**

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

Title of each class
Common Stock, $.01 Par Value

Indicate by a check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☐ No☒ .

Indicate by a check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes ☐ No☒ .

Indicate by a 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) 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 a 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 a check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2).

Yes ☐ No☒ .

The Registrant estimates that the aggregate market value of the Common Stock on June 30, 2005 (based upon the closing price shown on the Nasdaq National Market on June 30, 2005) held by non-affiliates was approximately $78,374,464. For this computation, the Registrant has excluded the market value of all shares of its Common Stock reported as beneficially owned by officers, directors and certain significant stockholders of the Registrant. Such exclusion shall not be deemed to constitute an admission that any such stockholder is an affiliate of the Registrant.

The number of shares of Common Stock, par value $.01, of the Registrant outstanding as of March 3, 2006 was 28,980,228 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive Proxy Statement to be filed in connection with the solicitation of proxies for its 2006 Annual Meeting of Stockholders are incorporated by reference into Items 10, 11, 12, 13 and 14 under Part III hereof.

PART I

ITEM 1. BUSINESS

Forward-Looking Statements and Risk Factors

This report includes forward-looking statements. In particular, statements about our expectations, beliefs, plans, objectives or assumptions of future events or performance are contained or incorporated by reference in this report. We have based these forward-looking statements on our current expectations about future events. While we believe these expectations are reasonable, forward-looking statements are inherently subject to risks and uncertainties, many of which are beyond our control. Our actual results may differ materially from those suggested by these forward-looking statements for various reasons, including those discussed in this report under the heading "Risk Factors" beginning at page 19. Given these risks and uncertainties, you are cautioned not to place undue reliance on forward-looking statements. The forward-looking statements included in this report are made only as of the date hereof. We do not undertake and specifically decline any obligation to update any of these statements or to publicly announce the results of any revisions to any forward looking statements to reflect future events or developments. When used in the report, unless otherwise indicated, "we," "our" and "us" refers to BioCryst Pharmaceuticals, Inc.

Overview

BioCryst Pharmaceuticals, Inc. a biotechnology company that designs, optimizes and develops novel drugs that block key enzymes involved in cancer, cardiovascular diseases, autoimmune diseases, and viral infections. BioCryst integrates the necessary disciplines of biology, crystallography, medicinal chemistry and computer modeling to effectively use structure-based drug design to discover and develop small molecule pharmaceuticals.

Our lead product candidate, Fodosine™, is a transition-state analog inhibitor of the target enzyme purine nucleoside phosphorylase ("PNP"). The compound is currently in a Phase IIa trial for patients with T-cell leukemia and a combination IV and oral Phase I pharmacokinetic trial in healthy volunteers was recently completed. We are negotiating a special protocol assessment ("SPA") with the U.S. Food and Drug Administration ("FDA") for a planned pivotal Phase IIb trial in relapsed or refractory T-cell leukemia patients. Additionally, Fodosine™ is currently being studied in a Phase I trial with an oral formulation in cutaneous T-cell lymphoma ("CTCL"), a Phase II trial in chronic lymphocytic leukemia ("CLL") and a Phase I/II trial in B-cell acute lymphoblastic leukemia ("B-ALL"). Fodosine™ has been granted Orphan Drug status by the FDA for three indications: T-cell non-Hodgkin's lymphoma, including CTCL; CLL and related leukemias including T-cell prolymphocytic leukemia, adult T-cell leukemia, and hairy cell leukemia; and for treatment of B-ALL. Additionally the FDA has granted "fast track" status to the development of Fodosine™ for the treatment of relapsed or refractory T-cell leukemia. In February 2006, we announced an exclusive licensing agreement with Mundipharma International Holdings Limited ("Mundipharma") to develop and commercialize Fodosine™ in markets across Europe, Asia and Australasia for use in oncology.

In August 2005, BioCryst initiated a Phase Ib study with its second-generation PNP inhibitor, BCX-4208, to evaluate the safety, tolerability and pharmacokinetics of multiple oral doses of BCX-4208. In November 2005, we entered into an exclusive worldwide licensing agreement with F.Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. ("Roche") to develop and commercialize BCX-4208 for the prevention of acute rejection in transplantation and for the treatment of autoimmune diseases.

Additionally, BioCryst has re-initiated clinical development of peramivir, an inhibitor of influenza neuraminidase, with a focus on intravenous and intramuscular delivery. Also, BioCryst has identified a clinical candidate, BCX-4678, in its hepatitis C polymerase inhibitor program, and is advancing that compound through preclinical testing with the goal of filing an investigational new drug application ("IND") and, if the IND becomes effective, commencing clinical trials in 2006.

BioCryst is a Delaware corporation originally founded in 1986. Our principal offices are located at 2190 Parkway Lake Drive, Birmingham, Alabama 35244, and our telephone number is (205) 444-4600. For more information about BioCryst, please visit our website at http://www.biocryst.com. The information on our website is not incorporated into this Form 10-K.

Our Business Strategy

Our business strategy is to use structure-based drug design technologies to develop innovative, small-molecule pharmaceuticals to treat a variety of diseases and disorders. We focus our drug development efforts on building potent, selective inhibitors of enzymes associated with targeted diseases. Enzymes are proteins that cause or enable biological reactions necessary for the progression of the disease or disorder. The specific enzymes on which we focus are called enzyme targets. We aim to design compounds that will inhibit an enzyme target by fitting the active site of a particular enzyme. Inhibition means interfering with the functioning of an enzyme target, thereby stopping or slowing the progression of the disease or disorder. The principal elements of our strategy are:

- ***Select and License Promising Enzyme Targets for the Development of Small-Molecule Pharmaceuticals.*** We use our technical expertise and network of academic and industry contacts to evaluate and select promising enzyme targets to license for the development of small-molecule pharmaceuticals. We choose enzyme targets that meet as many of the following criteria as possible:
  - serve important functions in disease pathways;
  - have known animal or cell-based models that would be indicative of results in humans;
  - address large potential markets and significant unmet medical needs, including pursuing niche markets where the results have potential application to broader markets and needs;
  - have multiple potential clinical applications; and
  - offer rapid development and commercialization opportunities.
- ***Focus on High Value-Added Structure-Based Drug Design Technologies.*** We focus our drug discovery activities and expenditures on applications of structure-based drug design technologies to design and develop drug candidates. Structure-based drug design is a process by which we design a drug candidate through detailed analysis of the enzyme target, which the drug candidate must inhibit in order to stop the progression of the disease or disorder. We believe that structure-based drug design is a powerful tool for efficient development of small-molecule drug candidates that have the potential to be safe, effective and relatively inexpensive to manufacture. Our structure-based drug design technologies typically allow us to design and synthesize multiple drug candidates that inhibit the same enzyme target. We believe this strategy can lead to broad patent protection and enhance the competitive advantages of our compounds.
- ***Develop or License Inhibitors that are Promising Candidates for Commercialization.*** We test multiple compounds to identify those that are most promising for clinical development. We base our selection of promising development candidates on desirable product characteristics, such as initial indications of safety and efficacy. We believe that this focused strategy allows us to eliminate unpromising candidates from consideration sooner without incurring substantial clinical costs. In addition, we select drug candidates on the basis of their potential for relatively efficient Phase I and Phase II clinical trials that require fewer patients to initially indicate safety and efficacy. We will consider, however, more complex candidates with longer development cycles if we believe that they offer promising commercial opportunities.

An important element of our business strategy is to control fixed costs and overhead through contracting and entering into license agreements with other parties. We maintain a streamlined corporate infrastructure that focuses on our strongest areas of expertise. By contracting with other specialty organizations, we believe that we can control costs, enable our drug candidates to reach the market more quickly and reduce our business risk. Key elements of our contracting strategy include:

- ***Entering Into Relationships with Academic Institutions and Biotechnology Companies.*** Many academic institutions and biotechnology companies perform extensive research on the molecular and structural biology of potential drug development targets. By entering into relationships with these institutions, we believe we can leverage this respective research to significantly reduce the time, cost and risks involved in drug development. Our collaborative relationships with such organizations may lead to the licensing of one or more drug targets or

compounds. Upon licensing a drug target or promising compound from one of these institutions, the scientists from the institution typically become working partners as members of our structure-based drug design teams. We believe this makes us a more attractive development partner to these scientists since they can continue to have some involvement in the continuing development of the program. In addition, we collaborate with outside experts in a number of areas, including crystallography, molecular modeling, combinatorial chemistry, biology, pharmacology, oncology, cardiology, immunology and infectious diseases. These collaborations enable us to complement our internal capabilities without adding costly overhead. We believe this strategy allows us to save valuable time and expense, and further diversify and strengthen our portfolio of drug candidates. An example of such a collaborative relationship is the arrangement that we have with Albert Einstein College of Medicine of Yeshiva University ("AECOM") and Industrial Research Limited ("IRL") who are the licensors of our PNP inhibitor programs.

- ***Developing Drug Development Candidates or Licensing Them to Other Parties.*** We generally plan to advance drug candidates through initial and/or early-stage drug development. For larger disease indications requiring complex clinical trials, our strategy is to license drug candidates to pharmaceutical or biotechnology partners for final development and global marketing. We believe partnerships are a good source of development payments, license fees, future event payments and royalties. They also reduce the costs and risks, and increase the effectiveness, of late-stage product development, regulatory approval, manufacturing and marketing. We believe that focusing on discovery and early-stage drug development while benefiting from our partners' proven development and commercialization expertise will reduce our internal expenses and allow us to have a larger number of drug candidates progress to later stages of drug development. However, after establishing a lead product candidate, we are willing to license that candidate during any stage of the development process we determine to be beneficial to the company and to the ultimate development and commercialization of that drug candidate. For some smaller niche disease indications markets, we may choose to develop, manufacture, and where appropriate market and distribute any approved drugs ourselves, such as Fodosine™ for certain T-cell and B-cell cancers in the U.S.

Products in Development

The following table summarizes BioCryst's active development projects as of February 24, 2006:

Program and Candidate Disease Category/Indication	Delivery Form	Development Stage	Worldwide Rights
PNP Inhibitor (Fodosine™)			
T-cell leukemia	IV/Oral	Phase IIa	BioCryst/Mundipharma
CLL	Oral	Phase II	
B-ALL	IV	Phase I/II	
CTCL	Oral	Phase I	
PNP Inhibitor (BCX-4208)	Oral	Phase I	Roche/BioCryst has co-promotion rights in the U.S. in limited indications
Autoimmune diseases			
Transplantation rejection			
Neuraminidase Inhibitor (peramivir)	IV	Phase I	BioCryst
Viral	IM	Preclinical	
Hepatitis C Polymerase Inhibitors	Oral	Preclinical	BioCryst
Viral			
Tissue Factor/Factor VIIa Inhibitors	Oral	Lead Optimization	BioCryst
Cardiovascular / Oncology			

PNP Inhibitors

T-cell Related Diseases

Overview . The human immune system employs specialized cells, including T-cells, to control infection by recognizing and attacking disease-causing viruses, bacteria and parasites. T-cells are an essential part of the body's immune system that serve a dual purpose to both orchestrate and participate in the body's immune response. For the most part, this system works flawlessly to protect the body. However, when T-cells multiply uncontrollably, T-cell proliferative diseases, such as T-cell cancers, can occur.

The link between T-cell proliferation and the purine nucleoside phosphorylase, or PNP, enzyme was first discovered approximately twenty-five years ago when a patient, who was genetically deficient in PNP, exhibited limited T-cell activity, but reasonably normal activity of other immune functions. In other patients lacking PNP activity, the T-cell population was selectively depleted; however, B-cell function tended to be normal. Based on these findings and the results of cell culture studies, inhibiting PNP appears to produce selective suppression of T-cells without significantly impairing the function of other cells.

Acute Lymphoblastic Leukemia . The most common form of leukemia in children is acute lymphoblastic leukemia ("ALL"). According to the American Cancer Society, 3,930 new cases (adult and children combined) will be diagnosed in the United States in 2006 (T-cell and B-cell). ALL results from an acquired injury to the DNA of a single cell in the bone marrow.

T-cell Lymphoma . Lymphoma is a general term for a group of cancers that originate in the lymphatic system. About 58,870 Americans will be diagnosed with a non-Hodgkin's lymphoma in 2006 and approximately 15% of these will be considered T-cell lymphomas. T-cell lymphoma results when a T-lymphocyte (a type of white blood cell) undergoes a malignant change and begins to multiply, eventually crowding out healthy cells and creating tumors, which enlarge the lymph nodes and invade other sites in the body. CTCL is a primary skin neoplasm and accounts for nearly 50% of all T-cell malignancies.

T-cell Mediated Autoimmune Diseases. There are more than 80 clinically distinct autoimmune diseases such as psoriasis, rheumatoid arthritis, multiple sclerosis, and Crohn's disease, which appear to have activated T-cells as a major part of their pathogenesis. These diseases occur when the immune system attacks the body's own cells rather than invading microorganisms. Therefore, inhibition and/or elimination of activated T-cells could have a beneficial effect on these diseases.

Transplant Rejection. The greatest threat to transplant patients is rejection of the transplanted organ by the body's own immune system. For this reason, transplant recipients must take drugs to suppress the immune response and prevent rejection usually for the rest of their lives. A regimen combining several drugs is usually given and this treatment has to be continued indefinitely. For kidney transplant recipients, rejection of the new kidney by the patient's immune system can lead to loss of the transplanted organ and a return to dialysis. For heart, lung and liver transplant patients, loss of the transplanted organ presents an immediate threat to life.

Our PNP Inhibitor(s)

PNP Inhibition . PNP is an enzyme that plays an important role in T-cell proliferation, because it is necessary to maintain normal DNA synthesis in human T-cells. Selective inhibition of PNP causes certain nucleosides, including deoxyguanosine, to accumulate. As the concentration of deoxyguanosine increases within T-cells, it is converted by specific enzymes to deoxyguanosine triphosphate. A high concentration of deoxyguanosine triphosphate in T-cells causes an imbalance in the intra-cellular trinucleotide pool and thus causes cell death.

In June 2000, we licensed a series of potent PNP inhibitors from AECOM and IRL. The lead drug candidate from this collaboration, Fodosine™, is a more potent inhibitor of human lymphocyte proliferation than other previously known PNP inhibitors. Clinical data in our past and ongoing clinical trials, plus extensive preclinical studies indicate that Fodosine™ can modulate T-cell activities. Fodosine™ is an investigational PNP inhibitor for the potential treatment of T-cell leukemias and lymphomas.

During 2002, we exercised the option to add a new compound, BCX-4208, to the series of inhibitors of PNP licensed from AECOM and IRL. Preclinical results indicated that BCX-4208 was a more potent inhibitor than Fodosine™. We completed a Phase I single ascending dose clinical trial in healthy volunteers early in 2005 and have recently added two additional dosing regimens to an ongoing Phase Ib multi-dose clinical trial in healthy volunteers that was initiated in the third quarter of 2005. We licensed BCX-4208 to Roche in November 2005 for the world wide development and commercialization in autoimmune diseases and transplant rejection.

PNP Inhibitor (Fodosine™)

Overview

The first clinical trial with an intravenous formulation of Fodosine™, which began in 2002, was a Phase I clinical trial that enrolled T-cell ALL patients at the M.D. Anderson Cancer Center in Houston, Texas. Simultaneously, there were preclinical studies being conducted at the M.D. Anderson Cancer Center which indicated that Fodosine™ induces the same biochemical changes in various other types of leukemia cells that are responsible for the inhibition of T-leukemia cells. The results of these preclinical studies led us to expand beyond the single starting trial in T-cell ALL by initiating additional clinical trials for refractory patients with B-ALL, CTCL, and hematologic malignancies. Based on the encouraging results of these initial studies, we have developed a strategy for the simultaneous development of Fodosine™ in multiple indications using intravenous, oral and combination dosing regimens.

Current Development Strategy (T-cell leukemia, B-ALL, CLL, and CTCL)

Fodosine™ Clinical Development for Aggressive T-cell Malignancies . During 2004, we initiated a Phase IIa trial to enroll patients with aggressive T-cell malignancies. Despite encouraging results observed with other T-cell specific agents, the prognosis for patients with relapsed or refractory leukemia or lymphoma is poor and treatment options remain limited. The goal of the Phase IIa clinical trial is to determine the therapeutic effect produced by Fodosine™ as it relates to the proposed mechanism of action in the inhibition of proliferating T-lymphocytes in patients with T-cell ALL. Through February 8, 2006, there have been 37 patients enrolled in this trial, some of which were still in the initial 30 day treatment period. The results of this trial, along with a Phase I oral and IV pharmacokinetic trial in healthy volunteers will assist in the final design of a planned Phase IIb pivotal trial.

Our strategy for future development is to continue negotiating with the FDA to design the planned Phase IIb clinical trial under an SPA, which depending on the results, could serve as the pivotal trial for the filing of a New Drug Application (“NDA”) in T-cell ALL. We have obtained orphan drug status for Fodosine™ in multiple indications and the FDA has granted “fast track” status to the development of Fodosine™ for the treatment of relapsed or refractory T-cell leukemia. Our current intent is to maintain significant rights in this program and for BioCryst itself to potentially market and distribute Fodosine™ in the United States for treatment of T-cell cancers.

In 2004, we initiated a Phase I trial with an oral formulation of Fodosine™ for treatment of patients with CTCL. This Phase I trial initially consisted of nine patients, including three cohorts of patients at three different dose levels, to determine the safety and pharmacokinetic profile of the oral formulation. This trial has been expanded to add additional cohorts of different dosing levels and to transition this trial into a Phase I/II study to determine the efficacy of this oral formulation and to establish the optimum dose that will be required for future clinical trials in CTCL.

During the third quarter of 2005, we initiated a Phase II trial with oral Fodosine™ in patients with CLL in an advanced stage and refractory to fludarabine, which is the current standard of therapy. Conducted at the University of Texas M.D. Anderson Cancer Center, this single-site Phase II, open label trial will evaluate the efficacy and safety of Fodosine™ as determined by response rate, time to disease progression, and patient tolerance. Patients will receive orally administered Fodosine™ at a dose of 200 mg for four weeks. After this first full cycle of therapy, patients will be evaluated. Responding patients or patients with stable disease will be allowed to receive further treatment cycles up to a maximum of six cycles.

During the fourth quarter of 2005, we initiated a Phase I/II clinical trial of Fodosine™ to determine the safety of repeat doses of an intravenous (IV) formulation of the drug in patients with B-ALL. This multi-center, open-label, repeat-dose study is scheduled to enroll 30 patients and consists of two periods, an Initial Treatment Period and an Extended Treatment Period. The Initial Treatment Period will last four weeks, during which patients will receive single daily infusions of 80mg/m2 of Fodosine™ for five consecutive days each week with at least two non-treatment days per week. This regimen will be extended by four additional weeks in the Extended Treatment Period if the patient continues to show benefit from the treatment. Additionally, patients who are responding to treatment with Fodosine™ at the end of the Extended Treatment Period may continue receiving the drug under compassionate use guidelines.

During 2006, we plan to initiate an additional Phase II trial of Fodosine™ in CLL at multiple sites in the U.S. and we plan to be in a Phase II trial in CTCL patients.

In February 2006, we and Mundipharma entered into an exclusive license agreement to develop and commercialize Fodosine™, in markets across Europe, Asia and Australasia for use in oncology. The agreement covers a number of markets in Asia and Australasia including Japan, Australia, New Zealand, China and India. This collaboration should help maximize the global development, commercialization, and market potential of Fodosine™ in a variety of serious medical conditions potentially including T-cell leukemia, CTCL, CLL, T-cell non-Hodgkin's lymphoma and B-cell non-Hodgkin's lymphoma.

PNP Inhibitor (BCX-4208)

Overview

We believe that the results to date from our Phase I trials of Fodosine™ support the principle that inhibition of PNP has a direct effect on proliferation of activated T-lymphocytes. During the fourth quarter of 2004, we began clinical development of BCX-4208, a second-generation PNP inhibitor, as a drug candidate for the treatment of T-cell mediated autoimmune diseases, including psoriasis. Although BCX-4208 and Fodosine™ are both investigational PNP inhibitors, BCX-4208 differs from Fodosine™ in significant ways. For example, BCX-4208 is more potent, and has the ability to suppress PNP for longer periods of time. Thus, BCX-4208 has potential advantages over Fodosine™ for the treatment of diseases requiring long-term, chronic administration of a PNP inhibitor.

Current Development Strategy

We completed a Phase I single dose pharmacokinetic trial in healthy volunteers early in 2005. During the third quarter of 2005, we initiated a Phase Ib multi dose trial in healthy volunteers to evaluate the safety, tolerability, and pharmacokinetics of multiple oral doses of BCX-4208 with the goal of beginning a Phase II trial during 2006 in psoriasis patients.

In November 2005, we and Roche announced an exclusive license agreement for the worldwide development and commercialization of BCX-4208 for the prevention of acute rejection in transplantation and for the treatment of autoimmune diseases. This collaboration provided substantial strategic and economic benefit to us and also all the essential elements for the rapid, comprehensive and competitive development of BCX-4208. The two companies have established a joint committee to set the clinical development strategy and the future development program for BCX-4208.

Neuraminidase Inhibitor

Influenza

Seasonal Influenza. Seasonal influenza, commonly known as the flu, is a viral infection characterized by symptoms including fever, cough, sore throat, fatigue, headache, and/or chills. According to the U.S. Centers for Disease Control and Prevention ("CDC"), an estimated 5% to 20% of the American population suffers from influenza annually, more than 200,000 people are hospitalized from flu complications, and approximately 36,000 people die from flu. Influenza is particularly dangerous to the elderly, young children and people with certain health conditions. Outbreaks of seasonal flu tend to follow predictable patterns usually occurring in the winter. New vaccines are developed annually based on known flu strains and are usually available for the annual flu season. There are also antiviral treatments available for the treatment of people infected with influenza.

Avian Influenza . According to information from the CDC, avian influenza, or bird flu is an infection caused by viruses which occur naturally among birds. This form of flu is very contagious among birds and can lead to serious illness and sometimes death. There are two main forms of disease that infect domestic poultry, one a low pathogenic form and the other a highly pathogenic form. The latter form can cause disease that affects multiple internal organs and with a mortality rate between 90-100% in these birds within 2 days.

While there are many different subtypes of the influenza A virus, only three subtypes are known to be currently circulating among humans. Avian influenza A viruses are found chiefly in birds, but there have been confirmed cases of infection in humans, generally as a result of contact with infected birds. These infections have led to symptoms of normal flu to more severe and life threatening conditions. Influenza A ("H5N1") is a subtype of an influenza virus that is highly contagious among birds and can be very deadly to them. Of the avian influenza viruses that have crossed the species barrier to infect humans, the H5N1 has caused the largest number of detected cases of severe disease and death in humans. Thus far, this virus has not been known to spread from one person to another, but as influenza A viruses constantly change, they could mutate over time to have the ability to spread among humans.

Pandemic Influenza . Pandemic flu is a global disease outbreak that occurs when a new influenza virus emerges so that people have had no previous exposure. This situation occurs very rarely and only occurred three times in the 20 th century.

Flu Prevention and Treatment . The development of effective therapeutics has challenged medical researchers due to the seasonal variation in viral strains and the highly infectious nature of influenza. Patients, therefore, have limited treatment options. Amantadine and rimantadine are used for treatment of influenza A but are ineffective against influenza B. In addition, these drugs cause some adverse side effects, and the virus tends to develop resistance to these drugs. For the 2005-2006 flu season, the CDC has recommended against the use of amantadine and rimantadine for the treatment or prophylaxis of influenza in the United States due to signs of resistance.

Vaccines are available against the disease but have limitations: people require advance vaccination; vaccines are limited by their specificity to particular strains of the virus; and vaccines offer little protection if the vaccine is inaccurate. In addition, many people decline the required injections because of fear and/or discomfort. The ability of the virus to change its structure to avoid the body's natural defenses is a serious obstacle to developing an effective vaccine against influenza. Different strains can arise when surface antigens on the virus (the portion of the virus that causes an immune reaction in humans) undergo minor genetic mutations each year as the virus replicates. Because of this mutability, the immunity acquired in response to infection by a particular strain of the virus does not provide adequate protection against viruses that subsequently arise. The production of a new vaccine each year is not only complex and expensive, but also an inefficient method of global disease control.

Inhibiting Influenza Neuraminidase. Research during the past two decades has seen dramatic advances in understanding the molecular structure and function of the influenza virus. Considerable attention has been focused on the enzyme neuraminidase, which is located on the surface of the virus. Neuraminidase assists in the release and spread of the flu virus by breaking the chemical strands that hold the new viruses to the cell surface, allowing the replicated virus to spread and infect other cells. This process progresses until the host's immune response can produce enough antibodies to bring the infection under control. Inhibiting the neuraminidase enzyme keeps new viruses attached to the cell surface, thereby preventing the spread of the virus and the further infection of other cells. The subsequent quantities of virus in the bloodstream are not enough to cause disease but are sufficient to induce the body to mount an immune response.

In addition to our neuraminidase inhibitor drug candidate, both Roche, in collaboration with Gilead Sciences, and GlaxoSmithKline ("GSK") have neuraminidase inhibitors. Roche's neuraminidase inhibitor is a twice-a-day, orally active neuraminidase inhibitor, while GSK's neuraminidase inhibitor is administered by dry powder inhaler twice a day. Both drugs are approved for marketing in the United States and other countries for treatment of influenza. Roche's neuraminidase inhibitor is also approved for prophylaxis use for prevention of influenza. In addition to these companies with neuraminidase inhibitors, there are other companies working to develop vaccines and other antiviral drugs to be used against various strains of influenza.

Some studies in laboratories suggest that some of these neuraminidase inhibitor drugs should work in treating avian influenza infections in humans, but additional studies are needed to demonstrate the effectiveness of these drugs.

Neuraminidase Inhibitor (peramivir)

Overview

Background . In 1987, scientists at The University of Alabama at Birmingham ("UAB"), in collaboration with our scientists, began determining the molecular structure of the influenza neuraminidase enzyme from several different strains of influenza, using X-ray crystallography. Subsequently, our scientists and UAB scientists developed numerous new inhibitors of these enzymes using structure-based drug design. We licensed the influenza neuraminidase program from UAB in 1994 and proceeded to complete the studies of the enzyme's molecular structure needed to advance the development of neuraminidase inhibitors. The structure of the active site of influenza neuraminidase is similar among different viral strains. Because of this similarity, we believe that our neuraminidase inhibitors may be effective in the treatment and prevention of influenza, regardless of changes in the virus.

By 1998, four patented compounds emerged as viable product development candidates. Preclinical studies determined the lead compound, peramivir, has the following benefits:

- good safety profile;
- inhibition of both influenza A and B;
- effective when given by injection or at large doses taken orally;
- once-a-day dosage; and
- can be made into a liquid form, allowing for oral use by the elderly and young children.

Previous Licensing History . In September 1998, we entered a worldwide license agreement with The R.W. Johnson Pharmaceutical Research Institute ("RWJPRI") and Ortho-McNeil Pharmaceutical Inc. ("Ortho-McNeil") both Johnson & Johnson companies, for development and commercialization of our influenza neuraminidase inhibitors, including peramivir. On April 30, 2001, we announced that Ortho-McNeil and RWJPRI, gave four months prior notice of termination of the worldwide license agreement with us to develop and market products to treat and prevent viral influenza. Subsequently, all rights to peramivir returned to us. Ortho-McNeil indicated that this business decision was not related to safety or efficacy of peramivir, but that other of its drug development programs were of a higher priority. The final termination of this agreement was effective on September 21, 2001.

Previous Clinical Development History

Phase II data – Summary. RWJPRI conducted two Phase II placebo-controlled, randomized studies for the treatment of healthy volunteers infected with a strain of either influenza A or influenza B. The primary endpoints were viral titers over time expressed as the area under the viral titer curve. Among infected subjects, peramivir produced a dose-dependent, anti-viral effect. In addition, oral, once daily peramivir was well tolerated and reported adverse events were similar for the active and placebo-treated groups.

Phase III clinical trial – Summary. Phase III clinical trials of peramivir were initiated in Europe in February 2000 by RWJPRI. The trials were continued, but not completed, during the 2000-2001 season, and remain blinded. On January 3, 2002, we announced that patient enrollment began in the United States in the Phase III trial with once-a-day orally administered peramivir. The multi-center, Phase III clinical trial enrolled approximately 1,200 healthy adults. In June 2002, we announced the initial findings of this Phase III trial demonstrated no statistically significant difference in the primary efficacy endpoint-the length of time from the first dose to the onset of clinically significant relief of influenza symptoms between groups treated with peramivir and groups treated with placebo. Based on these data, we had discontinued the development of peramivir in 2002.

Current status of peramivir. Due to the recent international concern about a potential influenza pandemic that could be initiated by avian strains of the virus, peramivir has received considerable attention, since it is positioned to be one of very few advanced antiviral alternatives behind oseltamivir, or Tamiflu, for addressing a potential pandemic. As a result, we have re-initiated the clinical development of peramivir.

Current Development Strategy

Preclinical studies comparing peramivir with other anti-influenza drugs have demonstrated that peramivir has outstanding broad-spectrum potency against multiple strains of influenza, including the avian strain H5N1. In addition, peramivir retains activity against nearly all Tamiflu-resistant strains of influenza that have been identified to date. We are currently focusing on injectable formulations of peramivir that may achieve high blood levels that should be effective against most strains of influenza, including strains that may be resistant to Tamiflu. Our IND for injectable peramivir became effective in December 2005, we received fast track designation from the FDA in January 2006 and initiated a Phase I clinical with IV peramivir in March 2006 at the NIH.

Our plan is to develop two injectable formulations, including intravenous peramivir for treating acutely ill patients, and an intramuscular injectable formulation for treatment of earlier-stage infected patients. Both of these development programs are being pursued in close collaboration with research groups at the National Institute of Allergy and Infectious Diseases ("NIAID") at the National Institutes of Health ("NIH"). Currently, the clinical division of the NIAID is planning to run our upcoming intravenous clinical trials, beginning in the first quarter of 2006, with Phase I studies in healthy volunteers at the clinical unit in NIH, and then assuming results are positive, proceeding into Phase II/III trials during 2006 at clinical sites in Southeast Asia.

We expect the intramuscular, or IM formulation of peramivir will follow a more classical development pathway with initial testing in patients infected with seasonal flu beginning in a placebo controlled trial during the 2006-2007 flu season. Preclinical studies have indicated that a single injection of peramivir is effective at preventing death in mice from infections with virulent strains of influenza. If this finding can be confirmed in clinical trials, we believe the IM formulation will have considerable potential for treating patients with normal influenza infections, in addition to providing an effective mechanism for treating large numbers of patients rapidly in the event of a flu pandemic.

Congress has recently approved an appropriation of $3.8 billion for 2006 to support the development of various countermeasures for a flu pandemic. The appropriation includes funding for the development of new antiviral agents, and we believe peramivir is eligible for funding under this appropriation. Health and Human Services recently issued a Request for Information regarding potential programs for the advanced development of antiviral agents for prophylactic/therapeutic usage during seasonal and pandemic influenza outbreaks. We have responded to this opportunity and believe that given the high quality of the science behind peramivir, the extensive preclinical and clinical data that we already have available, and the advanced development of our manufacturing process, we are in a strong position to compete for funds available under this pandemic preparedness initiative. We plan to continue working closely with scientists at NIAID to implement rapid and effective development of peramivir.

Hepatitis C Polymerase Inhibitors

Overview

Hepatitis C virus ("HCV") infection has been described in the New England Journal of Medicine as the nation's most common chronic blood-borne infection. According to the World Health Organization, 3% of the world's population are infected with HCV and are at risk of developing liver cirrhosis and/or liver cancer. The CDC estimates there are an estimated 3.9 million Americans (approximately 2% of the population) that have been infected with HCV, of whom 2.7 million are chronically infected. According to the CDC, as many as 55-85% of those infected with HCV will have chronic infection and 70% of those will develop chronic liver disease. While there are several approved treatments for chronic HCV using a combination therapy of interferon and ribavirin, there are some potentially severe side effects to these treatments.

Background . In June 2000, we licensed intellectual property from Emory University ("Emory") related to the hepatitis C polymerase target associated with hepatitis C viral infections. Under the original terms of the agreement, the research investigators from Emory provided us with materials and technical insight into the target.

Current Development Strategy

We are targeting HCV polymerase through collaborative and in-house efforts. Specifically, we are focused on development of orally active inhibitors against the RNA-dependent RNA polymerase. Competition for this target is less intense than for the HCV protease target and history suggests the likelihood of designing a useful inhibitor against this target may be better than designing inhibitors against the protease.

We have designed, synthesized and screened potential compounds against HCV polymerase. Specifically, our scientists have measured the potency and ability of potential drug candidates to block the replication of HCV polymerase in vitro, or in test tubes. These experiments measure the potency of each selected compound's ability to block replication. Advanced screening was also used to measure the fit of promising compounds in the HCV polymerase active site using X-ray crystallography and computer molecular modeling. The goal has been to identify a series of compounds that are potent in vitro inhibitors of the active site of the HCV polymerase for further testing and lead optimization.

During 2005, we identified a lead compound, BCX-4678, for which we have made progress in the preclinical development, plus major improvements in the large-scale synthesis. We now have adequate material on hand to initiate our final preclinical toxicology studies required for an IND filing during 2006. Assuming that our toxicology studies verify the safety profile seen in our earlier animal studies and the FDA accepts our IND, we plan to move directly into a clinical trial for hepatitis C infected patients during 2006.

We also have agreements in place with NIAID, and the U.S. Army Medical Research Institute of Infectious Diseases to assay promising inhibitors from the HCV polymerase program for activity against Severe Acute Respiratory Syndrome (SARS), West Nile and Ebola viruses.

Tissue Factor/Factor VIIa Inhibitors

Overview

A series of complicated reactions takes place in the body whenever a blood clot begins to form. The major initiator of these reactions is an enzyme system called the tissue factor/factor VIIa ("TF/FVIIa") complex. Animal tests show that various inhibitors of the TF/FVIIa complex can minimize blood clot formation as well as inflammatory responses. This sort of inhibition has been tested with a number of biological agents including the natural inhibitor of the pathway, synthetic peptides and protein inhibitors, and antibodies against tissue factor. However, there are no small molecule drugs currently on the market that intervene at the TF/FVIIa level.

We believe that small molecule inhibitors of TF/FVIIa may potentially be useful for treating acute coronary syndromes and complications associated with cardiovascular procedures, such as coronary angioplasty and stent insertions, because any type of damage to arteries and blood vessels exposes tissue factor, which then triggers clot formation. Myocardial infarction, unstable angina, and restenosis during and following angioplasty procedures are all potential treatment targets. In addition, tissue factor is involved in angiogenesis, or new blood vessel growth, and inhibitors of the TF/FVIIa complex are believed to have potential as anti-angiogenesis agents for use in oncology.

Background . We have an agreement with Altor BioScience Corporation ("Altor") formerly Sunol Molecular Corporation ("Sunol") to expedite the discovery of new drug candidates designed to inhibit TF/FVIIa. Under the terms of this agreement, Altor supplies us protein for our drug design program.

Current Development Strategy

We are continuing to design and synthesize groups of compounds that are potent and selective inhibitors of TF/FVIIa and further optimization is ongoing to identify a compound for preclinical development of a TF/FVIIa inhibitor in oral form.

Additional Products

In addition to our four active programs, we also retain exclusive rights to potent inhibitors of parainfluenza neuraminidase and maintain the patent portfolio for these inhibitors. We will continue to take the necessary steps to retain the value of these inhibitors.

Structure-Based Drug Design

Structure-based drug design is a drug discovery approach by which we design synthetic compounds from detailed structural knowledge of the active sites of enzyme targets associated with particular diseases. Enzymes are proteins that act as catalysts for many vital biological reactions. Our goal generally is to design a compound that will fit in the active site of an enzyme (the active site of an enzyme is the area into which a chemical or biological molecule fits to initiate a biochemical reaction) and thereby interfere with the progression of disease.

Our structure-based drug design involves the application of both traditional biology and medicinal chemistry and an array of advanced technologies. We use X-ray crystallography, computer modeling of molecular structures and advanced chemistry techniques to focus on the three-dimensional molecular structure and active site characteristics of the enzymes that control cellular biology.

We believe that structure-based drug design technologies are superior to drug screening techniques. By identifying the target enzyme in advance and by discovering the chemical and molecular structure of the enzyme, we believe it is possible to design a better drug to interact with the enzyme. In addition, the structural data obtained by X-ray crystallographic analysis allow additional analysis and compound modification at each stage of the biological evaluation. This capability makes structure-based drug design a powerful tool for efficient development of drugs that are highly specific for particular enzyme target sites.

Research and Development

We initiated our research and development program in 1986, with drug synthesis beginning in 1987. We have assembled a scientific research staff with expertise in a broad base of advanced research technologies including protein biochemistry, X-ray crystallography, chemistry and pharmacology. Our research facilities include protein biochemistry and organic synthesis laboratories, testing facilities, X-ray crystallography, computer and graphics equipment and facilities to make drug candidates on a small scale for early stage clinical trials.

During the years ended December 31, 2005, 2004 and 2003, we spent $23.6, $18.9 and $11.5 million, respectively on research and development. Approximately $9.1, $8.0 and $7.5 million of those respective amounts were spent on in-house research and development, and $14.5, $10.9 and $4.0 million, respectively were spent on contract research and development.

Collaboration and In-License Relationships

We seek to enter into collaborations with leading pharmaceutical and biotechnology companies when we feel it is advantageous to leverage these companies' resources to develop and commercialize our drug candidates on a global basis. This allows us to remain focused on our strength of early stage discovery and development of drug candidates. To date, we have two major collaborations for the development and commercialization of our lead PNP inhibitors.

Another important component of our strategy is to augment our internal discovery programs through the selective in-licensing of potential drug development targets or early stage compounds for these specific targets.

Corporate Alliances

Roche . In November 2005, we entered into an exclusive license with Roche for the development and commercialization of our second generation PNP inhibitor, BCX-4208, for the prevention of acute rejection in transplantation and for the treatment of autoimmune diseases. Under the terms of the agreement, Roche obtained worldwide rights to BCX-4208 in exchange for an up-front payment of $30 million, which included a payment as reimbursement for a limited supply of material during the first 24 months of the collaboration. There could also be future event payments for achieving specified development, regulatory and commercial milestones (including sales level milestones following a product's launch) for certain indications. In addition, we will receive royalties based on a percentage of net product sales, which varies depending upon when certain indications receive NDA approval in a major market country and can vary by country depending on the patent coverage or sales of generic compounds in a particular country. We licensed this compound and other PNP inhibitors from AECOM and IRL and will owe sublicense payments to these third parties on the upfront payment, future event payments and royalties received by us for the sublicense of these inhibitors.

Roche will have a right of first negotiation, under certain conditions, on existing backup PNP inhibitors we develop through Phase IIb in transplant rejection and autoimmune diseases, but any new PNP inhibitors will be exempt from this agreement and we will retain all rights to such compounds. We retain the right to co-promote BCX-4208 in the U.S. for several indications. Roche has certain obligations under the terms of the agreement to use commercially reasonable efforts to develop, manufacture and commercialize the licensed product. The agreement will be governed by a joint steering committee to oversee and review the research and development activities of both parties. The agreement may be terminated by either party following an uncured material breach by the other party or may be either fully or partially terminated by Roche without cause under certain conditions and all rights, data, materials, products and other information would be transferred to us at no cost.

Mundipharma. In February 2006, we entered into an exclusive, royalty bearing right and license in the specified territory (primarily Europe, Asia and Australasia) with Mundipharma for the development and commercialization of our lead PNP inhibitor, Fodosine™, for use in oncology. Under the terms of the agreement, Mundipharma obtained oncology rights to Fodosine™ in the specified territory in exchange for a $10 million up-front payment. Mundipharma will share 50% of the documented out of pocket development costs incurred by us in respect of our current and planned trials as of the effective date of the agreement provided that Mundipharma's maximum contribution to these trials shall be $10 million. In addition, Mundipharma will conduct additional clinical trials at their own cost up to a maximum of $15 million. The license provides for future event payments for achieving specified development, regulatory and commercial events (including certain sales level amounts following a product's launch) for certain indications. In addition, we will receive royalties based on a percentage of net product sales, which varies depending upon when certain indications receive NDA approval in a major market country and can vary by country depending on the patent coverage or sales of generic compounds in a particular country. Generally, all payments under the agreement are nonrefundable and non-creditable, but they are subject to audit. We licensed this compound and other PNP inhibitors from AECOM and IRL and will owe sublicense payments to these third parties on the upfront payment, future event payments and royalties received by us for the sublicense of these inhibitors.

For five years, Mundipharma will have a right of first negotiation on existing backup PNP inhibitors we develop through Phase IIb in oncology, but any new PNP inhibitors will be exempt from this agreement and we will retain all rights to such compounds. We retain the rights to Fodosine™ in the United States ("U.S.") and Mundipharma is obligated by the terms of the agreement to use commercially reasonable efforts to develop the licensed product in the territory specified by the agreement. The agreement will be governed by a Joint Steering Committee to oversee and review the research and development activities of both parties. The agreement will continue for the commercial life of the licensed products, but may be terminated by either party following an uncured material breach by the other party or in the event the pre-existing third party license with AECOM and IRL expires. It may be terminated by Mundipharma upon 60 days written notice without cause or under certain other conditions as specified in the agreement and all rights, data, materials, products and other information would be transferred to us at no cost. In the event we terminate the agreement for material default or insolvency, we could have to pay Mundipharma 50% of the costs of any independent data owned by Mundipharma in accordance with the terms of the agreement.

Sunol . In April 1999, we entered into an agreement with Sunol which requires Sunol to conduct research and supply us with protein targets for drug design to expedite the discovery of new drug candidates designed to inhibit tissue factor/factor VIIa for our cardiovascular program. During 2005, the assets and obligations of Sunol were transferred to Altor BioScience Corporation.

Academic Alliances

Albert Einstein College of Medicine of Yeshiva University and Industrial Research, Ltd, New Zealand . In June 2000, we licensed a series of potent inhibitors of PNP from AECOM and IRL. The lead drug candidates from this collaboration are Fodosine™ and BCX-4208. We have obtained worldwide exclusive rights to develop and ultimately distribute these, or any other, drug candidates that might arise from research on these inhibitors. We have agreed to pay certain milestone payments for future development of these inhibitors, certain royalties on sales of any resulting product, and to share in future payments received from other third-party collaborators, if any. In addition, we have agreed to pay an annual license fee that is non-refundable, but is creditable against actual royalties and other payments due to AECOM/IRL. This agreement may be terminated by us at any time by giving 60 days advance notice or in the event of material uncured breach by AECOM/IRL.

The University of Alabama at Birmingham . We have had a close relationship with UAB since our formation. Our Chairman and Chief Executive Officer, Dr. Charles E. Bugg, was the previous Director of the UAB Center for Macromolecular Crystallography, and our President, Chief Operating Officer and Medical Director, Dr. J. Claude Bennett, was the former President of UAB, the former Chairman of the Department of Medicine at UAB and a former Chairman of the Department of Microbiology at UAB. Several of our consultants are employed by UAB. UAB has a large X-ray crystallography center with approximately 121 full-time staff members and they expect to receive approximately $18.0 million in research grants and contract funding for their programs in 2006. Several of our early programs originated at UAB.

We currently have agreements with UAB for influenza neuraminidase and complement inhibitors. Under the terms of these agreements, UAB performed specific research for us in return for research payments and license fees. UAB has granted us certain rights to any discoveries in these areas resulting from research developed by UAB or jointly developed with us. We have agreed to pay royalties on sales of any resulting product and to share in future payments received from other third-party collaborators. We have completed the research under the UAB influenza agreement. We funded the research program under the complement inhibitors agreement through March 2002, which entitled us to an assignment of, or a right to an exclusive license for, any inhibitors of specified complement enzymes developed by UAB scientists during the period of support or for a one-year period thereafter. These two agreements have initial 25-year terms, are automatically renewable for five-year terms throughout the life of the last patent and are terminable by us upon three months notice and by UAB under certain circumstances. There is currently no activity between us and UAB on these agreements, but in the event we license technology or commercialize products related to these programs we could owe sublicense fees or royalties on amounts we receive.

Emory. In June 2000, we licensed intellectual property from Emory related to the HCV polymerase target associated with hepatitis C viral infections. Under the original terms of the agreement, the research investigators from Emory provided us with materials and technical insight into the target. We have agreed to pay Emory royalties on sales of any resulting product and to share in future payments received from other third party collaborators, if any. We can terminate this agreement at any time by giving 90 days advance notice.

Patents and Proprietary Information

Our success will depend in part on our ability to obtain and enforce patent protection for our products, methods, processes and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. We own or have rights to certain proprietary information, proprietary technology, issued and allowed patents and patent applications which relate to compounds we are developing. We actively seek, when appropriate, protection for our products, proprietary technology and proprietary information by means of U.S. and foreign patents, trademarks and contractual arrangements. In addition, we rely upon trade secrets and contractual arrangements to protect certain of our proprietary information, proprietary technology and products.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective patent claims and enforcing those claims once granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated, rendered unenforceable or circumvented, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. In addition, the rights granted under any issued patents may not provide us with competitive advantages against competitors with similar compounds or technology. Furthermore, our competitors may independently develop similar technologies or duplicate any technology developed by us in a manner that does not infringe our patents or other intellectual property. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our drug candidates or those developed by our collaborators can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

As of February 20, 2006, we have been issued 28 U.S. patents that expire between 2009 and 2023 and that relate to our PNP, serine protease and neuraminidase inhibitor compounds. We have licensed six additional composition of matter patents and two pending composition of matter patents from AECOM and IRL for our PNP inhibitors, plus additional manufacturing patents related to these PNP inhibitors and one patent from Emory related to hepatitis C. Additionally, we have 13 U.S. patent applications pending related to PNP, neuraminidase, RNA viral polymerase, paramyxovirus neuraminidase, and serine protease inhibitors. Our pending applications may not result in issued patents, and our patents may not provide us with sufficient protection against competitive products or otherwise be commercially viable.

Our success is also dependent upon the skills, knowledge and experience of our scientific and technical personnel, none of which is patentable. To help protect our rights, we require all employees, consultants, advisors and collaborators to enter into confidentiality agreements, which prohibit the disclosure of confidential information to anyone outside of our company and requires disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information.

Marketing and Sales

We currently plan to market, distribute and sell Fodosine™ in the U.S. for use in treatment of T-cell and B-cell cancers. Although our general strategy is to rely on major marketing companies for worldwide commercialization of most products we may develop, we believe that we can manage the highly specialized oncology market for Fodosine™ within the U.S. Most patients with advanced T-cell malignancies in the U.S. are treated at major referral cancer centers, and we expect that many of these centers will be participating in our Phase II trials and will thus be familiar with Fodosine™ if it reaches the market. However, we lack experience in marketing, distributing and selling pharmaceutical products. Our general strategy is to rely on collaborators, licensees or arrangements with others to provide for the marketing, distribution and sales of products we may develop. We may not be able to establish and maintain acceptable commercial arrangements with collaborators, licensees or others to perform such activities.

Competition

The pharmaceutical and biotechnology industries are intensely competitive. Many companies, including biotechnology, chemical and pharmaceutical companies, are actively engaged in activities similar to ours, including research and development of drugs for the treatment of cancer, infectious, autoimmune, inflammatory and cardiovascular diseases and disorders. Many of these companies have substantially greater financial and other resources, larger research and development staffs, and more extensive marketing and manufacturing organizations than we do. In addition, some of them have considerable experience in preclinical testing, clinical trials and other regulatory approval procedures. For example, in October 2005, the FDA announced the approval of Arranon (nelarabine) for the treatment of adults and children with T-cell acute lymphoblastic leukemia. This drug was approved under the FDA's orphan drug and accelerated approval (fast track) programs and will be distributed and marketed by GSK. We are currently testing Fodosine™ in T-cell ALL and have also received both orphan drug and fast track designation from the FDA. There are also academic institutions, governmental agencies and other research organizations that are conducting research in areas in which we are working. They may also market commercial products, either on their own or through collaborative efforts.

We expect to encounter significant competition for any of the pharmaceutical products we plan to develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage. Such is the case with GSK's Arranon for T-cell ALL and the current neuraminidase inhibitors marketed by GSK and Roche for influenza. In addition, several pharmaceutical and biotechnology firms, including major pharmaceutical companies and specialized structure-based drug design companies, have announced efforts in the field of structure-based drug design and in the fields of PNP, HCV, influenza, and TF/FVIIa.

In order to compete successfully, we must develop proprietary positions in patented drugs for therapeutic markets that have not been satisfactorily addressed by conventional research strategies and, in the process, expand our expertise in structure-based drug design. Our products, even if successfully tested and developed, may not be adopted by physicians over other products and may not offer economically feasible alternatives to other therapies.

Government Regulation

The FDA regulates the pharmaceutical and biotechnology industries in the U.S., and our drug candidates are subject to extensive and rigorous domestic government regulations prior to commercialization. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of pharmaceutical products. In foreign countries, our products are also subject to extensive regulation by foreign governments. These government regulations will be a significant factor in the production and marketing of any pharmaceutical products that we develop. Failure to comply with applicable FDA and other regulatory requirements at any stage during the regulatory process may subject us to sanctions, including:

- delays;
- warning letters;
- fines;
- product recalls or seizures;
- injunctions;
- penalties;
- refusal of the FDA to review pending market approval applications or supplements to approval applications;
- total or partial suspension of production;
- civil penalties;
- withdrawals of previously approved marketing applications; and
- criminal prosecutions.

The regulatory review and approval process is lengthy, expensive and uncertain. Before obtaining regulatory approvals for the commercial sale of any products, we or our licensees must demonstrate that our product candidates are safe and effective for use in humans. The approval process takes many years, substantial expenses may be incurred and significant time may be devoted to clinical development.

Before testing potential candidates in humans, we carry out laboratory and animal studies to determine safety and biological activity. After completing preclinical trials, we must file an IND, including a proposal to begin clinical trials, with the FDA. We have filed twelve INDs to date and plan to file, or rely on future partners to file, additional INDs in the future as our potential drug candidates advance to that stage of development. Thirty days after filing an IND, a Phase I human clinical trial can start, unless the FDA places a hold on the study.

Our Phase I trials are designed to determine safety in a small group of patients or healthy volunteers. We also assess tolerances and the metabolic and pharmacologic actions of our drug candidates at different doses. After we complete the initial trials, we conduct Phase II trials to assess safety and efficacy and establish the optimal dose in patients. If Phase II trials are successful, we or our licensees conduct Phase III trials to verify the results in a larger patient population. Phase III trials are required for FDA approval to market a drug. A Phase III trial may require hundreds or even thousands of patients and is the most expensive to conduct. The goal in Phase III is to collect enough safety and efficacy data to obtain FDA approval of a drug for treatment of a particular disease. For some clinical indications that are especially serious and for which there are no effective treatments, such as refractory cancers, conditional approval can be obtained following Phase II trials.

Initiation and completion of the clinical trial phases are dependent on several factors including things that are beyond our control. For example, the clinical trials cannot begin at a particular site until that site receives approval from its Institutional Review Board (“IRB”), which reviews the protocol and related documents. This process can take from several weeks to several months. In addition, clinical trials are dependent on patient enrollment, but the rate at which patients enroll in the study depends on:

- willingness of investigators to participate in a study;
- ability of clinical sites to obtain approval from their IRB;
- the size of the patient population we intend to treat;
- the availability of patients;
- the willingness of patients to participate; and
- the patients meeting the eligibility criteria.

Delays in planned patient enrollment may result in increased expense and longer development timelines.

After completion of the clinical trials of a product, we or our licensees must submit a NDA to the FDA for marketing approval before commercialization of the product. The FDA may not grant approval on a timely basis, if at all. The FDA, as a result of the Food and Drug Administration Modernization Act of 1997, has six months to review and act upon license applications for priority therapeutics that are for life-threatening or unmet medical needs. Standard reviews can take between one and two years, and can even take longer if significant questions arise during the review process. The FDA may withdraw any required approvals, once obtained.

In addition to clinical development regulations, we and our contract manufacturers and collaborators must comply with the applicable FDA current good manufacturing practice ("GMP") regulations. GMP regulations include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. Such facilities must be approved before we can use them in commercial manufacturing of our potential products. We or our contract manufacturers may not be able to comply with the applicable GMP requirements and other FDA regulatory requirements. If we or our contract manufacturers fail to comply, our business, financial condition and results of operations will be materially adversely affected.

Human Resources

As of February 28, 2005, we had 52 employees, of whom 37 were engaged in research and development and 15 were in general and administrative functions. Our scientific staff, 20 of whom hold Ph.D. or M.D. degrees, has diversified experience in biochemistry, pharmacology, X-ray crystallography, synthetic organic chemistry, computational chemistry, and medicinal chemistry. We consider our relations with our employees to be satisfactory.

Scientific Advisory Board and Consultants

Our scientific advisory board is comprised of five scientific advisors who are leaders in certain of our core disciplines or who otherwise have specific expertise in our therapeutic focus areas. We also have consulting agreements with a number of other scientists with expertise in our core disciplines or who are specialists in diseases or treatments on which we focus. The scientific advisory board meets as a group at scheduled meetings and the consultants meet more frequently, on an individual basis, with our scientific personnel and management to discuss our ongoing research and drug discovery and development projects. The scientific advisory board consists of the following individuals:

Name	Position
Albert F. LoBuglio, M.D. (Chairman)	Director Emeritus and Distinguished Professor of The University Of Alabama at Birmingham Comprehensive Cancer Center.
Gordon N. Gill, M.D.	Professor of Medicine *Emeritus* at the University of California, San Diego School of Medicine.
Lorraine J. Gudas, Ph.D.	Professor and Chairman, Department of Pharmacology Weill Medical College of Cornell University, Revlon Pharmaceutical Professor of Pharmacology and Toxicology.

Name	Position
Herbert A. Hauptman, Ph.D.	President of the Hauptman-Woodward Medical Research Institute, Inc. (formerly the Medical Foundation (Buffalo), Inc.), and Research Professor in Biophysical Sciences and Distinguished Professor in Structural Biology at the State University of New York (Buffalo). Recipient of the Nobel Prize in Chemistry (1985).
Hamilton O. Smith, M.D.	Professor, Molecular Biology and Genetics Department at The Johns Hopkins University School of Medicine, retired, and Scientific Director of the Synthetic Biology and Biological Energy Groups at the J. Craig Venter Institute in Rockville, Maryland. Recipient of the Nobel Prize in Medicine (1978).

The scientific advisors and the consultants are reimbursed for their expenses and receive nominal cash compensation in connection with their service and have been issued options to purchase shares of common stock. The scientific advisors and the consultants are all employed by or have consulting agreements with entities other than us, some of which may compete with us in the future. The scientific advisors and the consultants are expected to devote only a small portion of their time to our business, although no specific time commitment has been established. They are not expected to participate actively in our affairs or in the development of our technology. Several of the institutions with which the scientific advisors and the consultants are affiliated may adopt new regulations or policies that limit the ability of the scientific advisors and the consultants to consult with us. The loss of the services of the scientific advisors and the consultants could adversely affect us to the extent that we are pursuing research or development in areas relevant to the scientific advisors' and consultants' expertise. To the extent members of our scientific advisory board or the consultants have consulting arrangements with or become employed by any of our competitors, we could be materially adversely affected.

Any inventions or processes independently discovered by the scientific advisors or the consultants may not become our property and will probably remain the property of such persons or of such persons' employers. In addition, the institutions with which the scientific advisors and the consultants are affiliated may make available the research services of their personnel, including the scientific advisors and the consultants, to our competitors pursuant to sponsored research agreements. We require the scientific advisors and the consultants to enter into confidentiality agreements which prohibit the disclosure of confidential information to anyone outside of our company and require disclosure and assignment to us of their ideas, developments, discoveries or inventions. However, our competitors may gain access to trade secrets and other proprietary information developed by us and disclosed to the scientific advisors and the consultants.

Available Information

We have available a website on the Internet. Our address is www.biocryst.com. We make available at our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. We also make available at our website copies of our audit committee charter, compensation committee charter, corporate governance and nominating committee charter and our code of business conduct, which applies to all employees of BioCryst as well as the members of our Board of Directors.

ITEM 1A. RISK FACTORS

An investment in our stock involves a high degree of risk. You should consider carefully the following risks, along with all of the other information included in our other filings with the Securities and Exchange Commission, before deciding to buy our common stock. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also impair our business operations. If we are unable to prevent events that have a negative effect from occurring, then our business may suffer. Negative events are likely to decrease our revenue, increase our costs, make our financial results poorer and/or decrease our financial strength, and may cause our stock price to decline. In that case, you may lose all or a part of your investment in our common stock.

Risks Relating to Our Business

We have incurred substantial losses since our inception in 1986, expect to continue to incur such losses, and may never be profitable.

Since our inception in 1986, we have not been profitable. We expect to incur additional losses for the foreseeable future, and our losses could increase as our research and development efforts progress. As of December 31, 2005, our accumulated deficit was approximately $151.9 million. To become profitable, we must successfully develop drug product candidates, enter into profitable agreements with other parties and our product candidates must receive regulatory approval. We or these other parties must then successfully manufacture and market our product candidates. It could be several years, if ever, before we receive royalties from any current or future license agreements or revenues directly from product sales.

Because of the numerous risks and uncertainties associated with developing our product candidates and their potential for commercialization, we are unable to predict the extent of any future losses or when we will become profitable, 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. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

If we fail to obtain additional financing, we may be unable to complete the development and commercialization of our product candidates or continue our research and development programs.

To date, we have financed our operations primarily from sale of our equity securities and, to a lesser extent, revenues from collaborations and interest. In 2005, our operations consumed approximately $2.0 million per month. Our initial projection for 2006 is that our average burn rate for 2006 will be approximately $2.5 million per month. We expect that our monthly cash used by operations will continue to increase for the next couple of years as our clinical programs are expanded. We are planning to be in a Phase IIb pivotal trial with Fodosine™ in 2006 in T-cell leukemia and are in the early stages of clinical trials in several other indications with Fodosine™. As these trials increase in size and patient enrollment increases, our costs will increase. In addition, we expect our neuraminidase inhibitor, peramivir, to be in clinical trials in the first quarter of 2006 and our hepatitis C drug candidate, BCX-4678 to be in clinical trials during 2006. These additional trials and the related manufacturing, personnel resources and testing required to support these studies will consume significant capital resources and will increase our expenses and our net loss.

This monthly burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our existing partnerships for our drug candidates, the amount of funding or assistance we receive from governmental agencies or other new partnerships with third parties for the development of our drug candidates in general and for peramivir specifically, the progress and results of our current and proposed clinical trials for Fodosine™, peramivir and BCX-4678, the progress made in the manufacturing of our products and the progression of our other programs. As of December 31, 2005, we had $60.0 million in cash, cash equivalents and securities. We raised $30 million (approximately $29.9 million, net of expenses) in December 2005 through a sale of equity to provide the resources necessary to continue the development of our existing programs, while prudently maintaining our cash position. In addition, we established a collaborative relationship with Roche in November 2005 and a collaborative relationship with Mundipharma in February 2006, which provided additional cash in 2006, net of third party license fees, totaling approximately $32 million. Our long-term capital requirements and the adequacy of our available funds will depend upon many factors, including:

- the progress of our research, drug discovery and development programs;
- changes in existing collaborative relationships;
- our ability to establish additional collaborative relationships with academic institutions, biotechnology or pharmaceutical companies, governmental agencies or other third parties;
- the extent to which our collaborators, including governmental agencies will share in the costs associated with the development of our programs or run the development programs themselves;
- our ability to negotiate favorable development and marketing alliances for our drug product candidates;
- the magnitude of our research and development programs;
- the scope and results of preclinical studies and clinical trials to identify drug product candidates and the costs of manufacturing drug product to support these studies and trials;
- competitive and technological advances;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- our dependence on others for development and commercialization of our product candidates; and
- successful commercialization of our products consistent with our licensing strategy.

We will be required to raise additional capital to complete the development and commercialization of our current product candidates. Additional funding, whether through additional sales of securities or collaborative or other arrangements with corporate partners, governmental agencies or from other sources, may not be available when needed or on terms acceptable to us. The issuance of preferred or common stock or convertible securities, with terms and prices significantly more favorable than those of the currently outstanding common stock, could have the effect of diluting or adversely affecting the holdings or rights of our existing stockholders. In addition, collaborative arrangements may require us to transfer certain material rights to such corporate partners as described in the following risk factor related to collaborative relationships. Insufficient funds may require us to delay, scale-back or eliminate certain of our research and development programs.

If we fail to establish collaborative relationships to commercialize certain of our drug product candidates or if any collaborator terminates or fails to perform its obligations under agreements with us, the commercialization of our product candidates could be delayed or terminated.

A key aspect of our business strategy is to enter into successful collaborative arrangements with pharmaceutical companies, research institutions, the United States government and universities for the preclinical development, clinical development, regulatory approval, marketing, domestic and international sales and distribution of our drug product candidates. Our general strategy is to rely upon other parties for all of these steps so that we can focus exclusively on the key areas of our expertise. For some smaller niche markets, we may perform these steps ourselves and outsource those functions where we do not have the internal expertise.

Currently, we have established collaborative relationships with two pharmaceutical companies, Roche and Mundipharma for development and commercialization of BCX-4208 and Fodosine™, respectively. There is currently work being both planned and performed by various governmental agencies for the development of one of our drug candidates, peramivir, for the potential use in avian influenza. Any contracts with governmental agencies may not be completed on terms favorable to us, or at all, and any revenues under such contracts may not cover the development costs of our programs. The process of establishing collaborative relationships is difficult, time-consuming and involves significant uncertainty. Heavy reliance upon collaborative relationships with these third parties for these critical functions presents several risks, including:

- our collaborators may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements may expire;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration;
- we do not have day to day control over the activities of our collaborators and have limited control over their decisions;
- our ability to generate future event payments and royalties from our collaborators depends upon our collaborators' abilities to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and achieve market acceptance of products developed from our drug candidates;
- our collaborators may not properly maintain or defend our intellectual property rights, where applicable, or they may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our product candidates; and
- our partners may not comply with applicable government regulatory requirements.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our commercialization efforts related to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development of one or more of our product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our compounds would severely affect our business, because if our compounds do not progress through the development process or reach the market in a timely manner, or at all, we may not receive additional future event payments and may never receive product or royalty payments.

We have not commercialized any products or technologies and our future revenue generation is uncertain.

We have not yet commercialized any products or technologies, and we may never be able to do so. Our revenue from collaborative agreements is dependent upon the status of our preclinical and clinical programs. If we fail to advance these programs to the point of being able to enter into successful collaborations, we will not receive any future milestone or other collaborative payments.

Any future revenue directly from product sales would depend on our ability to successfully complete clinical studies, obtain regulatory approvals, manufacture, market and commercialize any approved drugs.

If our development collaborations with other parties fail, the development of our drug product candidates will be delayed or stopped.

We rely heavily upon other parties for many important stages of our drug development programs, including:

- discovery of proteins that cause or enable biological reactions necessary for the progression of the disease or disorder, called enzyme targets;
- licensing or design of enzyme inhibitors for development as drug product candidates;
- execution of some preclinical studies and late-stage development for our compounds and product candidates;

- management of our clinical trials, including medical monitoring and data management;
- execution of additional toxicology studies that may be required to obtain approval for our product candidates;
- manufacturing the starting materials required to formulate our drug products and the drug products to be used in both our clinical trials and toxicology studies;
- management of our regulatory function; and
- manufacturing, sales, marketing and distribution of our product candidates.

Our failure to engage in successful collaborations at any one of these stages would greatly impact our business. If we do not license enzyme targets or inhibitors from academic institutions or from other biotechnology companies on acceptable terms, our product development efforts would suffer. Similarly, if the contract research organizations that conduct our initial or late-stage clinical trials, conduct our toxicology studies, manufacture our starting materials and drug products or manage our regulatory function breached their obligations to us, this would delay or prevent the development of our product candidates.

Our development of both intravenous and intramuscular dosing of peramivir for avian flu is subject to all disclosed drug development and potential commercialization risks and numerous additional risks. Any potential revenue benefits to us are highly speculative.

We have reinitiated development of our influenza neuraminidase inhibitor, peramivir. Further development and potential commercialization of peramivir is subject to all the risks and uncertainties disclosed in our other risk factors relating to drug development and commercialization. In addition, potential commercialization of peramivir is subject to further risks, including the following:

- the injectable version of peramivir is at an early stage of development, has not been tested in humans and may not be safe or effective;
- necessary government or other third party funding and clinical testing for further development of peramivir may not be available timely, at all, or in sufficient amounts;
- the avian flu prevention or treatment concerns may not materialize at all, or in the near future;
- advances in flu vaccines could substantially replace potential demand for an antiviral such as peramivir;
- any substantial demand for avian flu treatments may occur before peramivir can be adequately developed and tested in clinical trials;
- numerous large and well-established pharmaceutical and biotech companies will be competing to meet the market demand for avian flu drugs and vaccines;
- regulatory authorities may not make needed accommodations to accelerate the drug testing and approval process for peramivir; and
- in the next few years, it is expected that a limited number of governmental entities will be the primary potential customers for peramivir. If we are not successful at marketing peramivir to these entities for any reason, we will not receive substantial revenues.

If any or all of these and other risk factors occur, we will not attain significant revenues or gross margins from peramivir and our stock price will be adversely affected.

Because we have limited manufacturing experience, we depend on third-party manufacturers to manufacture our drug product candidates and the materials for our product candidates. If we cannot rely on third-party manufacturers, we will be required to incur significant costs and potential delays in finding new third-party manufacturers.

We have limited manufacturing experience and only a small scale manufacturing facility. We currently rely upon third-party manufacturers to manufacture the materials required for our drug product candidates and most of the preclinical and clinical quantities of our product candidates. We depend on these third-party manufacturers to perform their obligations in a timely manner and in accordance with applicable governmental regulations. Our third-party manufacturers may encounter difficulties with meeting our requirements, including problems involving:

- inconsistent production yields;
- interruption of the delivery of materials required for the manufacturing process;
- scheduling of plant time with other vendors or unexpected equipment failure;
- potential catastrophes that could strike their facilities;
- poor quality control and assurance or inadequate process controls; and
- lack of compliance with regulations and specifications set forth by the FDA or other foreign regulatory agencies.

These contract manufacturers may not be able to manufacture the materials required or our drug product candidates at a cost or in quantities necessary to make them commercially viable. We also have no control over whether third-party manufacturers breach their agreements with us or whether they may terminate or decline to renew agreements with us. To date, our third party manufacturers have met our manufacturing requirements, but they may not continue to do so. Furthermore, changes in the manufacturing process or procedure, including a change in the location where the drug is manufactured or a change of a third-party manufacturer, may require prior review and approval in accordance with the FDA's current Good Manufacturing Practices, or cGMPs, and comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a product. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties.

If we are unable to enter into agreements with additional manufacturers on commercially reasonable terms, or if there is poor manufacturing performance on the part of our third party manufacturers, we may not be able to complete development of, or market, our product candidates.

Our raw materials, drug substances, and drug products are manufactured by a limited group of suppliers and some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of drugs for further preclinical testing and clinical trials.

We may be unable to establish sales, marketing and distribution capabilities necessary to successfully commercialize products we may successfully develop.

We currently have no marketing capability and no direct or third-party sales or distribution capabilities. If we successfully develop a drug product candidate and decide to commercialize it ourselves rather than relying on third parties, as we are considering doing in the United States for Fodosine™, we may be unable to establish marketing, sales and distribution capabilities necessary to commercialize and gain market acceptance for that product.

If the clinical trials of our drug product candidates fail, our product candidates will not be marketed, which would result in a complete absence of product related revenue.

To receive the regulatory approvals necessary for the sale of our product candidates, we or our licensees must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective. If we or other third party collaborators are unable to demonstrate that our product candidates are safe and effective, our product candidates will not receive regulatory approval and will not be marketed, which would result in a complete absence of product related revenue. The clinical trial process is complex and uncertain. Because of the cost and duration of clinical trials, we may decide to discontinue development of product candidates that are either unlikely to show good results in the trials or unlikely to help advance a product to the point of a meaningful collaboration. Positive results from preclinical studies and early clinical trials do not ensure positive results in clinical trials designed to permit application for regulatory approval, called pivotal clinical trials. We may suffer significant setbacks in pivotal clinical trials, even after earlier clinical trials show promising results. Any of our product candidates may produce undesirable side effects in humans. These side effects could cause us or regulatory authorities to interrupt, delay or halt clinical trials of a product candidate. These side effects could also result in the FDA or foreign regulatory authorities refusing to approve the product candidate for any targeted indications. We, our licensees, the FDA or foreign regulatory authorities may suspend or terminate clinical trials at any time if we or they believe the trial participants face unacceptable health risks. Clinical trials may fail to demonstrate that our product candidates are safe or effective.

We are negotiating a special protocol assessment, or SPA, of the clinical trial protocol for the proposed Phase IIb clinical trial of Fodosine™ in T-cell leukemia. An SPA is an agreement between an applicant and the FDA on the design and the size of clinical trials that is intended to form the basis of a New Drug Application ("NDA"). In connection with an SPA, an applicant may decide, or the FDA may require the applicant, to modify the proposed protocol by, for example, changing the proposed primary endpoint, the size of the study or otherwise, which may result in a delay in the initiation or completion of the clinical trials that are the subject of the SPA. These changes could arise from a change in the standard of care for the proposed indication or other aspects of the protocol for the proposed clinical trials. If the FDA and an applicant reach an agreement on an SPA, the SPA cannot be changed after the clinical trial begins, except in limited circumstances such as a change in the science or clinical knowledge about the conditions being studied. Any significant change to the protocols for a clinical trial subject to an SPA would require prior FDA approval, which could delay implementation of such a change and continuation and completion of the related clinical trial.

Clinical trials are lengthy and expensive. We or our collaborators incur substantial expense for, and devote significant time to, preclinical testing and clinical trials, yet cannot be certain that the tests and trials will ever result in the commercial sale of a product. For example, clinical trials require adequate supplies of drug and sufficient patient enrollment. Delays in patient enrollment can result in increased costs and longer development times. Even if we or our licensees successfully complete clinical trials for our product candidates, we or our licensees might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the product candidate.

If we or our licensees do not obtain and maintain governmental approvals for our products under development, we or our partners will not be able to sell these potential products, which would significantly harm our business because we will receive no revenue.

We or our licensees must obtain regulatory approval before marketing or selling our future drug products. If we or our licensees are unable to receive regulatory approval and do not market or sell our future drug products, we will never receive any revenue from such product sales. In the United States, we or our partners must obtain FDA approval for each drug that we intend to commercialize. The FDA approval process is typically lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. The FDA or foreign regulatory agencies have not approved any of our drug product candidates. If we or our licensees fail to obtain regulatory approval we will be unable to market and sell our future drug products. We have several drug products in various stages of preclinical and clinical development; however, we are unable to determine when, if ever, any of these products will be commercially available. Because of the risks and uncertainties in biopharmaceutical development, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. If the FDA delays regulatory approval of our product candidates, our management's credibility, our company's value and our operating results may suffer. Even if the FDA or foreign regulatory agencies approve a product candidate, the approval may limit the indicated uses for a product candidate and/or may require post-marketing studies.

The FDA regulates, among other things, the record keeping and storage of data pertaining to potential pharmaceutical products. We currently store most of our preclinical research data at our facility. While we do store duplicate copies of most of our clinical data offsite, we could lose important preclinical data if our facility incurs damage. If we get approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements. These requirements are wide ranging and govern, among other things:

- adverse drug experience reporting regulations;
- product promotion;
- product manufacturing, including good manufacturing practice requirements; and
- product changes or modifications.

Our failure to comply with existing or future regulatory requirements, or our loss of, or changes to, previously obtained approvals, could have a material adverse effect on our business because we will not receive product or royalty revenues if we or our licensees do not receive approval of our products for marketing.

In June 1995, we notified the FDA that we submitted incorrect data for our Phase II studies of BCX-34 applied to the skin for CTCL and psoriasis. The FDA inspected us in November 1995 and issued us a List of Inspectional Observations, Form FDA 483, which cited our failure to follow good clinical practices. The FDA also inspected us in June 1996. The focus was on the two 1995 Phase II dose-ranging studies of topical BCX-34 for the treatment of CTCL and psoriasis. As a result of the investigation, the FDA issued us a Form FDA 483, which cited our failure to follow good clinical practices. We are no longer developing BCX-34; however, as a consequence of these two investigations, our ongoing and future clinical studies may receive increased scrutiny, which may delay the regulatory review process.

If our drug product candidates do not achieve broad market acceptance, our business may never become profitable.

Our drug product candidates may not gain the market acceptance required for us to be profitable even if they successfully complete initial and final clinical trials and receive approval for sale by the FDA or foreign regulatory agencies. The degree of market acceptance of any product candidates that we or our partners develop will depend on a number of factors, including:

- our clinical evidence of safety and efficacy;
- cost-effectiveness, convenience and ease of use of our product candidates;
- their safety, availability and effectiveness relative to alternative treatments;
- the actual and potential side effects or other reactions;
- reimbursement policies of government and third-party payers; and
- the effectiveness of marketing and distribution support for our product candidates.

Physicians, patients, payers or the medical community in general may not accept or use our product candidates even after the FDA or foreign regulatory agencies approve the drug candidates. If our product candidates do not achieve significant market acceptance, we will not have enough revenues to become profitable.

We face intense competition, and if we are unable to compete effectively, the demand for our products, if any, may be reduced.

The biotechnology and pharmaceutical industries are highly competitive and subject to rapid and substantial technological change. We face, and will continue to face, competition in the licensing of desirable disease targets, licensing of desirable drug product candidates, and development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things:

- other drug development technologies;
- methods of preventing or reducing the incidence of disease, including vaccines; and
- new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive.

We and our licensees are performing research on or developing products for the treatment of several disorders including T-cell mediated disorders (T-cell cancers, psoriasis, transplant rejection, and rheumatoid arthritis), oncology, influenza, hepatitis C and cardiovascular disorders. We expect to encounter significant competition for any of the pharmaceutical products we plan to develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage. Such is the case with GSK's Arranon for T-cell ALL and the current neuraminidase inhibitors marketed by GSK and Roche for influenza. In addition, several pharmaceutical and biotechnology firms, including major pharmaceutical companies and specialized structure-based drug design companies, have announced efforts in the field of structure-based drug design and in the fields of PNP, hepatitis C, influenza, and tissue factor/factor VIIa. If one or more of our competitors' products or programs are successful, the market for our products may be reduced or eliminated.

Compared to us, many of our competitors and potential competitors have substantially greater:

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- preclinical study and clinical testing experience;
- manufacturing and marketing experience; and
- production facilities.

Any of these competitive factors could reduce demand for our products.

If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of those rights would diminish.

Our success will depend in part on our ability and the abilities of our collaborators to obtain patent protection for our products, methods, processes and other technologies we may license or develop, to preserve our trade secrets, and to operate without infringing the proprietary rights of third parties both domestically and abroad. The patent position of biotechnology and pharmaceutical companies is generally highly uncertain, involves complex legal and factual questions and has recently been the subject of much litigation. Neither the United States Patent and Trademark Office ("USPTO"), nor the courts have a consistent policy regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology and pharmaceutical patents. The validity, enforceability and commercial value of these rights, therefore, is highly uncertain.

Our success depends in part on avoiding the infringement of other parties' patents and proprietary rights as well as avoiding the breach of any licenses relating to our technologies and products. In the U.S., patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third-party patents or proprietary rights. These third parties could bring claims against us, our collaborators or our licensors that even if

resolved in our favor, could cause us to incur substantial expenses and, if resolved against us, could additionally cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, our collaborators or our licensors, we or they could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent we infringe, unless we can obtain a license from the patent holder. Such a license may not be available on acceptable terms, or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we, our collaborators or our licensors were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

If we or our partners are unable to adequately protect or enforce our intellectual property rights for our products, methods, processes and other technologies, the value of the drug product candidates that we license to derive revenue would diminish. Additionally, if our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO has issued to us a number of U.S. patents for our various inventions and we have in-licensed several patents from various institutions. We have filed additional patent applications and provisional patent applications with the USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U.S. patent applications, as appropriate. We cannot assure you as to:

- the degree and range of protection any patents will afford against competitors with similar products;
- if and when patents will issue; or
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

If the USPTO upholds patents issued to others or if the USPTO grants patent applications filed by others, we may have to:

- obtain licenses or redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in those patents; or
- pay damages.

We may initiate, or others may bring against us, litigation or administrative proceedings related to intellectual property rights, including proceedings before the USPTO. Any judgment adverse to us in any litigation or other proceeding arising in connection with a patent or patent application could materially and adversely affect our business, financial condition and results of operations. In addition, the costs of any such proceeding may be substantial whether or not we are successful.

Our success is also dependent upon the skills, knowledge and experience, none of which is patentable, of our scientific and technical personnel. To help protect our rights, we require all employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to anyone outside of our company and require disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information, and if any of our proprietary information is disclosed, our business will suffer because our revenues depend upon our ability to license our technology and any such events would significantly impair the value of such a license.

If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our drug product candidates and the expansion of our business will be delayed or stopped.

We are highly dependent upon our senior management and scientific team, the loss of whose services might impede the achievement of our development and commercial objectives. Competition for key personnel with the experience that we require is intense and is expected to continue to increase. Our inability to attract and retain the required number of skilled and experienced management, operational and scientific personnel, will harm our business because we rely upon these personnel for many critical functions of our business. In addition, we rely on members of our scientific advisory

board and consultants to assist us in formulating our research and development strategy. All of the members of the scientific advisory board and all of our consultants are otherwise employed and each such member or consultant may have commitments to other entities that may limit their availability to us.

If users of our drug products are not reimbursed for use, future sales of our drug products will decline.

The lack of reimbursement for the use of our product candidates by hospitals, clinics, patients or doctors will harm our business. Medicare, Medicaid, health maintenance organizations and other third-party payers may not authorize or otherwise budget for the reimbursement of our products. Governmental and third-party payers are increasingly challenging the prices charged for medical products and services. We cannot be sure that third-party payers would view our product candidates as cost-effective, that reimbursement will be available to consumers or that reimbursement will be sufficient to allow our product candidates to be marketed on a competitive basis. Changes in reimbursement policies, or attempts to contain costs in the health care industry could limit or restrict reimbursement for our product candidates and would materially and adversely affect our business, because future product sales would decline and we would receive less product or royalty revenue.

The Medicare prescription drug coverage legislation and future legislative or regulatory reform of the healthcare system may affect our ability to sell our products profitably.

In the United States, there have been a number of legislative and regulatory proposals, at both the federal and state government levels, to change the healthcare system in ways that could affect our ability to sell our products profitably, if approved. For example, the Medicare Prescription Drug and Modernization Act of 2003 ("MMA"), went into effect on January 1, 2006 and has changed the types of drugs covered by Medicare, and the methodology used to determine the price for such drugs. Further federal and state proposals and healthcare reforms are likely. Our business could be harmed by the MMA, by the possible effect of this legislation on amounts that private payors will pay and by other healthcare reforms that may be enacted or adopted in the future.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face even greater risks upon any commercialization by us of our product candidates. We have product liability insurance covering our clinical trials in the amount of $7 million, which we currently believe is adequate to cover any product liability exposure we may have. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available;
- an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, or at all;
- withdrawal of clinical trial volunteers or patients;
- damage to our reputation and the reputation of our products, resulting in lower sales;
- regulatory investigations that could require costly recalls or product modifications;
- litigation costs; and
- the diversion of management's attention from managing our business.

If our computer systems fail or our facility incurs damage, our business will suffer.

Our drug development activities depend on the security, integrity and performance of the computer systems supporting them, and the failure of our computer systems could delay our drug development efforts. We currently store most of our preclinical and clinical data at our facility. Duplicate copies of most critical data are stored off-site in a bank vault. Any significant degradation or failure of our computer systems could cause us to inaccurately calculate or lose our data. Loss of data could result in significant delays in our drug development process and any system failure could harm our business and operations.

In addition, we store numerous clinical and stability samples at our facility that could be damaged if our facility incurred physical damage or in the event of an extended power failure. We have backup power systems in addition to backup generators to maintain power to all critical functions, but any loss of these samples could result in significant delays in our drug development process.

If, because of our use of hazardous materials, we violate any environmental controls or regulations that apply to such materials, we may incur substantial costs and expenses in our remediation efforts.

Our research and development involves the controlled use of hazardous materials, chemicals and various radioactive compounds. We are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and some waste products. Accidental contamination or injury from these materials could occur. In the event of an accident, we could be liable for any damages that result and any liabilities could exceed our resources. Compliance with environmental laws and regulations could require us to incur substantial unexpected costs, which would materially and adversely affect our results of operations.

Risks Relating to Our Common Stock

Our stock price is likely to be highly volatile and the value of your investment could decline significantly.

The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future. Moreover, our stock price has fluctuated frequently, and these fluctuations are often not related to our financial results. For the twelve months ended December 31, 2005, the 52-week range of the market price of our stock was from $3.68 to $18.64 per share. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- announcements of technological innovations or new products by us or our competitors;
- developments or disputes concerning patents or proprietary rights;
- status of new or existing licensing or collaborative agreements;
- we or our licensees achieving or failing to achieve development milestones;
- publicity regarding actual or potential medical results relating to products under development by us or our competitors;
- publicity regarding certain public health concerns for which we are or may be developing treatments;
- regulatory developments in both the United States and foreign countries;
- public concern as to the safety of pharmaceutical products;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- changes in the structure of healthcare payment systems, including developments in price control legislation;

- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- additions or departures of key personnel or members of our board of directors;
- sales of substantial amounts of our stock by existing stockholders, including officers or directors;
- economic and other external factors or other disasters or crises; and
- period-to-period fluctuations in our financial results.

Because stock ownership is concentrated, you and other investors will have limited influence on stockholder decisions.

As of December 31, 2005, our directors, executive officers and some principal stockholders and their affiliates beneficially owned approximately 34.1% of our outstanding common stock and common stock equivalents. As a result, these holders, if acting together, are able to significantly influence matters requiring stockholder approval, including the election of directors. This concentration of ownership may delay, defer or prevent a change in our control.

We have anti-takeover provisions in our corporate charter documents that may result in outcomes with which you do not agree.

Our board of directors has the authority to issue up to 3,178,500 shares of undesignated preferred stock and to determine the rights, preferences, privileges and restrictions of those shares without further vote or action by our stockholders. The rights of the holders of any preferred stock that may be issued in the future may adversely affect the rights of the holders of common stock. The issuance of preferred stock could make it more difficult for third parties to acquire a majority of our outstanding voting stock.

In addition, our certificate of incorporation provides for staggered terms for the members of the board of directors and supermajority approval of the removal of any member of the board of directors and prevents our stockholders from acting by written consent. Our certificate also requires supermajority approval of any amendment of these provisions. These provisions and other provisions of our by-laws and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us.

In June 2002, our board of directors adopted a stockholder rights plan and, pursuant thereto, issued preferred stock purchase rights ("Rights") to the holders of our common stock. The Rights have certain anti-takeover effects. If triggered, the Rights would cause substantial dilution to a person or group of persons who acquires more than 15% (19.9% for William W. Featheringill, a Director who owned approximately 9.95% as of December 31, 2005, but owned more than 15% at the time the Rights were put in place) of our common stock on terms not approved by the board of directors.

We have never paid dividends on our common stock and do not anticipate doing so in the foreseeable future.

We have never paid cash dividends on our stock. We currently intend to retain all future earnings, if any, for use in the operation of our business. Accordingly, we do not anticipate paying cash dividends on our common stock in the foreseeable future.

Information Regarding Forward-Looking Statements

This discussion contains forward-looking statements, which are subject to risks and uncertainties. These forward-looking statements can generally be identified by the use of words such as "may," "will," "intends," "plans," "believes," "anticipates," "expects," "estimates," "predicts," "potential," the negative of these words or similar expressions. Statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements are principally contained in "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations", as well as any amendments we make to those sections in filings with the SEC. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical and clinical trials, research and development programs;
- the further preclinical or clinical development and commercialization of our product candidates;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our ability to establish and maintain collaborations with biotechnology or pharmaceutical companies and governmental agencies or other third parties;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our ability to operate our business without infringing the intellectual property rights of others;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the timing or likelihood of regulatory filings and approvals;
- our negotiations with the FDA for a special protocol assessment;
- our financial performance; and
- competitive companies, technologies and our industry.

These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail in “Risk Factors.” Also, these forward-looking statements represent our estimates and assumptions only as of the date of this document.

You should read this discussion completely and with the understanding that our actual future results may be materially different from what we expect. We may not update these forward-looking statements, even though our situation may change in the future. We qualify all of our forward-looking statements by these cautionary statements.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our administrative offices and principal research facility are located in 50,150 square feet of leased office space in Riverchase Industrial/Research Park in Birmingham, Alabama. The lease runs through June 30, 2010 with an option to lease for an additional five years at current market rates. We believe that our facilities are adequate for our current operations.

ITEM 3. LEGAL PROCEEDINGS

None.

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

None.

PART II

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

Our common stock trades on the Nasdaq National Market tier of The Nasdaq Stock MarketSM under the symbol BCRX. The following table sets forth the low and high bid prices of our common stock as reported by Nasdaq for each quarter in 2005 and 2004:

	2005		2004	
	Low	High	Low	High
First quarter	$ 4.32	$ 6.91	$ 6.24	$ 8.75
Second quarter	3.68	5.25	6.75	11.25
Third quarter	4.90	10.44	4.37	7.56
Fourth quarter	9.70	18.64	4.63	6.94

The last sale price of the common stock on March 3, 2006 as reported by Nasdaq was $20.75 per share.

As of March 3, 2006, there were approximately 285 holders of record of our common stock.

We have never paid cash dividends and does not anticipate paying cash dividends in the foreseeable future.

ITEM 6. SELECTED FINANCIAL DATA

Statement of Operations Data:	Years Ended December 31, (Dollars in thousands, except per share data) 2005	2004	2003	2002	2001
Total revenues	$ 152	$ 337	$ 653	$ 0	$ 7,737
Research and development expenses	23,643	18,868	11,522	15,473	13,091
Net loss	(26,099)	(21,104)	(12,700)	(16,929)	(4,986)
Amounts per common share:					
Basic and diluted net loss per share	$ (1.01)	$ (1.00)	$ (.72)	$ (.96)	$ (.28)
Weighted average shares outstanding (in thousands)	25,721	21,165	17,703	17,643	17,560

Balance Sheet Data:	December 31, (Dollars in thousands) 2005	2004	2003	2002	2001
Cash, cash equivalents and securities	$ 59,988	$ 28,704	$ 25,732	$ 36,163	$ 52,941
Total assets	99,248	32,469	30,096	41,300	59,096
Long-term deferred revenue	29,426	300	300	300	300
Accumulated deficit	(151,863)	(125,764)	(104,660)	(91,960)	(75,031)
Total stockholders' equity	58,440	29,334	28,447	40,128	56,814

Note: In 2001, the license agreement for the development and commercialization of the Company's influenza neuraminidase inhibitors with RWJPRI and Ortho-McNeil was terminated. At the date of termination, all non-refundable license fees and milestone payments that had been deferred, but not yet recognized were fully recognized as revenue in the current period.

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

This Annual Report on Form 10-K contains certain statements of a forward-looking nature relating to future events or the future financial performance of BioCryst. Such statements are only predictions and the actual events or results may differ materially from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include those discussed below as well as those discussed in other filings made by BioCryst with the Securities and Exchange Commission.

This discussion of our financial condition and results of operations should be read together with Item 1, Business and the financial statements, including the notes thereto, contained in Item 8 of this Form 10-K.

Overview

Since our inception in 1986, we have been engaged in research and development activities and organizational efforts, including:

- identifying and licensing enzyme targets;
- drug discovery;
- structure-based design of drug candidates;
- small-scale synthesis of compounds;
- conducting preclinical studies and clinical trials;
- establishing collaborative relationships with third parties for contract research related to the development of our drug candidates to support manufacturing, clinical development and regulatory compliance;
- establishing collaborative relationships with biotechnology or pharmaceutical companies and governmental agencies or other third parties for the further development and potential commercialization of our compounds;
- recruiting our scientific and management personnel;
- establishing laboratory facilities; and
- raising capital.

Our revenues have generally been limited to license fees, milestone payments, research and development fees, and interest income. Revenue is recognized in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* ("SAB No. 104") and Emerging Issues Task Force Issue 00-21, *Revenue Arrangements with Multiple Deliverables* ("EITF Issue 00-21"). License fees, milestone payments, and research and development fees are recognized as revenue when the earnings process is complete and we have no further continuing performance obligations or we have completed the performance obligations under the terms of the agreement. Fees received under licensing agreements that are related to future performance are deferred and recognized as earned over an estimated period determined by management based on the terms of the agreement and the products licensed. For example, in the Roche and Mundipharma licenses agreements, we have determined to defer the upfront payments over the remaining life of the patents which are 17 years and 12 years, respectively. In the event a license agreement contains multiple deliverables, we evaluate whether the deliverables are separate or combined units of accounting in accordance with EITF Issue 00-21. Revisions to revenue or profit estimates as a result of changes in the estimated revenue period are recognized prospectively.

Milestone payments are recognized as revenue upon the achievement of specified milestone events if (1) the milestone is substantive in nature and the achievement of the milestone was not reasonably assured at the inception of the agreement and (2) the fees are non-refundable and non-creditable. Any milestone payments received prior to satisfying these criteria are recorded as deferred revenue.

Significant direct costs incurred upon entering into a licensing arrangement are deferred and charged to expense in proportion to the revenue recognized. Under the guidance of Emerging Issues Task Force Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* ("EITF Issue 99-19"), and Emerging Issues Task Force Issue 01-14, *Income Statement Characterization of Reimbursements Received for "Out-of-Pocket" Expenses* ("EITF Issue 01-14"), reimbursements received for direct out-of-pocket expenses related to research and development costs are recorded as revenue in the income statement rather than as a reduction in expenses.

Royalty revenue is recognized based on estimates of royalties earned during the applicable period and adjusted for differences between the estimated and actual royalties in the following period. If royalties can not be reasonably estimated, revenue is recognized upon receipt of royalty statements from the licensee. We have not received any royalties from the sale of licensed pharmaceutical products.

It could be several years, if ever, before we will recognize significant revenue from royalties received pursuant to our license agreements or revenue directly from product sales. Future revenues, if any, are likely to fluctuate substantially from quarter to quarter.

We have incurred operating losses since our inception. Our accumulated deficit at December 31, 2005 was $151.9 million. We expect to incur substantial expenditures relating to the development of our current and future drug candidates. During the three years ended December 31, 2005, we spent 54.6% of our research and development expenses on contract research and development, including:

- payments to consultants;
- funding of research at academic institutions;
- toxicology studies on existing and potential drugs;
- manufacturing of our raw materials, drug substance and drug products;
- large scale synthesis and formulation of compounds;
- preclinical studies;
- engaging investigators to conduct clinical trials;
- hiring contract research organizations for regulatory and clinical functions; and
- using statisticians to evaluate the results of clinical trials.

The above expenditures for contract research and development for our current and future drug candidates will vary from quarter-to-quarter depending on the status of our research and development projects. For example, during the third quarter of 2005, we initiated a Phase I trial in healthy volunteers for our lead drug candidate, Fodosine™, an inhibitor of purine nucleoside phosphorylase ("PNP"). Results from this trial will be used to assist in facilitating the design of a proposed Phase IIb pivotal clinical program in patients with T-cell leukemia, using a combination of intravenous and oral formulations of Fodosine™. In addition, during the third quarter of 2005, we initiated a Phase II clinical trial of Fodosine™ in patients with advanced, fludarabine-refractory chronic lymphocytic leukemia ("CLL") and in the fourth quarter of 2005 we announced the initiation of a Phase I/II clinical trial of Fodosine™ in patients with B-cell ALL. As these trials progress and additional trials are started in other indications, our costs for clinical studies will increase significantly. In addition, the costs associated with the manufacturing of Fodosine™, peramivir and BCX-4678 will increase as we scale up to the larger production runs required for both clinical development and additional toxicology studies required for each of these programs.

Changes in our existing and future research and development and collaborative relationships also will impact the status of our research and development projects. For example, in November 2005 we entered into a license agreement with Roche for the worldwide development and commercialization for our second PNP inhibitor, BCX-4208. In addition to an upfront payment plus an advance payment for some manufacturing we will perform, Roche will take over the development and pay all costs associated with this program. In February 2006, we licensed Fodosine™ to Mundipharma for the development and commercialization of this drug in Europe, Asia and Australasia. In addition to the upfront payment of $10 million, Mundipharma will pay 50% of the clinical development costs we will incur for Fodosine™ on existing and planned clinical trials, but their portion shall not exceed $10 million.

Although we may, in some cases, be able to control the timing of development expenses, in part by accelerating or decelerating certain of these costs, many of these costs will be incurred irrespective of whether we are able to discover drug candidates or obtain collaborative partners for commercialization. As a result, we believe that quarter-to-quarter comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of future performance. If we fail to meet the research, clinical and financial expectations of securities analysts and investors, it could have a material adverse effect on the price of our common stock.

Year Ended December 31, 2005 Compared with the Year Ended December 31, 2004

Collaborative and other research and development revenue was $152,000 for the year compared to $337,000 for 2004 due to completion of work performed under the NIH grant for hepatitis C during 2005. Also, there was an NIH grant during 2004 for our TF/FVIIa program that totaled approximately $100,000, which was completed in 2004.

Research and development expenses for 2005 were $23,642,000, a 25.3% increase from 2004 expenses of $18,868,000, which is directly related to the additional contract research, clinical trial and toxicology expenses required for the further development of our lead drug candidates during 2005 and an increase in personnel costs.

General and administrative expenses for 2005 were $3,686,000, an increase of 14.4% over the 2004 expense of $3,221,000, primarily due to an increase in legal fees related to our recently announced partnerships and an increase in personnel related expenses.

Interest income for 2005 was $1,078,000, a 66.4% increase compared to $648,000 in 2004. This increase was due to a higher average cash balance during 2005 and a more favorable interest rate environment as compared to 2004.

The net loss for the year ended December 31, 2005 was $26,099,000, or $1.01 per share, compared to a net loss of $21,104,000, or $1.00 per share in 2004.

Year Ended December 31, 2004 Compared with the Year Ended December 31, 2003

Collaborative and other research and development revenues decreased in 2004 to $337,000 compared to $653,000 in 2003, primarily due to a payment in 2003 from 3-Dimensional Pharmaceuticals Inc. (“3DP”), a wholly-owned subsidiary of Johnson & Johnson, for certain rights related to complement system inhibitors discovered during the term of our collaborative research agreement. Our 2004 revenue was entirely related to grants from the NIH for support of our HCV and TF/FVIIa programs, while for 2003 our revenue included only $153,000 from the NIH.

Research and development expenses increased 63.8% to $18,868,000 for 2004 from $11,522,000 in 2003. The increase in expenses during 2004 was directly related to contract and clinical costs associated with the development of both of our lead drug candidates during 2004. These costs primarily consisted of manufacturing, toxicology, clinical development and regulatory affairs charges, which were essential to the continuing development of these programs.

General and administrative expenses increased 14.5% to $3,221,000 in 2004 from $2,812,000 in 2003, primarily due to an increase in consulting and professional fees related to compliance with section 404 of the Sarbanes-Oxley Act of 2002 and for the strategic development of our lead drug candidate.

Interest income for 2004 was $648,000, a 33.9% decrease compared to $980,000 in 2003. This decrease was due to a lower interest rate environment in 2004.

The net loss for the year ended December 31, 2004 was $21,104,000, or $1.00 per share, compared to a net loss of $12,700,000, or $0.72 per share in 2003.

Liquidity and Capital Resources

Cash expenditures have exceeded revenues since our inception. Our operations have principally been funded through public offerings and private placements of equity and debt securities. For example, during February 2005, we raised $23.9 million (approximately $22.7 million net of expenses) through the sale of 4,350,000 shares of our common stock and during December 2005, we raised $30.0 million (approximately $29.9 million net of expenses) through a sale of 2,228,829 shares of our common stock. Other sources of funding have included the following:

- equipment lease financing;
- facility leases;
- collaborative and other research and development agreements (such as the Roche and Mundipharma licenses);
- research grants; and
- interest income.

In addition, we have attempted to contain costs and reduce cash flow requirements by renting scientific equipment and facilities, contracting with other parties to conduct certain research and development and using consultants. We expect to incur additional expenses, potentially resulting in significant losses, as we continue to pursue our research and development activities, undertake additional preclinical studies and clinical trials of compounds which have been or may be discovered and as we increase the manufacturing of our compounds for clinical trials and toxicology studies. We also expect to incur substantial expenses related to the filing, prosecution, maintenance, defense and enforcement of patent and other intellectual property claims and additional regulatory costs as our clinical products advance through later stages of development.

We invest our excess cash principally in U.S. marketable securities from a diversified portfolio of institutions with strong credit ratings and in U.S. government and agency bills and notes, and by policy, limit the amount of credit exposure at any one institution. These investments are generally not collateralized and mature within three years. We have not realized any losses from such investments. In addition, at December 31, 2005, approximately $21.9 million was invested in the Merrill Lynch Premier Institutional Fund, a money market mutual fund that invests in near cash securities with weighted average maturities of less than 90 days. The Merrill Lynch Premier Institutional Fund is not insured.

We have financed some of our equipment purchases with lease lines of credit. In July 2000, we renegotiated our lease for our current facilities, which will expire on June 30, 2010. We have an option to renew the lease for an additional five years at the current market rate in effect on June 30, 2010 and a one-time option to terminate the lease on June 30, 2008 for a termination fee of approximately $124,000. The lease, as amended effective December 1, 2005 for a reduction of 7,200 square feet, requires us to pay monthly rent starting at $36,855 per month in December 2005 and escalating annually to a minimum of $41,481 per month in the final year, plus our pro rata share of operating expenses and real estate taxes in excess of base year amounts. As part of the lease, we have deposited a U.S. Treasury security in escrow for the payment of rent and performance of other obligations specified in the lease. This pledged amount is currently $196,000, which can be decreased by $65,000 annually throughout the term of the lease. Currently, we have approximately 3,600 square feet being subleased, which can be terminated with 30 days written notice.

We have not incurred any significant charges related to new equipment or building renovations since 2001 and currently have no plans for any significant renovations, but our purchases of additional equipment during 2006 could exceed $1 million.

At December 31, 2005, we had long-term operating lease obligations, which provide for aggregate minimum payments of $533,904 in 2006, $486,119 in 2007 and $496,834 in 2008. These obligations include the future rental of our operating facility.

We plan to finance our needs principally from the following:

- our existing capital resources and interest earned on that capital;
- payments under collaborative and licensing agreements with corporate partners; and
- lease or loan financing and future public or private financing.

We believe that our currently available funds will be sufficient to fund our operations at least through 2008. However, this is a forward looking statement, and there may be changes that would consume available resources significantly before such time. Our long-term capital requirements and the adequacy of our available funds will depend upon many factors, including:

- the progress and magnitude of our research, drug discovery and development programs;
- changes in existing collaborative relationships;
- our ability to establish additional collaborative relationships with academic institutions, biotechnology or pharmaceutical companies and governmental agencies or other third parties;
- the extent to which our collaborators, including governmental agencies will share in the costs associated with the development of our programs or run the development programs themselves;
- our ability to negotiate favorable development and marketing strategic alliances for our drug candidates;
- the scope and results of preclinical studies and clinical trials to identify drug candidates;
- the scope of manufacturing of our drug candidates to support our preclinical research and clinical trials;
- the scope of validation for the manufacturing of our drug substance and drug products required for future NDA filings;
- competitive and technological advances;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- our dependence on others for development and commercialization of our product candidates; and
- successful commercialization of our products consistent with our licensing strategy.

To date, we have financed our operations primarily from sale of our equity securities and, to a lesser extent, revenues from collaborations and interest. In 2005, our operations consumed approximately $2.0 million per month. Our initial projection for 2006 is that our average burn rate for 2006 will be approximately $2.5 million per month. We expect that our monthly cash used by operations will continue to increase for the next couple of years as our clinical programs are expanded. We are planning to be in a Phase IIb pivotal trial with Fodosine™ in 2006 in T-cell leukemia and are in the early stages of clinical trials in several other indications with Fodosine™. As these trials increase in size and patient enrollment increases, our costs will increase. In addition, we expect our neuraminidase inhibitor, peramivir, to be in clinical trials in the first quarter of 2006 and our HCV drug candidate, BCX-4678 to be in clinical trials during 2006. These additional trials and the related manufacturing, personnel resources and testing required to support these studies will consume significant capital resources and will increase our expenses and our net loss.

This monthly burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our existing partnerships for our drug candidates, the amount of funding or assistance we receive from governmental agencies or other new partnerships with third parties for the development of our drug candidates in general and for peramivir specifically, the progress and results of our current and proposed clinical trials for Fodosine™, peramivir and BCX-4678, the progress made in the manufacturing of our products and the progression of our other programs.

As of December 31, 2005, we had $60.0 million in cash, cash equivalents and securities. This includes approximately $30 million raised in December 2005 through a sale of equity, which provided additional resources to continue the development of our existing programs, while prudently maintaining our cash position. In addition, we established a collaborative relationship with Roche in November 2005 and a collaborative relationship with Mundipharma in February 2006, which provided additional cash in 2006, net of third party license fees, totaling approximately $32 million.

The collaboration with Roche for the worldwide development and commercialization of BCX-4208 provided an upfront payment plus an advance payment for specific manufacturing we will perform. This initial $30 million was recorded as a receivable on our balance sheet at December 31, 2005 and was received in January 2006. Roche will take over the development and pay all costs associated with this program. The agreement also provides for future event payments and royalties to be made by Roche upon the achievement of certain clinical, regulatory and sales events.

In February 2006, we licensed Fodosine™ to Mundipharma for the development and commercialization of this drug in Europe, Asia and Australasia. In addition to the upfront payment of $10 million, Mundipharma will pay 50% of the clinical development costs we will incur for Fodosine™ on existing and planned clinical trials, but their portion shall not exceed $10 million. In addition, Mundipharma will conduct additional clinical trials at their own cost up to a maximum of $15 million. The agreement also provides for future event payments and royalties to be made by Mundipharma upon the achievement of certain clinical, regulatory and sales events.

Due to the nature of the potential milestones in our collaborations, it is difficult to predict if and when particular milestones will be achieved by us or our collaborators. However, we hope to reach at least one milestone in each of the collaborations during 2006, which would provide additional cash upon the achievement of the specific milestone reached. All future event payments are non-refundable under our current collaborations, net of sublicense payments, and would be fully available to offset our projected burn rate.

We will be required to raise additional capital to complete the development and commercialization of our current product candidates. Additional funding, whether through additional sales of securities or collaborative or other arrangements with corporate partners or from other sources, may not be available when needed or on terms acceptable to us. The issuance of preferred or common stock or convertible securities, with terms and prices significantly more favorable than those of the currently outstanding common stock, could have the effect of diluting or adversely affecting the holdings or rights of our existing stockholders. In addition, collaborative arrangements may require us to transfer certain material rights to such corporate partners. Insufficient funds may require us to delay, scale-back or eliminate certain of our research and development programs.

Off-Balance Sheet Arrangements

As part of our ongoing business, we do not participate in transactions that generate relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities (“SPEs”), which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. As of December 31, 2005, we are not involved in any material unconsolidated SPE or off-balance sheet arrangements.

Contractual Obligations

In the table below, we set forth our enforceable and legally binding obligations and future commitments and obligations related to all contracts that we are likely to continue regardless of the fact that they are cancelable as of December 31, 2005. Some of the amounts we include in this table are based on management’s estimates and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties, and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table.

Contractual Obligations	Payments due by period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating Lease Obligations	$ 2,258,569	$ 533,904	$ 982,953	$ 741,712	—
Purchase Obligations (1)	9,479,977	8,379,977	400,000	400,000	300,000
Other Long-Term Liabilities Reflected on BioCryst's Balance Sheet Under GAAP	300,000	—	—	—	300,000
Total	$ 12,038,546	$ 8,913,881	$ 1,382,953	$ 1,141,712	$ 600,000

(1) Purchase obligations include commitments related to clinical development, manufacturing and research operations and other significant purchase commitments.

In addition to the above, we have committed to make potential future "sublicense" payments to third-parties as part of in-licensing and development programs. Payments under these agreements generally become due and payable only upon achievement of certain developmental, regulatory and/or commercial milestones. Because the achievement of these milestones is neither probable nor reasonably estimable, such contingencies have not been recorded on our balance sheet.

Critical Accounting Policies

We have established various accounting policies that govern the application of accounting principles generally accepted in the United States, which were utilized in the preparation of our financial statements. Certain accounting policies involve significant judgments and assumptions by management that have a material impact on the carrying value of certain assets and liabilities; management considers such accounting policies to be critical accounting policies. The judgments and assumptions used by management are based on historical experience and other factors, which are believed to be reasonable under the circumstances. Because of the nature of the judgments and assumptions made by management, actual results could differ from these judgments and estimates, which could have a material impact on the carrying values of assets and liabilities and the results of operations.

While our significant accounting policies are more fully described in Note 1 to our financial statements included later in this Form 10-K, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our reported financial results and affect the more significant judgments and estimates that we use in the preparation of our financial statements.

Revenue Recognition

Our revenues have generally been limited to license fees, milestone payments, research and development fees, and interest income. Revenue is recognized in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* ("SAB No. 104") and Emerging Issues Task Force Issue 00-21, *Revenue Arrangements with Multiple Deliverables* ("EITF Issue 00-21"). License fees, milestone payments, and research and development fees are recognized as revenue when the earnings process is complete and we have no further continuing performance obligations or we have completed the performance obligations under the terms of the agreement. Fees received under licensing agreements that are related to future performance are deferred and recognized as earned over an estimated period determined by management based on the terms of the agreement and the products licensed. For example, in the Roche and Mundipharma licenses agreements, we have determined to defer the upfront payments over the remaining life of the patents which are 17 years and 12 years, respectively. In the event a license agreement contains multiple deliverables, we evaluate whether the deliverables are separate or combined units of accounting in accordance with EITF Issue 00-21. Revisions to revenue or profit estimates as a result of changes in the estimated revenue period are recognized prospectively.

Milestone payments are recognized as revenue upon the achievement of specified milestone events if (1) the milestone is substantive in nature and the achievement of the milestone was not reasonably assured at the inception of the agreement and (2) the fees are non-refundable and non-creditable. Any milestone payments received prior to satisfying these criteria are recorded as deferred revenue.

Significant direct costs incurred upon entering into a licensing arrangement are deferred and charged to expense in proportion to the revenue recognized. Under the guidance of Emerging Issues Task Force Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* ("EITF Issue 99-19"), and Emerging Issues Task Force Issue 01-14, *Income Statement Characterization of Reimbursements Received for "Out-of-Pocket" Expenses* ("EITF Issue 01-14"), reimbursements received for direct out-of-pocket expenses related to research and development costs are recorded as revenue in the income statement rather than as a reduction in expenses.

Royalty revenue is recognized based on estimates of royalties earned during the applicable period and adjusted for differences between the estimated and actual royalties in the following period. If royalties can not be reasonably estimated, revenue is recognized upon receipt of royalty statements from the licensee.

Research and Development Expenses

Major components of R&D expenses consist of personnel costs, including salaries and benefits, manufacturing costs, clinical, regulatory, and toxicology services performed by contract research organizations (CRO's), materials and supplies, and overhead allocations consisting of various administrative and facilities related costs. We charge these costs to expense when incurred, consistent with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs* . These costs are a significant component of R&D expenses. Most of our manufacturing and our clinical and preclinical studies are performed by third-party CRO's. We accrue costs for studies performed by CRO's over the service periods specified in the contracts and adjust our estimates, if required, based upon our on-going review of the level of services actually performed by the CRO. We expense both our internal and external research and development costs as incurred. We expect our research and development expense to increase as we continue to develop our drug candidates.

Additionally, we have license agreements with third parties, such as AECOM/IRL that require maintenance fees or fees related to sublicense agreements. These fees are generally expensed as incurred unless they are related to revenues that have been deferred in which case the expenses will be deferred and recognized over the related revenue recognition period.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. To date, we have not adjusted our estimate at any particular balance sheet date in any material amount. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of our raw materials, drug substance and drug products; and
- professional service fees.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Stock-Based Compensation

We account for stock-based compensation under Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* ("APB No. 25"). Under APB No. 25, our stock option and employee stock purchase plans qualify as noncompensatory plans. Under Financial Accounting Standards Board Interpretation No. 44, *Accounting for Certain Transactions involving Stock Compensation, an Interpretation of APB No. 25* ("FIN No. 44"), outside directors are considered employees for purposes of applying APB No. 25, if they are elected by the shareholders. Consequently, no compensation expense for employees and directors is recognized unless there has been a modification to their grants as was the case for the directors in May 2004, resulting in an additional recognized expense of $457,000 during 2004. Stock issued to non-employees is compensatory and compensation expense is recognized under Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* ("Statement No. 123"), as amended by Statement of Financial Accounting Standards No. 148, *Accounting for Stock-Based Compensation-Transition and Disclosure* ("Statement No. 148").

In December 2004, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* ("Statement No. 123R"), which is a revision of Statement No. 123, supersedes APB No. 25, and amends Statement No. 95. Generally, the approach in Statement No. 123R is similar to the approach described in Statement No. 123. However, Statement No. 123R requires all share-based payments to employees, including grants of stock options, to be recognized in the income statement based on their fair values. Pro forma disclosure is no longer an alternative.

In March 2005, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 107, *Share-Based Payment* , which provided further clarification on the implementation of Statement No. 123R. Statement No. 123R originally required adoption no later than July 1, 2005. In April 2005, the Securities and Exchange Commission issued a release that amends the compliance dates for Statement No. 123R. Under the release, we were required to, and did, apply Statement No. 123R as of January 1, 2006.

7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

The primary objective of our investment activities is to preserve principal while maximizing the income we receive from our investments without significantly increasing our risk. We invest excess cash principally in U.S. marketable securities from a diversified portfolio of institutions with strong credit ratings and in U.S. government and agency bills and notes, and by policy, limit the amount of credit exposure at any one institution. Some of the securities we invest in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. To minimize this risk, we schedule our investments to have maturities that coincide with our expected cash flow needs, thus avoiding the need to redeem an investment prior to its maturity date. Accordingly, we believe we have no material exposure to interest rate risk arising from our investments. Therefore, no quantitative tabular disclosure is provided.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

BALANCE SHEETS

	December 31,	
	2005	2004
Assets		
Cash and cash equivalents	$ 29,156,827	$ 8,838,464
Securities held-to-maturity	21,103,572	14,334,631
Receivable from collaboration	30,000,000	—
Prepaid expenses and other current assets	839,662	699,284
Total current assets	81,100,061	23,872,379
Securities held-to-maturity	9,727,501	5,530,452
Furniture and equipment, net	2,407,954	2,817,154
Patents and licenses, net of accumulated amortization of $13,076 in 2005 and $3,934 in 2004	187,635	248,586
Deferred collaboration expense	5,825,243	—
Total assets	$ 99,248,394	$ 32,468,571
Liabilities and Stockholders' Equity		
Accounts payable	$ 8,812,985	$ 1,970,443
Accrued expenses	1,252,018	563,961
Accrued vacation	442,977	299,955
Deferred revenue	873,786	—
Total current liabilities	11,381,766	2,834,359
Deferred revenue	29,426,214	300,000
Stockholders' equity:		
Preferred stock: shares authorized - 5,000,000		
Series A Convertible Preferred stock, $.01 par value; shares authorized - 1,800,000; shares issued and outstanding - none		
Series B Junior Participating Preferred stock, $.001 par value; shares authorized - 45,000; shares issued and outstanding - none		
Common stock, $.01 par value; shares authorized - 45,000,000; shares issued and outstanding - 28,813,533 – 2005; 21,758,287 – 2004	288,135	217,583
Additional paid-in capital	210,014,946	154,880,528
Accumulated deficit	(151,862,667)	(125,763,899)
Total stockholders' equity	58,440,414	29,334,212
Total liabilities and stockholders' equity	$ 99,248,394	$ 32,468,571

See accompanying notes to financial statements .

STATEMENTS OF OPERATIONS

	Years Ended December 31,		
	2005	2004	2003
Revenues:			
Collaborative and other research and development	$ 151,867	$ 336,901	$ 653,255
Expenses:			
Research and development	23,642,377	18,868,112	11,521,982
General and administrative	3,686,323	3,220,655	2,811,605
Total expenses	27,328,700	22,088,767	14,333,587
Loss from operations	(27,176,833)	(21,751,866)	(13,680,332)
Interest and other income	1,078,065	647,745	980,249
Net loss	$ (26,098,768)	$ (21,104,121)	$ (12,700,083)
Basic and diluted net loss per common share	$ (1.01)	$ (1.00)	$ (.72)
Weighted average shares outstanding	25,721,031	21,165,311	17,703,441

See accompanying notes to financial statements.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock	Additional Paid-in Capital	Accumulated Deficit	Total Stock-holders' Equity
Balance at December 31, 2002	**$ 176,571**	**$ 131,910,935**	**$ (91,959,695)**	**$ 40,127,811**
Exercise of stock options, 186,228 shares, net	1,862	877,198	—	879,060
Employee stock purchase plan sales, 27,964 shares	280	20,399	—	20,679
Stock-based compensation expense	—	119,676	—	119,676
Net loss	—	—	(12,700,083)	(12,700,083)
Balance at December 31, 2003	**178,713**	**132,928,208**	**(104,659,778)**	**28,447,143**
Sale of common stock, 3,571,667 shares	35,717	20,244,133	—	20,279,850
Exercise of stock options, 283,636 shares, net	2,836	1,077,500	—	1,080,336
Employee stock purchase plan sales, 31,695 shares	317	118,260	—	118,577
Stock-based compensation expense	—	512,427	—	512,427
Net loss	—	—	(21,104,121)	(21,104,121)
Balance at December 31, 2004	**217,583**	**154,880,528**	**(125,763,899)**	**29,334,212**
Sale of common stock, 6,578,829 shares	65,788	52,498,067	—	52,563,855
Exercise of stock options, 450,717 shares, net	4,507	2,473,395	—	2,477,902
Employee stock purchase plan sales, 25,700 shares	257	136,564	—	136,821
Stock-based compensation expense	—	26,392	—	26,392
Net loss	—	—	(26,098,768)	(26,098,768)
Balance at December 31, 2005	**$ 288,135**	**$ 210,014,946**	**$ (151,862,667)**	**$ 58,440,414**

See accompanying notes to financial statements.

STATEMENTS OF CASH FLOWS

	Years Ended December 31,		
	2005	2004	2003
Operating activities:			
Net loss	$ (26,098,768)	$ (21,104,121)	$ (12,700,083)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization of furniture and equipment	854,269	955,548	1,101,311
Impairment of furniture and equipment	52,215	10,922	—
Amortization of patents and licenses	10,298	2,979	202
Impairment of patents and licenses	101,437	8,339	—
Stock-based compensation expense	26,392	512,427	119,676
Changes in operating assets and liabilities:			
Receivable from collaboration	(30,000,000)	—	—
Prepaid expenses and other current assets	(140,378)	(23,377)	(193,287)
Deferred collaboration expense	(5,825,243)	—	—
Accounts payable	6,842,542	1,330,094	384,311
Accrued expenses	688,057	96,271	24,166
Accrued vacation	143,022	59,583	67,357
Deferred revenue	30,000,000	—	—
Net cash used in operating activities	**(23,346,157)**	**(18,151,335)**	**(11,196,347)**
Investing activities:			
Acquisitions of furniture and equipment	(497,284)	(275,919)	(51,729)
Purchases of patents and licenses	(50,784)	(80,443)	(82,140)
Purchases of marketable securities	(29,695,358)	(18,879,234)	(13,187,900)
Maturities of marketable securities	18,729,368	16,398,629	21,690,778
Net cash (used in) provided by investing activities	**(11,514,058)**	**(2,836,967)**	**8,369,009**
Financing activities:			
Sale of common stock, net of issuance costs	52,563,855	20,279,850	—
Exercise of stock options	2,477,902	1,080,336	879,060
Employee stock purchase plan sales	136,821	118,577	20,679
Net cash provided by financing activities	**55,178,578**	**21,478,763**	**899,739**
Increase (decrease) in cash and cash equivalents	20,318,363	490,461	(1,927,599)
Cash and equivalents at beginning of year	8,838,464	8,348,003	10,275,602
Cash and cash equivalents at end of year	**$ 29,156,827**	**$ 8,838,464**	**$ 8,348,003**

See accompanying notes to financial statements .

NOTES TO FINANCIAL STATEMENTS

Note 1 - Accounting Policies

The Company

BioCryst Pharmaceuticals, Inc., a Delaware corporation (the "Company"), is a biotechnology company that designs, optimizes, and develops novel drugs that block key enzymes involved in cancer, cardiovascular diseases, autoimmune diseases, and viral infections. The Company integrates the necessary disciplines of biology, crystallography, medicinal chemistry, and computer modeling to effectively use structure-based drug design to discover and develop small molecule pharmaceuticals. The Company has four research projects in different stages of development from early discovery to an ongoing Phase II trial of the Company's most advanced drug candidate, Fodosine™. While the prospects for a project may increase as the project advances to the next stage of development, a project can be terminated at any stage of development. Until the Company generates revenues from either a research project or an approved product, the Company's ability to continue research projects is dependent upon its ability to raise funds through the sale of equity securities or through collaborative arrangements with government agencies or third-party partners.

Cash and Cash Equivalents

The Company generally considers cash equivalents to be all cash held in money market accounts or investments in debt instruments with maturities of three months or less at the time of purchase in accordance with Statement of Financial Accounting Standards No. 95, *Statement of Cash Flows* ("Statement No. 95").

Securities Held-to-Maturity

The Company is required to classify securities as held-to-maturity, available-for-sale or trading. The appropriateness of each classification is reassessed at each reporting date. As of December 31, 2005 and 2004, the Company classified all securities as held-to-maturity. The only dispositions of securities classified as held-to-maturity related to actual maturities or securities called prior to their maturity. At December 31, 2005 securities held-to-maturity totaling to $30,831,073 consisted entirely of U.S. Treasury and Agency securities carried at amortized cost. At December 31, 2004, securities held-to-maturity totaling $19,865,083 consisted of U.S. Treasury and Agency securities carried at amortized cost of $17,775,804 and certificates of deposit from financial institutions of $2,089,279. At December 31, 2005, all of the non-current portions of securities held-to-maturity are U.S. Agency securities that mature in 2007. The estimated fair value of all held-to-maturity securities at December 31, 2005 and 2004, respectively, was approximately $30,737,609 and $19,712,365. The Company has deposited a U.S. Treasury security of $196,000 in escrow for the payment of rent and performance of other obligations specified in its lease dated July 12, 2000 (see Note 5). The amount deposited in escrow for the lease decreases $65,000 annually throughout the term of the lease.

Fair value of held-to-maturity investment securities are based on independent quoted market prices. While these securities have an unrealized loss position at December 31, 2005, management does not believe the loss represents an other-than-temporary impairment. The Company has the ability and the intent to hold the securities until maturity, at which time the cost of the investments will be recovered. These unrealized losses are mainly attributed to changes in interest rates and are individually less than one percent of their respective amortized cost.

Furniture and Equipment

Furniture and equipment are recorded at cost. Depreciation is computed using the straight-line method with estimated useful lives of five and seven years. Laboratory equipment, office equipment, leased equipment and software are depreciated over a life of five years. Furniture and fixtures are depreciated over a life of seven years. Leasehold improvements are amortized over their estimated useful lives or the remaining lease term, whichever is lesser. The Company periodically reviews its furniture and equipment for impairment in accordance with Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* ("Statement No. 144"), to determine any impairment that needs to be recognized.

Patents and Licenses

Patents and licenses are recorded at cost and amortized on a straight-line basis over their estimated useful lives or 20 years, whichever is lesser. The Company periodically reviews its patents and licenses for impairment in accordance with Statement No. 144 to determine any impairment that needs to be recognized. During 2005 and 2004, the Company identified certain patents and licenses that no longer met its strategic objectives, which were determined to be unrecoverable and for which the Company had no alternative future uses. Accordingly, the Company recorded impairment losses for such patents and licenses totaling $101,437 and $8,339 for the years ended December 31, 2005 and 2004, respectively. These impairment losses are included in general and administrative expenses in the statements of operations.

Research and Development Expenses

Major components of research and development expenses consist of personnel costs, including salaries and benefits, clinical, regulatory and toxicology services performed by contract research organizations (CRO's), materials and supplies, and overhead allocations consisting of

various administrative and facilities related costs. The Company charges clinical and preclinical study costs to expense when incurred, consistent with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs* . These costs are a significant component of R&D expenses. Most of the Company's manufacturing and clinical and preclinical studies are performed by third-party CRO's. The Company accrues costs for studies performed by CRO's over the service periods specified in the contracts and adjusts estimates, if required, based upon the Company's on-going review of the level of services actually performed by the CRO.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. To date, we have not adjusted our estimate at any particular balance sheet date in any material amount. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of our raw materials, drug substance and drug products; and
- professional service fees.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Income Taxes

The liability method is used in accounting for income taxes in accordance with Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes* (“Statement No. 109”). Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Revenue Recognition

The Company’s revenues have generally been limited to license fees, milestone payments, research and development fees, and interest income. Revenue is recognized in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (“SAB No. 104”) and Emerging Issues Task Force Issue 00-21, *Revenue Arrangements with Multiple Deliverables* (“EITF Issue 00-21”). License fees, future event payments, and research and development fees are recognized as revenue when the earnings process is complete and the Company has no further continuing performance obligations or the Company has completed the performance obligations under the terms of the agreement. Fees received under licensing agreements that are related to future performance are deferred and recognized as earned over an estimated period determined by management. In the event a license agreement contains multiple deliverables, the Company evaluates whether the deliverables are separate or combined units of accounting in accordance with EITF Issue 00-21. Revisions to revenue or profit estimates as a result of changes in the estimated revenue period are recognized prospectively.

Future event payments are recognized as revenue upon the achievement of specified events if (1) the event is substantive in nature and the achievement of the event was not reasonably assured at the inception of the agreement and (2) the fees are non-refundable and non-creditable. Any event payments received prior to satisfying these criteria are recorded as deferred revenue.

Significant direct costs incurred upon entering into a licensing arrangement are deferred and charged to expense in proportion to the revenue recognized. Under the guidance of Emerging Issues Task Force Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* (“EITF Issue 99-19”), and Emerging Issues Task Force Issue 01-14, *Income Statement Characterization of Reimbursements Received for “Out-of-Pocket” Expenses* (“EITF Issue 01-14”), reimbursements received for direct out-of-pocket expenses related to research and development costs are recorded as revenue in the income statement rather than as a reduction in expenses.

Royalty revenue is recognized based on estimates of royalties earned during the applicable period and adjusted for differences between the estimated and actual royalties in the following period. If royalties can not be reasonably estimated, revenue is recognized upon receipt of royalty statements from the licensee. The Company has not received any royalties from the sale of licensed pharmaceutical products.

Net Loss Per Share

The Company computes net loss per share in accordance with Statement of Financial Accounting Standards No. 128, *Earnings Per Share* . Net loss per share is based upon the weighted average number of common shares outstanding during the period. Diluted loss per share is equivalent to basic net loss per share for all periods presented herein because common equivalent shares from unexercised stock options and common shares expected to be issued under the Company's employee stock purchase plan were anti-dilutive.

Stock-Based Compensation

The Company accounts for stock-based compensation under Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* ("APB No. 25"). Under APB No. 25, the Company's stock option and employee stock purchase plans qualify as noncompensatory plans. Under Financial Accounting Standards Board Interpretation No. 44, *Accounting for Certain Transactions involving Stock Compensation, an Interpretation of APB No. 25* ("FIN No. 44"), outside directors are considered employees for purposes of applying APB No. 25, if they are elected by the shareholders. Consequently, no compensation expense for employees and directors is recognized unless there has been a modification to their grants as was the case for the directors in May 2004, resulting in an additional recognized expense of $457,000 during 2004. Stock issued to non-employees is compensatory and compensation expense is recognized under Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* ("Statement No. 123"), as amended by Statement of Financial Accounting Standards No. 148, *Accounting for Stock-Based Compensation-Transition and Disclosure* ("Statement No. 148").

The following table illustrates the pro forma effect on net loss and net loss per share had the Company applied the fair value recognition provisions of Statement No. 123 for the years ended December 31, 2005, 2004, and 2003. See Note 7 for the assumptions used to compute the pro forma amounts.

	2005	2004	2003
Net loss as reported	$ (26,098,768)	$ (21,104,121)	$ (12,700,083)
Add stock-based employee compensation expense included in reported net loss	26,392	512,427	119,676
Deduct total stock-based employee compensation expense determined under Statement No. 123	(1,779,991)	(2,260,551)	(2,178,781)
Pro forma net loss	$ (27,852,367)	$ (22,852,245)	$ (14,759,188)
Amounts per common share:			
Net loss per share, as reported	$ (1.01)	$ (1.00)	$ (.72)
Pro forma net loss per share	$ (1.08)	$ (1.08)	$ (.83)

In December 2004, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* ("Statement No. 123R"), which is a revision of Statement No. 123, supersedes APB No. 25, and amends Statement No. 95. Generally, the approach in Statement No. 123R is similar to the approach described in Statement No. 123. However, Statement No. 123R requires all share-based payments to employees, including grants of stock options, to be recognized in the income statement based on their fair values. Pro forma disclosure is no longer an alternative.

In March 2005, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 107, *Share-Based Payment* , which provided further clarification on the implementation of Statement No. 123R. Statement No. 123R originally required adoption no later than July 1, 2005. In April 2005, the Securities and Exchange Commission issued a release that amends the compliance dates for Statement No. 123R. Under the release, the Company was required to and did apply Statement No. 123R as of January 1, 2006.

Statement No. 123R permits public companies to adopt its requirements using one of two methods, a “modified prospective” method or a “modified retrospective” method. Both methods are similar, except that the modified retrospective method permits entities to restate, based on the amounts previously recognized under Statement No. 123 for purposes of pro forma disclosures, either (a) all prior periods presented or (b) prior interim periods of the year of adoption. The Company plans to adopt Statement No. 123R using the modified prospective basis in which compensation cost is recognized beginning with the effective date (a) based on the requirements of Statement No. 123R for all share based payments granted after the effective date and (b) based on the requirements of Statement No. 123 for all awards granted to employees prior to the effective date of Statement No. 123R that remain unvested on the effective date.

As permitted by Statement No. 123, the Company currently accounts for share-based payments to employees using APB No. 25’s intrinsic value method and, as such, generally recognizes no compensation cost for employee stock options. Accordingly, the adoption of Statement No. 123R’s fair value method will have a significant impact on the Company’s results of operations, although it will have no impact on the Company’s overall financial position. The impact of adoption of Statement No. 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 Statement No. 123R in prior periods, the impact of that standard would have approximated the impact of Statement No. 123 as described in the disclosure of pro forma net income and earnings per share. Statement No. 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under current literature. This requirement could reduce net operating cash flows and increase net financing cash flows in periods after adoption if the Company is able to benefit from these tax deductions. The Company cannot estimate what those amounts will be in the future because they depend on other things such as the Company having net income and when employees may exercise stock options. Since the Company has always maintained a net operating loss, the benefit of these tax deductions has never been realized.

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 amounts reported in the financial statements. Examples include accrued clinical and preclinical expenses. Actual results could differ from those estimates.

Reclassifications

Certain amounts in the 2004 and 2003 financial statements have been reclassified to conform to the 2005 financial statement presentation. The changes had no effect on the results of operations previously reported.

Note 2 - Furniture and Equipment

Furniture and equipment consisted of the following at December 31:

	2005	2004
Furniture and fixtures	$ 339,635	$ 330,677
Office equipment	589,702	581,520
Software	485,554	489,873
Laboratory equipment	4,013,708	3,595,859
Leased equipment	62,712	62,712
Leasehold improvements	4,624,324	4,670,008
	10,115,635	9,730,649
Less accumulated depreciation and amortization	(7,707,681)	(6,913,495)
Furniture and equipment, net	$ 2,407,954	$ 2,817,154

Long-lived assets and certain identifiable intangible assets to be held and used are reviewed for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values. Long-lived assets and certain identifiable intangible assets to be disposed of are reported at the lower of carrying amount or fair value less cost to sell.

The Company reviewed its furniture and equipment for possible impairment in accordance with Statement No. 144 for the year ended December 31, 2005. As a result, the Company recorded an impairment charge of $52,215 to write down impaired assets to their estimated fair values. The impairment charge was primarily related to leasehold improvements on space that is no longer under lease by the Company and was included in general and administrative expenses in the statements of operations.

Note 3 - Concentration of Credit and Market Risk

The Company invests its excess cash principally in U.S. marketable securities from a diversified portfolio of institutions with strong credit ratings and in U.S. government and agency bills and notes and, by policy, limits the amount of credit exposure at any one institution. These investments are generally not collateralized and mature within less than three years. The Company has not realized any losses from such investments. At December 31, 2005, $21,895,909 was invested in the Merrill Lynch Premier Institutional Fund, a money market mutual fund that invests in near cash securities with weighted average maturities of less than 90 days. The Merrill Lynch Premier Institutional Fund is not insured.

The Company's raw materials, drug substances, and drug products are manufactured by a limited group of suppliers and some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact the Company's supply of drugs for further preclinical testing and clinical trials.

Note 4 - Accrued Expenses

Accrued expenses were comprised of the following at December 31:

	2005	2004
Accrued clinical trials	$ 877,882	$ 330,920
Accrued legal fees	189,430	20,000
Accrued consulting fees	66,621	128,509
Stock purchase plan withholdings	81,460	54,476
Other	36,625	30,056
Accrued expenses	$ 1,252,018	$ 563,961

Note 5 - Lease Obligations and Other Contingencies

The Company has the following lease obligations at December 31, 2005:

	Operating Leases
2006	$ 533,904
2007	486,119
2008	496,834
2009	492,825
2010	248,887
Total minimum payments	$ 2,258,569

Rent expense for operating leases was $560,322, $583,969, and $603,996 in 2005, 2004 and 2003, respectively. The commitment for operating leases is primarily related to the building lease, which expires in June 2010. The lease, as amended effective December 1, 2005 for a reduction in occupied space, requires monthly rents of $36,855 beginning in

December 2005 and escalates annually to a minimum of $41,481 per month in the final year. The Company has an option to renew the lease for an additional five years at the current market rate on the date of termination and a one-time option to terminate the lease on June 30, 2008, subject to a reasonable termination fee.

On August 5, 2002, at the request of the compensation committee, the Company's Board of Directors approved a reduction in salary of 25% for Dr. Charles E. Bugg, Chairman and Chief Executive Officer and Dr. J. Claude Bennett, President, Chief Operating Officer and Medical Director, effective August 1, 2002. In the event of any change of control of the Company, any cumulative salary reductions up to the date of the change of control would become due and payable. The monthly amount of the reduction was $14,677 combined. On December 8, 2003, the Board of Directors approved the recommendation of the compensation committee to restore their salaries to their previous amounts effective January 1, 2004, leaving the cumulative reduction of $249,509 outstanding in the event of a change in control.

Note 6 - Income Taxes

The provision for income taxes differs from the amounts computed by applying the statutory federal income tax rate to income before income taxes. The sources and tax effects of the differences are as follows:

	2005	2004	2003
Federal taxes benefit at statutory rate on income before income taxes	$ (9,134,569)	$ (7,386,442)	$ (4,445,029)
State taxes benefit, net of federal income tax benefit	(1,120,784)	(917,879)	(559,421)
Increase in valuation allowance	12,706,721	9,786,925	5,484,477
Permanent items (federal effect)	1,488,588	882,830	366,469
R&D credit	(4,237,250)	(2,514,344)	(1,038,165)
Other-net	297,294	148,910	191,669
Total tax expense (benefit)	$ —	$ —	$ —

The Company has not had taxable income since incorporation and, therefore, has not paid any income taxes. Significant components of the Company's deferred tax assets and liabilities are as follows:

	2005	2004
Deferred tax assets:		
Net operating losses	$ 51,727,869	$ 43,136,163
General business credits	16,536,933	12,299,683
Fixed assets	594,432	511,002
Accrued expenses	168,386	159,556
Reserve for doubtful accounts	—	—
Deferred revenue	113,400	113,400
Other	—	193,697
Total deferred tax assets	69,141,020	56,413,501
Total deferred tax liabilities	—	—
Net deferred tax asset	69,141,020	56,413,501
Valuation allowance	(69,141,020)	(56,413,501)
Net deferred tax assets	$ —	$ —

Because the majority of the deferred tax assets relate to net operating loss (NOL) carryforwards that can only be realized if the Company is profitable in future periods and because the Company has never been profitable in the past, it is uncertain whether the Company will realize any tax benefit related to the NOL carryforwards. Accordingly, the Company has provided a valuation allowance against the net deferred tax assets due to uncertainties as to their ultimate realization. The valuation allowance will remain at the full amount of the deferred tax asset until it is more likely than not that the related tax benefits will be realized.

As of December 31, 2005, the Company had net operating loss and research and development credit carryforwards of approximately $136,300,000 and $16,500,000, respectively, which expire at various dates from 2006 through 2025.

Use of the Carryforward Tax Benefits will be subject to a substantial annual limitation due to the change of ownership provisions of the Tax Reform Act of 1986. The annual limitation is expected to result in the expiration of a portion of the Carryforward Tax Benefits before utilization. The ownership change which occurred in 1996 has been considered by the Company in its computations under Statement No. 109. Due to recent stock issuances, it is possible that additional limitations could currently apply. The Company has not performed a detailed analysis to determine if an additional ownership change has occurred under the tax code or to determine its impact on its ability to use these net operating loss and research credit carryforwards. However, it is not anticipated that any such analysis would have a material impact on the balance sheet as a result of offsetting changes in the deferred tax valuation allowance.

Note 7 – Stockholders' Equity

On December 14, 2005, the Company entered into a stock purchase agreement with Kleiner Perkins Caufield & Byers Holdings, LLC, KPTV, LLC and TPG Biotechnology Partners, L.P. in connection with a registered direct offering of 2,228,829 shares of its common stock at an offering price of $13.46 per share. The common stock was issued pursuant to prospectus supplements filed with the Securities and Exchange Commission pursuant to Rule 424(b)(2) of the Securities Act of 1933, as amended ("the Securities Act"), in connection with a shelf takedown from the Company's registration statement on Form S-3 (333-111226), which was filed on December 16, 2003 and which became effective on January 5, 2004, and the Company's registration statement on Form S-3 (333-128087), which was filed on September 2, 2005 and which became effective on September 20, 2005. On December 16, 2005, the Company issued the total 2,228,829 shares of common stock to the aforementioned investors and received total proceeds of approximately $30 million (approximately $29.9 million net of expenses).

On February 9, 2005, the Company entered into a Placement Agency Agreement with Leerink Swann & Company in connection with a registered direct offering of 4,350,000 shares of its common stock at an offering price of $5.50 per share. The common stock was issued pursuant to a prospectus supplement filed with the Securities and Exchange Commission pursuant to Rule 424(b)(2) of the Securities Act in connection with a shelf takedown from the Company's registration statement on Form S-3 (333-111226), filed on December 16, 2003 and which became effective on January 5, 2004.

On February 17, 2005, the Company entered into stock purchase agreements with a number of institutional investors for an aggregate of 4,350,000 shares of common stock at a gross purchase price of $5.50 per share or approximately $23.9 million (approximately $22.7 million net of expenses). One of these agreements was with Baker Brothers Investments, L.P., Baker Brothers Investments II, L.P., Baker Biotech Fund I, L.P., Baker Biotech Fund II, L.P., Baker Biotech Fund II (Z), L.P., Baker Biotech Fund III, L.P., Baker Biotech Fund III (Z), L.P., Baker/Tisch Investments, L.P., and 14159, L.P., or the Baker investors, for a total of 1,454,545 shares.

On February 4, 2004, the Company entered into a Placement Agency Agreement with Leerink Swann & Company in connection with a registered direct offering of 3,571,667 shares of its common stock at an offering price of $6.00 per share. The common stock was issued pursuant to a prospectus supplement filed with the Securities and Exchange Commission pursuant to Rule 424(b)(2) of the Securities Act in connection with a shelf takedown from the Company's registration statement on Form S-3 (333-111226), filed on December 16, 2003 and which became effective on January 5, 2004.

On February 17, 2004, the Company entered into a Stock Purchase Agreement with Caduceus Private Investments II, LP, Caduceus Private Investments II (QP), LP and UBS Juniper Crossover Fund, L.L.C. As part of this agreement, the Company granted these investors the right to appoint a member to its board of directors effective as of the closing of the offering. On February 18, 2004, the Company completed a $21.4 million registered direct offering of 3,571,667 shares of its common stock to a group of institutional investors.

In June 2002, the Board of Directors adopted a stockholder rights plan and, pursuant thereto, issued preferred stock purchase rights ("Rights") to the holders of the Company's common stock. The Rights have certain anti-takeover effects. If triggered, the Rights would cause substantial dilution to a person or group of persons who acquires more than 15% (19.9% for William W. Featheringill, a Director who owned approximately 9.95% at December 31, 2005, but

owned more than 15% at the time the Rights were put in place) of the Company's common stock on terms not approved by the Board of Directors. The rights are not exercisable until the distribution date, as defined in the Rights Agreement by and between the Company and American Stock Transfer & Trust Company, as Rights Agent. The Rights will expire at the close of business on June 24, 2012, unless that final expiration date is extended or unless the rights are earlier redeemed or exchanged by the Company.

Each Right entitles the registered holder to purchase from the Company one one-thousandth of a share of Series B Junior Participating Preferred Stock ("Series B"), par value $0.001 per share, at a purchase price of $26.00, subject to adjustment. Shares of Series B purchasable upon exercise of the Rights will not be redeemable. Each share of Series B will be entitled to a dividend of 1,000 times the dividend declared per share of common stock. In the event of liquidation, each share of Series B will be entitled to a payment of 1,000 times the payment made per share of common stock. Each share of Series B will have 1,000 votes, voting together with the common stock. Finally, in the event of any merger, consolidation, or other transaction in which shares of common stock are exchanged, each share of Series B will be entitled to receive 1,000 times the amount received per share of common stock. Effective in December 2005, we increased the authorized shares available under these rights to 45,000 to match the authorized common shares of 45,000,000.

In November 1991, the Board of Directors adopted the 1991 Stock Option Plan (the "Plan") for key employees and consultants of the Company and reserved 500,000 shares of common stock for issuance under the Plan. The Plan was approved by the stockholders on December 19, 1991. The original term of the Plan was for ten years and included provisions for issuance of both incentive stock options and non-statutory options. The exercise price of options granted under the Plan shall not be less than the fair market value of common stock on the grant date. Options granted under the Plan generally vest 25% after one year and monthly thereafter on a pro rata basis over the next three years until fully vested after four years and expire ten years after the grant date. Options are generally granted to all full-time employees.

The Plan was amended and restated in February 1993 to effect the following changes: (i) divide the Plan into two separate incentive programs: the Discretionary Option Grant Program and the Automatic Option Grant Program (for outside Directors), (ii) increase the number of shares of the Company's common stock available for issuance under the Plan by 500,000 shares and (iii) expand the level of benefits available under the Plan. The Board amended the Plan on December 23, 1993 to increase the number of shares issuable under the Plan by 500,000 shares and subsequently amended and restated the Plan in its entirety on February 8, 1994. On March 16, 1995, the Board authorized another 500,000 shares for issuance under the Plan. The Plan was subsequently amended and restated effective March 3, 1997, which amendment and restatement included an increase of 1,000,000 shares. The Plan (as so amended and restated) was further amended March 1, 1999 to increase the share reserve by 400,000 shares. The Board amended and restated the Plan in its entirety on March 6, 2000, which increased the reserved shares by 1,200,000 and extended the term of the Plan for ten years from the date of the amendment. This restatement was approved by the Company's stockholders on May 17, 2000. The Plan was amended March 8, 2004 to increase the number of shares reserved for issuance by 1,000,000 and to amend the automatic option grant program related to initial grants, vesting and option terms. The automatic option grant program grants options to purchase 10,000 shares to new non-employee Board members, prorated from their initial appointment to the next Annual Meeting, and an additional 10,000 shares annually over such period of continued service all of which vest one-twelfth per month. Directors receiving options under the automatic option grant program will have the full term of the original option to exercise all options vested at the time of their cessation from service. This amendment was approved by the Company's stockholders on May 12, 2004. The vesting and exercise provisions of options granted under the Plan are subject to acceleration in the event of certain stockholder-approved transactions, or upon the occurrence of a Change in Control as defined by the Plan.

The following is an analysis of stock options for the three years ended December 31, 2005:

	Options Available	Options Outstanding	Weighted Average Exercise Price
Balance December 31, 2002	606,494	2,998,485	$ 8.45
Options granted	(546,000)	546,000	1.27
Options exercised	—	(186,228)	4.72
Options canceled	440,325	(440,325)	8.83
Balance December 31, 2003	500,819	2,917,932	7.29
Option plan amended	1,000,000	—	—
Options granted	(499,197)	499,197	8.76
Options exercised	—	(283,636)	3.81
Options canceled	34,149	(34,149)	4.10
Balance December 31, 2004	1,035,771	3,099,344	7.88
Options granted	(653,801)	653,801	4.66
Options exercised	—	(450,717)	5.50
Options canceled	61,077	(61,077)	5.96
Balance December 31, 2005	443,047	3,241,351	7.60

There were 2,199,129, 2,220,583, and 1,979,152 options exercisable at December 31, 2005, 2004 and 2003, respectively. The weighted-average exercise price for options exercisable was $8.81, $8.94, and $9.71 at December 31, 2005, 2004 and 2003, respectively.

The following table summarizes, at December 31, 2005, by price range: (1) for options outstanding, the number of options outstanding, their weighted-average remaining life and their weighted-average exercise price; and (2) for options exercisable, the number of options exercisable and their weighted-average exercise price:

	Outstanding			Exercisable	
Price Range	**Number**	**Life**	**Price**	**Number**	**Price**
$ 0 to 3	594,942	7.0	$ 1.12	414,365	$ 1.19
3 to 6	830,408	8.6	4.36	227,164	3.79
6 to 9	1,197,932	5.5	7.87	947,864	7.62
9 to 12	17,953	4.4	9.71	13,787	9.67
12 to 15	276,515	1.2	14.15	276,515	14.15
15 to 18	98,061	1.4	16.34	93,894	16.38
21 to 24	205,920	3.9	22.84	205,920	22.84
24 to 30	19,620	4.4	26.83	19,620	26.83
$ 0 to 30	3,241,351	5.9	7.60	2,199,129	8.81

As of December 31, 2005, there were an aggregate of 3,809,999 shares reserved for future issuance under both the Plan and the Employee Stock Purchase Plan (“ESPP”) discussed in Note 8.

The Company follows APB No. 25 in accounting for both the Plan and the ESPP and, accordingly, does not recognize any compensation cost related to options granted to employees or non-employee Directors, unless there is a modification to the original option that would require recognition of compensation cost under FIN No. 44. For example, in May 2004, the stockholders approved an amendment to Automatic Option Grant Program for directors, which resulted in the Company recognizing $457,000 in compensation expense related to this amendment during 2004. The Company has adopted the disclosure requirements of Statement No. 123, as amended by Statement No. 148. The fair value of each option is estimated on the grant date using the Black-Scholes option-pricing method with the following weighted-average assumptions used for grants in 2005, 2004 and 2003, respectively: no dividends; expected volatility of 96.6, 103.1, and 104.4 percent; risk-free interest rate of 3.9, 4.0, and 3.0 percent; and expected lives of five years. The weighted-average grant-date fair values of options granted during 2005 under the Plan and ESPP were $3.48 and $2.55, respectively. The compensation cost recorded for options issued to non-employee consultants, was $26,392, $512,427, and $119,676 for the years ended December 31, 2005, 2004 and 2003, respectively, which included $456,787 in 2004 related to the modification of options for outstanding directors as a result of the amendment to the Plan during 2004.

Note 8 - Employee Benefit Plans

On January 1, 1991, the Company adopted an employee retirement plan (the “401(k) Plan”) under Section 401(k) of the Internal Revenue Code covering all employees. Employee contributions may be made to the 401(k) Plan up to limits established by the Internal Revenue Service. Company matching contributions may be made at the discretion of the Board of Directors. The Company made matching contributions of $205,524, $171,601, and $158,425 in 2005, 2004 and 2003, respectively.

On May 29, 1995, the stockholders approved the ESPP effective February 1, 1995. On May 15, 2002, the stockholders approved an amendment to the ESPP to reserve an additional 200,000 shares and eliminate the January 2005 termination date. The Company has reserved a total of 400,000 shares of common stock under the ESPP, of which 125,601 shares remain available for purchase at December 31, 2005. Eligible employees may authorize up to 15% of their salary to purchase common stock at the lower of 85% of the beginning or 85% of the ending price during the six-month purchase intervals. No more than 3,000 shares may be purchased by any one employee at the six-month purchase dates and no employee may purchase stock having a fair market value at the commencement date of $25,000 or more in any one calendar year. There were 25,700, 31,695, and 27,964 shares of common stock purchased under the ESPP in 2005, 2004 and 2003, respectively, at a weighted average price per share of $5.06, $3.82, and $0.74, respectively.

Note 9 - Collaborative and Other Research and Development Contracts

Roche. In November 2005, the Company entered into an exclusive license with Roche for the development and commercialization of the Company's second generation purine nucleoside phosphorylase ("PNP") inhibitor, BCX-4208, for the prevention of acute rejection in transplantation and for the treatment of autoimmune diseases. Under the terms of the agreement, Roche obtained worldwide rights to BCX-4208 in exchange for a $25 million up-front payment and a $5 million payment as reimbursement for a limited supply of material during the first 24 months of the collaboration. According to the terms of the license, there could also be future event payments for achieving specified development, regulatory and commercial milestones (including sales level milestones following a product's launch) for certain indications. In addition, the Company will receive royalties based on a percentage of net product sales, which varies depending upon when certain indications receive NDA approval in a major market country and can vary by country depending on the patent coverage or sales of generic compounds in a particular country. The Company licensed this compound and other PNP inhibitors from the Albert Einstein College of Medicine of Yeshiva University ("AECOM") and Industrial Research, Ltd. New Zealand ("IRL") and will owe sublicense payments to these third parties on the upfront payment, future event payments and royalties received by the Company for the sublicense of these inhibitors.

Roche will have a right of first negotiation, under certain conditions, on existing backup PNP inhibitors the Company develops through Phase IIb in transplant rejection and autoimmune diseases, but any new PNP inhibitors will be exempt from this agreement and the Company will retain all rights to such compounds. We retain the right to co-promote BCX-4208 in the U.S. for several indications. Roche has certain obligations under the terms of the agreement to use commercially reasonable efforts to develop, manufacture and commercialize the licensed product. The agreement will be governed by a joint steering committee to oversee and review the research and development activities of both parties. The agreement may be terminated by either party following an uncured material breach by the other party or may be either fully or partially terminated by Roche without cause under certain conditions and all rights, data, materials, products and other information would be transferred to the Company at no cost.

At December 31, 2005, the Company recorded a receivable of $30 million due from Roche for the $25 million up-front payment and the $5 million payment as reimbursement for supply. These amounts were received from Roche in January 2006. In accordance with SAB No. 104 and EITF Issue 00-21, the Company also recorded deferred revenue of $30 million related to the Roche collaboration at December 31, 2005. The Company's management anticipates that this deferred revenue will be amortized to revenue beginning in July 2006 and ending in August 2023, which is the date of expiration for the last-to-expire patent covered by the agreement. Therefore, at December 31, 2005, $873,786 of the deferred revenue is classified as short-term while the remaining $29,126,214 is classified as long-term.

Albert Einstein College of Medicine and Industrial Research, Ltd. In June 2000, the Company licensed a series of potent inhibitors of PNP from AECOM and IRL. The lead drug candidates from this collaboration are Fodosine™ and BCX-4208. The Company has obtained worldwide exclusive rights to develop and ultimately distribute these, or any other, drug candidates that might arise from research on these inhibitors. The Company has agreed to pay certain milestone payments for future development of these inhibitors, certain royalties on sales of any resulting product, and to share in future payments received from other third-party collaborators, if any. In addition, the Company agreed to pay an annual license fee that is non-refundable, but is creditable against actual royalties and other payments due to AECOM and IRL. This agreement may be terminated by the Company at any time by giving 60 days advance notice or in the event of material uncured breach by AECOM and IRL.

Upon completion of the collaboration with Roche for BCX-4208, the Company was obligated to pay AECOM/IRL approximately $6 million, which was included in accounts payable at December 31, 2005. The payment to AECOM/IRL was capitalized as a deferred expense at December 31, 2005. The deferred expense will be amortized into expense in proportion to the revenue recognized from the Roche agreement.

The University of Alabama at Birmingham ("UAB"). The Company currently has agreements with UAB for influenza neuraminidase and complement inhibitors. Under the terms of these agreements, UAB performed specific research for the Company in return for research payments and license fees. UAB has granted the Company certain rights to any discoveries in these areas resulting from research developed by UAB or jointly developed with the company. The Company has agreed to pay royalties on sales of any resulting product and to share in future payments received from other third-party collaborators. The Company has completed the research under the UAB influenza agreement. The Company funded the research program under the complement inhibitors agreement through March 2002, which entitled the Company to an assignment of, or a right to an exclusive license for, any inhibitors of specified complement enzymes developed by UAB scientists during the period of support or for a one-year period thereafter. These two agreements have initial 25-year terms, are automatically renewable for five-year terms throughout the life of the last patent and are terminable by the Company upon three months notice and by UAB under certain circumstances. There is currently no activity between us and UAB on these agreements, but in the event we license technology or commercialize products related to these programs we could owe sublicense fees or royalties on amounts we receive.

Emory University ("Emory") . In June 2000, the Company licensed intellectual property from Emory related to the hepatitis C polymerase target associated with hepatitis C viral infections. Under the original terms of the agreement, the research investigators from Emory provided the Company with materials and technical insight into the target. The Company has agreed to pay Emory royalties on sales of any resulting product and to share in future payments received from other third party collaborators, if any. The Company can terminate this agreement at any time by giving 90 days advance notice.

3-Dimensional Pharmaceuticals, Inc. ("3DP"). In December 2003, the Company transferred to 3DP, a wholly owned subsidiary of Johnson & Johnson, certain rights related to complement system inhibitors discovered during the Company's collaborative research agreement with 3DP, which was terminated by the Company on October 18, 2003. BioCryst received an initial payment from 3DP, and will receive royalties on any future sales of complement inhibitors covered under the assignment.

Sunol Molecular Corporation ("Sunol"). In April 1999, the Company entered into an agreement with Sunol. This agreement requires Sunol to conduct research and supply the Company with protein targets for drug design to expedite the discovery of new drug candidates designed to inhibit tissue factor/factor VIIa for the Company's cardiovascular program. In 2005, the assets and obligations of Sunol were transferred to Altor BioScience Corporation.

Novartis Corporation ("Novartis)". The Company granted Novartis, formerly Ciba-Geigy Corporation, an option in 1990 to acquire exclusive licenses to a class of inhibitors arising from research performed by the Company by February 1991. The option was exercised and a $500,000 fee was paid to the Company in 1993. Milestone payments are due upon approval of a new drug application. The Company will also receive royalties based upon a percentage of sales of any resultant products. Up to $300,000 of the initial fee received is refundable if sales of any resultant products are below specified levels and has been recorded as deferred revenue. This agreement has been inactive for several years.

Note 10 – Subsequent Events

In February 2006, the Company entered into an exclusive, royalty bearing right and license agreement with Mundipharma International Holdings Limited ("Mundipharma") for the development and commercialization of the Company's lead PNP inhibitor, Fodosine™, for use in oncology. Under the terms of the agreement, Mundipharma obtained rights in to Fodosine™ in markets across Europe, Asia, and Australasia in exchange for a $10 million up-front payment. Mundipharma will share 50% of the documented out of pocket development costs incurred by the Company in respect of the current and planned trials as of the effective date of the agreement provided that Mundipharma's maximum contribution to these trials shall be $10 million. In addition, Mundipharma will conduct additional clinical trials at their own cost up to a maximum of $15 million. The license provides for future event payments for achieving specified development, regulatory and commercial events (including certain sales level amounts following a product's launch) for certain indications. In addition, the Company will receive royalties based on a percentage of net product

sales, which varies depending upon when certain indications receive NDA approval in a major market country and can vary by country depending on the patent coverage or sales of generic compounds in a particular country. Generally, all payments under the agreement are nonrefundable and non-creditable, but they are subject to audit. The Company licensed Fodosine™ and other PNP inhibitors from AECOM and IRL and will owe sublicense payments to these third parties on the upfront payment, future event payments and royalties received by the Company from Mundipharma.

For five years, Mundipharma will have a right of first negotiation on existing backup PNP inhibitors the Company develops through Phase IIb in oncology, but any new PNP inhibitors will be exempt from this agreement and the Company will retain all rights to such compounds. The Company retained the rights to Fodosine™ in the U.S. and Mundipharma is obligated by the terms of the agreement to use commercially reasonable efforts to develop the licensed product in the territory specified by the agreement. The agreement is governed by a Joint Steering Committee to oversee and review the research and development activities of both parties. The agreement will continue for the commercial life of the licensed products, but may be terminated by either party following an uncured material breach by the other party or in the event the pre-existing third party license with AECOM and IRL expires. It may be terminated by Mundipharma upon 60 days written notice without cause or under certain other conditions as specified in the agreement and all rights, data, materials, products and other information would be transferred back to the Company at no cost. In the event the Company terminates the agreement for material default or insolvency, the Company could have to pay Mundipharma 50% of the costs of any independent data owned by Mundipharma in accordance with the terms of the agreement.

In accordance with SAB No. 104 and EITF Issue 00-21, the Company plans to defer the $10 million up-front payment that was received from Mundipharma in February 2006. The Company's management anticipates that this deferred revenue will be amortized to revenue beginning in February 2006 and ending in October 2017, which is the date of expiration for the last-to-expire patent covered by the agreement. In accordance with EITF Issue 99-19 and EITF Issue 01-14, the costs reimbursed by Mundipharma for the current and planned trials of Fodosine™ will be recorded as revenue when the expense is incurred up to the $10 million limit stipulated in the agreement. Upon completion of the collaboration with Mundipharma for Fodosine™, the Company is obligated to pay AECOM and IRL approximately $2 million.

Also in February 2006, the Company obtained a $1.8 million letter of credit. This letter of credit was obtained for a customs bond that was required in order to import into the country compound that was manufactured abroad. The Company does not anticipate drawing any funds against this letter of credit in the future, but it could remain in force for up to one year or until customs closes the file on the particular receipt of goods for which the bond was required.

Note 11 – Recent Accounting Pronouncements

As outlined in Note 1, the FASB issued Statement No. 123R, which is a revision of Statement No. 123 in December 2004. Statement No. 123R requires all share-based payments to employees and directors to be recognized in the financial statements based on their fair values, superseding APB No. 25 and its related implementation guidance. Under APB No. 25, issuing stock options to employees could have resulted in no compensation cost. Statement No. 123R eliminates this alternative and requires entities to expense the cost of employee services received in exchange for stock options based on the grant date fair value of those awards. The Company currently accounts for its employee stock options in accordance with APB No. 25 while disclosing the pro forma effect of the options had they been recorded under the fair value method. The Company adopted this accounting standard on January 1, 2006. It is anticipated that the adoption of this statement will have a significant impact on the Company's results of operations, although it will have no impact on the Company's financial position.

Note 12 - Quarterly Financial Information (Unaudited) (In thousands, except per share)

	First	Second	Third	Fourth
2005 Quarters				
Revenues	$ 41	$ 58	$ 32	$ 21
Net loss	(5,645)	(5,648)	(7,645)	(7,161)
Net loss per share	(.24)	(.22)	(.29)	(.27)
2004 Quarters				
Revenues	$ 0	$ 43	$ 116	$ 178
Net loss	(5,462)	(5,057)	(5,296)	(5,289)
Net loss per share	(.28)	(.23)	(.24)	(.24)

Net loss and net loss per share each year may differ from the total of the individual quarters due to rounding.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM ON FINANCIAL STATEMENTS

The Board of Directors and Shareholders
BioCryst Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of BioCryst Pharmaceuticals, Inc. as of December 31, 2005 and 2004, and the related statements of operations, stockholders' equity 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 an 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 BioCryst Pharmaceuticals, Inc. as of 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 BioCryst Pharmaceuticals, 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 March 8, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Birmingham, Alabama
March 8, 2006

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM ON INTERNAL CONTROL

The Board of Directors and Shareholders
BioCryst Pharmaceuticals, Inc.

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that BioCryst Pharmaceuticals, 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"). BioCryst Pharmaceuticals, 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 BioCryst Pharmaceuticals, 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, BioCryst Pharmaceuticals, 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 2005 financial statements of BioCryst Pharmaceuticals, Inc. and our report dated March 8, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Birmingham, Alabama
March 8, 2006

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain a set of disclosure controls and procedures that are designed to ensure that information relating to BioCryst Pharmaceuticals, Inc. required to be disclosed in our periodic filings under the Securities Exchange Act is recorded, processed, summarized and reported in a timely manner under the Securities Exchange Act of 1934. We carried out an evaluation, under the supervision and with the participation of management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures. Based upon that evaluation, the Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2005, our disclosure controls and procedures are effective to ensure that information required to be disclosed by BioCryst in the reports filed or submitted by it under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, and include controls and procedures designed to ensure that information required to be disclosed by BioCryst in such reports is accumulated and communicated to our management, including the Chairman and Chief Executive Officer and Chief Financial Officer of BioCryst, as appropriate to allow timely decisions regarding required disclosure.

Management's Report on Internal Control Over Financial Reporting

Management of BioCryst Pharmaceuticals, Inc. (the "Company") is responsible for establishing and maintaining adequate internal control over financial reporting and for the assessment of the effectiveness of internal control over financial reporting. As defined by the Securities and Exchange Commission, internal control over financial reporting is a process designed by, or under the supervision of our principal executive and principal financial officers and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of the consolidated financial statements in accordance with U.S. generally accepted accounting principles.

Our internal control over financial reporting is supported by written policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of the consolidated financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of BioCryst are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the consolidated 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 connection with the preparation of our annual financial statements, management has undertaken an assessment of the effectiveness of our 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 Framework). Management's assessment included an evaluation of the design of our internal control over financial reporting and testing of the operational effectiveness of those controls.

Based on this assessment, management has concluded that as of December 31, 2005, our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles.

Ernst & Young LLP, the independent registered public accounting firm that audited our financial statements included in this report, have issued an attestation report on management's assessment of internal control over financial reporting, a copy of which appears on page 61 of this annual report.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2005 that have materially affected, or are reasonably likely to materially affect, BioCryst's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The directors and executive officers of BioCryst are as follows:

Name	Age	Position(s) with the Company
Charles E. Bugg, Ph.D.	64	Chairman, Chief Executive Officer and Director
J. Claude Bennett, M.D.	72	President, Chief Operating Officer, Medical Director and Director
Michael A. Darwin	44	Chief Financial Officer, Secretary and Treasurer
Jonathan M. P. Nugent	38	Vice President, Corporate Communications
Randall B. Riggs	39	Senior Vice President, Business Development
Stephen R. Biggar, M.D., Ph.D.	35	Director
William W. Featheringill	63	Director
Carl L. Gordon, CFA, Ph.D. (2)	41	Director
John L. Higgins (1)(2)	36	Director
Zola P. Horovitz, Ph.D. (1)	71	Director
Beth C. Seidenberg, M.D.	48	Director
Joseph H. Sherrill, Jr. (2)	65	Director
William M. Spencer, III	85	Director
Randolph C. Steer, M.D., Ph.D. (1)	56	Director

(1) Member of the Compensation Committee ("Compensation Committee").

(2) Member of the Audit Committee ("Audit Committee").

Charles E. Bugg, Ph.D., was named Chairman of the Board, Chief Executive Officer and Director in November 1993 and President in January 1995. He relinquished the position of President in December 1996 when Dr. J. Claude Bennett joined us in that position. Prior to joining us, Dr. Bugg had been a member of the faculty of the University of Alabama at Birmingham ("UAB") since 1968, having served as Professor of Biochemistry, Director of the Center for Macromolecular Crystallography, and Associate Director of the Comprehensive Cancer Center. He was a founder of BioCryst and served as our first Chief Executive Officer from 1987-1988 while on a sabbatical from UAB. Dr. Bugg also served as Chairman of our Scientific Advisory Board from January 1986 to November 1993. He continues to hold the position of Professor Emeritus in Biochemistry and Molecular Genetics at UAB, a position he has held since January 1994.

J. Claude Bennett, M.D., was named President and Chief Operating Officer in December 1996 and elected a Director in January 1997. Since 2001, Dr. Bennett has also served as the Medical Director. Prior to joining us, Dr. Bennett was President of The University of Alabama at Birmingham ("UAB") from October 1993 to December 1996 and Professor and Chairman of the Department of Medicine of UAB from January 1982 to October 1993. Dr. Bennett served on our Scientific Advisory Board from 1989-96. He is a former co-editor of the *Cecil Textbook of Medicine* and former President of the Association of American Physicians. He is a past chair of the Scientific Advisory Committee of the Massachusetts General Hospital, a member of the Scientific Advisory Board of Zycogen, LLC, and continues to hold the position of Distinguished University Professor Emeritus at UAB, a position he has held since January 1997.

Michael A. Darwin joined BioCryst in June 2000 as Controller. Effective November 1, 2002, Mr. Darwin was appointed Chief Financial Officer, Secretary and Treasurer. Prior to joining BioCryst, from June 1990 to June 2000, Mr. Darwin was Chief Financial Officer of a privately held company in the food services industry. He began his career at Ernst & Young and spent six years in public accounting practice.

Randall B. Riggs joined BioCryst in February 2005 as Vice President, Business Development and was promoted to Senior Vice President, Business Development effective January 2006. Mr. Riggs served as Vice President, Business Development at TransMolecular, Inc. an emerging oncology company from September 2004 to February 2005. Before joining TransMolecular, he served as a Corporate Licensing and Business Development consultant for TRUBION Pharmaceuticals, Inc. from March 2004 to August 2004. Mr. Riggs was previously Senior Vice President, Corporate Licensing and Business Development at Lexicon Genetics Incorporated from February 2000 to March 2004 and served as Vice President, Business Development from December 1998 to February 2000. Prior to joining Lexicon Genetics, Mr. Riggs was Director of Business Development for the Infectious Disease Unit of GeneMedicine, Inc. Mr. Riggs began his pharmaceutical and biotechnology business development career with Eli Lilly and Company; starting as a District Sales Manager and advancing to Manager, Corporate Business Development.

Jonathan M. P. Nugent joined BioCryst in May 2005 as Vice President, Corporate Communications. Mr. Nugent served as Senior Vice President at Burns McClellan, Inc., Investor Relations Division, since April 1999, except for a period from August 2003 to December 2003 when he served as Director of Investor Relations for Eyetech Pharmaceuticals, Inc. and from January 2004 to March 2004 when he was performing volunteer services. He also served as Account Supervisor from April 1996 to April 1999, Account Manager from April 1994 to April 1996, and Senior Account Executive from April 1993 to April 1994 at Burns McClellan.

Stephen R. Biggar, M.D., Ph.D. was appointed to the Board in October 2005. Dr. Biggar has served as a Principal at Baker Brothers Investments, a family of long-term investment funds for major university endowments and foundations, which is focused on publicly traded life sciences companies, since April 2002 and served as an Associate from April 2000 to April 2002. Prior to joining Baker Brothers, Dr. Biggar received an M.D. and a Ph.D. in Immunology from Stanford University. He attended the University of Rochester where he achieved a B.S. degree in Genetics. Dr. Biggar serves as a director of one private biotechnology company.

William W. Featheringill was elected a Director in May 1995. Mr. Featheringill is President, Chief Executive Officer and director, since 1973, of Private Capital Corporation, a venture capital company. He currently serves as Chairman of Electronic Healthcare Systems, Inc., a system solutions provider to the ambulatory care industry, since June 1995, and Momentum Business Solutions, Inc., a telecom and VoIP company, since May 2001. Mr. Featheringill is a Director of Altec Industries, Inc., Southern Research Institute and the Birmingham Museum of Art, and serves as a Trustee of Vanderbilt University. Mr. Featheringill received a BE in Mechanical Engineering from Vanderbilt University and a J.D. degree from the Columbia University School of Law and a M.B.A. from the Columbia University Graduate School of Business.

Carl L. Gordon, CFA, Ph.D ., was elected a Director in March 2004. Dr. Gordon is a founding General Partner of OrbiMed Advisors LLC, an asset management firm focused on the global healthcare industry, and has served in such capacity since 1998. Dr. Gordon was previously a senior biotechnology analyst at Mehta and Isaly, the predecessor firm to OrbiMed, from 1995-1997. Dr. Gordon received a Bachelor's degree from Harvard College, a Ph.D. in molecular biology from the Massachusetts Institute of Technology, and was a Fellow at the Rockefeller University.

John L. Higgins was elected a Director in May 2004. Mr. Higgins joined Connetics as Chief Financial Officer in 1997, and has served as Executive Vice President, Finance and Administration and Corporate Development since January 2002. He served as Executive Vice President, Finance and Administration, from January 2000 to December 2001, and as Vice President, Finance and Administration from September 1997 through December 1999. Before joining Connetics, he was a member of the executive management team at BioCryst. Before joining BioCryst in 1994, Mr. Higgins was a member of the healthcare banking team of Dillon, Read & Co. Inc., an investment banking firm. He currently serves as a director of a private company. He received his A.B. from Colgate University.

Zola P. Horovitz, Ph.D., was elected a Director in August 1994. Dr. Horovitz was Vice President of Business Development and Planning at Bristol-Myers Squibb from 1991 until his retirement in April 1994 and previously was Vice President of Licensing at the same company from 1990 to 1991. Prior to that he spent over 30 years with The Squibb Institute for Medical Research, most recently as Vice President Research, Planning, & Scientific Liaison. He has been an independent consultant in pharmaceutical sciences and business development since his retirement from Bristol-Myers Squibb in April 1994. He serves as non executive Chairman on the Board of Directors of Avigen, Inc., and also serves on the Boards of Directors of Genaera Pharmaceuticals, Inc., Palatin Technologies, Inc., DOV Pharmaceuticals, GenVec, Inc., NitroMed, Inc. and Immunicon Corporation.

Beth C. Seidenberg, M.D., was appointed to the Board in December 2005. Dr. Seidenberg has served as Partner of Kleiner Perkins Caufield and Byers ("KPCB") since May 2005. Prior to joining KPCB, Dr. Seidenberg served as Amgen's Chief Medical Officer and Senior Vice President, Global Development from January 2002 to December 2004, at Bristol-Myers Squibb Company as Senior Vice President, Global Development from September 2001 to January 2002, Senior Vice President, Clinical Development & Life Cycle Management from May 2000 to September 2001 and Vice President, Clinical Immunology/Pulmonary/Dermatology from April 2000 to May 2000 and at Merck/Merck Research Laboratories as Vice President, Pulmonary-Immunology from July 1998 to March 2000, Executive Director from March 1996 to June 1998, Senior Director from September 1993 to February 1996 and also served as both Director and Associate Director of Clinical Pharmacology from September 1991 to August 1993 and from June 1989 to August 1991, respectively. She received her M.D. from University of Miami; completed post-doctoral training at Johns Hopkins Medical Center and specialty training in immunology and infectious diseases at the National Institutes of Health. Dr. Seidenberg also has a B.S. degree in Biology and Anthropology from Barnard College.

Joseph H. Sherrill, Jr., was elected a Director in May 1995. Mr. Sherrill served as Chief Executive Officer and President of R. J. Reynolds ("RJR") Asia Pacific, based in Hong Kong, where he oversaw RJR operations across Asia, including licensing, joint ventures and a full line of operating companies from August 1989 to his retirement in October 1994. Prior management positions with RJR include Senior Vice President of Marketing for R.J. Reynolds International, President and Chief Executive Officer of R.J. Reynolds Tabacos do Brazil, and President and General Manager of R.J. Reynolds Puerto Rico. Mr. Sherrill received his M.B.A. from Columbia University.

William M. Spencer, III, has been a Director of BioCryst since our inception. Mr. Spencer, who is retired, is also a private investor in Birmingham, Alabama. Mr. Spencer is a Founder of BioCryst, and served as our Chairman of the Board from our founding in 1986 until April 1992. He co-founded and operated Motion Industries from 1946 through its merger into Genuine Parts Company in 1976. He has founded several businesses and has served on the Board of Directors of numerous public and private corporations.

Randolph C. Steer, M.D., Ph.D., was elected a Director in February 1993. Dr. Steer has been an independent pharmaceutical and biotechnology consultant since 1989, having a broad background in business development, medical marketing and regulatory affairs. He was formerly Chairman, President and CEO of Advanced Therapeutics Communications International, a leading drug regulatory group, and served as associate director of medical affairs at Marion Laboratories, and medical director at Ciba Consumer Pharmaceuticals. Dr. Steer serves on the Board of Directors of Techne Corporation and several privately held companies.

In accordance with the terms of our Certificate of Incorporation, the Board of Directors has been divided into three classes with members of each class holding office for staggered three-year terms. In accordance with our By-Laws, a director elected to fill a vacancy shall be elected for the unexpired term of his predecessor in office, and a director chosen to fill a position resulting from an increase in the number of directors shall hold office until the annual meeting of stockholders of the Corporation at which term of the class of directors for which he has been chosen expires. During 2005, the Board by resolution increased the size of the Board to add Dr. Biggar in October who was chosen for the 2006

class and Dr. Seidenberg who was chosen for the 2007 class of directors. Dr. Bennett's, Dr. Biggar's, Dr. Horovitz's and Dr. Steer's terms expire at the 2006 annual meeting. Dr. Bugg's, Dr. Gordon's, Mr. Higgins's, and Dr. Seidenberg's terms expire at the 2007 annual meeting, and Mr. Featheringill's, Mr. Sherrill's, and Mr. Spencer's terms expire at the 2008 annual meeting (in all cases subject to the election and qualification of their successors or to their earlier death, resignation or removal). At each annual stockholder meeting, the successors to the Directors whose terms expire are elected to serve from the time of their election and qualification until the third annual meeting of stockholders following their election and until a successor has been duly elected and qualified. The provisions of our Certificate of Incorporation governing the staggered Director election procedure can be amended only by a shareholder's vote of at least 75% of the eligible voting securities. There are no family relationships among any of our directors and executive officers. The Board has by resolution established the number of directors of BioCryst at eleven (11) commencing December 16, 2005. Currently, nine of our directors (Biggar, Featheringill, Gordon, Higgins, Horovitz, Seidenberg, Sherrill, Spencer and Steer) are independent as defined by the current Nasdaq rules.

We have an Audit Committee, consisting of Messrs. Gordon, Higgins and Sherrill, which is responsible for the review of internal accounting controls, financial reporting and related matters. The Audit Committee also recommends to the Board the independent accountants selected to be our auditors and reviews the audit plan, financial statements and audit results. The Board has adopted an Amended and Restated Audit Committee Charter that meets all the applicable rules of the Nasdaq National Market and the Securities and Exchange Commission. The Audit Committee Charter can be found on our website at www.biocryst.com. The Audit Committee members are "independent" directors as defined by the Nasdaq National Market listing standards in effect as of the date hereof and meet Nasdaq's financial literacy requirements for audit committee members. The Board of Directors has determined that Mr. Higgins qualifies as the "audit committee financial expert".

We also have a Compensation Committee consisting of Messrs. Higgins, Horovitz and Steer. The Compensation Committee is responsible for the annual review of officer compensation and other incentive programs and is authorized to award options under our Stock Option Plan. The Board has adopted a Compensation Committee Charter that meets all the applicable rules of the Nasdaq National Market and the Securities and Exchange Commission. The Charter can be found on our website at www.biocryst.com. The Compensation Committee members are "independent" directors as defined by the Nasdaq National listing standards in effect as of the date hereof.

We have a Corporate Governance and Nominating Committee comprised of all independent directors with terms not expiring in the current year. The current members of the committee are Directors Featheringill, Gordon, Higgins, Seidenberg, Sherrill and Spencer. The Committee nominates persons for election or re-election as directors. The Board has adopted a Corporate Governance and Nominating Committee Charter that meets all the applicable rules of the Nasdaq National Market and the Securities and Exchange Commission and is available on our website at www.biocryst.com. The Committee has established procedures/qualifications for selecting nominees and will consider nominees recommended in writing, including biographical information and personal references, by stockholders. All submissions by shareholders should be sent directly to the Chairman of the Board, Dr. Bugg at the corporate address.

We have adopted a Code of Business Conduct (the "Code") applicable to all employees, including executive officers, and all Board members. The Code is publicly available on our website at www.biocryst.com. Any waivers of the Code will be disclosed through a Form 8-K filing with the Securities and Exchange Commission.

Section 16(a) Beneficial Ownership Reporting Compliance

Incorporated by reference from our definitive Proxy Statement to be filed in connection with the solicitation of proxies for our 2006 Annual Meeting of Stockholders.

ITEM 11. EXECUTIVE COMPENSATION

Incorporated by reference from our definitive Proxy Statement to be filed in connection with the solicitation of proxies for our 2006 Annual Meeting of Stockholders.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

Incorporated by reference from our definitive Proxy Statement to be filed in connection with the solicitation of proxies for our 2006 Annual Meeting of Stockholders.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Incorporated by reference from our definitive Proxy Statement to be filed in connection with the solicitation of proxies for our 2006 Annual Meeting of Stockholders.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Incorporated by reference from our definitive Proxy Statement to be filed in connection with the solicitation of proxies for our 2006 Annual Meeting of Stockholders.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) Financial Statements

No financial statement schedules are included because the information is either provided in the financial statements or is not required under the related instructions or is inapplicable and such schedules therefore have been omitted.

(b) Exhibits

Number	Description
3.1	Composite Certificate of Incorporation of Registrant. Incorporated by reference to Exhibit 3.1 to the Company's Form 10-Q for the second quarter ending June 30, 1995 dated August 11, 1995.
3.2	Bylaws of Registrant as amended December 15, 2005. Incorporated by reference to Exhibit 3.1 to the Company's Form 8-K filed December 16, 2005.
4.1	Rights Agreement, dated as of June 17, 2002, by and between the Company and American Stock Transfer & Trust Company, as Rights Agent, which includes the Certificate of Designation for the Series B Junior Participating Preferred Stock as Exhibit A and the form of Rights Certificate as Exhibit B. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-A dated June 17, 2002.
10.1&	1991 Stock Option Plan, as amended and restated effective March 8, 2004. Incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q for the second quarter ending June 30, 2004 dated August 10, 2004.
10.2#	License Agreement dated April 15, 1993 between Ciba-Geigy Corporation (now merged into Novartis) and the Registrant. Incorporated by reference to Exhibit 10.40 to the Company's Form S-1 Registration Statement (Registration No. 33-73868).
10.3&	Employee Stock Purchase Plan. Incorporated by reference to Exhibit 99.1 to the Company's Form S-8 Registration Statement dated June 14, 2002 (Registration No. 333-90582).

10.4	Warehouse Lease dated July 12, 2000 between RBP, LLC an Alabama Limited Liability Company and the Registrant for office/warehouse space. Incorporated by reference to Exhibit 10.8 to the Company's Form 10-Q for the second quarter ending June 30, 2000 dated August 8, 2000.
10.5	Stock Purchase Agreement, dated as of February 17, 2004, by and among BioCryst Pharmaceuticals, Inc., Caduceus Private Investments II, LP, Caduceus Private Investments II (QP), LP and UBS Juniper Crossover Fund, L.L.C. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K dated February 17, 2004.
10.6&	Employment Agreement dated March 17, 2004 between the Registrant and Charles E. Bugg, Ph.D. Incorporated by reference to Exhibit 10.9 to the Company's Form 10-Q for the first quarter ending March 31, 2004 dated May 11, 2004.
10.7&	Employment Letter Agreement dated February 1, 2005 between the Registrant and Randall B. Riggs. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K dated February 7, 2005.
10.8	Stock Purchase Agreement, dated as of February 17, 2005, by and among BioCryst Pharmaceuticals, Inc., Baker Bros. Investments, L.P., Baker Biotech Fund II, L.P., Baker Bros. Investments II, L.P., Baker Biotech Fund II (Z), L.P., Baker/Tisch Investments, L.P., Baker Biotech Fund III, L.P., Baker Biotech Fund I, L.P., Baker Biotech Fund III (Z), L.P. and 14159, L.P. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-K dated February 17, 2005.
10.9&	Employment Letter Agreement dated May 4, 2005 between the Registrant and Jonathan M. Nugent. Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K dated May 10, 2005.
10.10*	License Agreement dated as of June 27, 2000, by and among Albert Einstein College of Medicine, Industrial Research, Ltd. and BioCryst Pharmaceuticals, Inc., as amended by the First Amendment Agreement dated as of July 26, 2002 and the Second Amendment Agreement dated as of April 15, 2005. (Portions omitted pursuant to request for confidential treatment.) Incorporated by reference to Exhibit 10.1 to the Company's Form 8-K dated November 30, 2005.
10.11*	Development and License Agreement dated as of November 29, 2005, by and between BioCryst Pharmaceuticals, Inc. and F.Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (Portions omitted pursuant to request for confidential treatment.) Incorporated by reference to Exhibit 10.2 to the Company's Form 8-K/A dated November 30, 2005.
10.12	Stock Purchase Agreement, dated as of December 14, 2005, by and among BioCryst Pharmaceuticals, Inc., Kleiner Perkins Caufield & Byers, Texas Pacific Group Ventures and KPTV, LLC. Incorporated by reference to Exhibit 4.1 to the Company's Form 8-K dated December 16, 2005.
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10.14&	Officer salaries for 2006. Incorporated by reference to Exhibit 1.01 to the Company's Form 8-K dated December 13, 2005.
23	Consent of Ernst & Young, Independent Registered Public Accounting Firm.
31.1	Certification of the Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

Confidential treatment granted.
& Management contracts.
* Confidential treatment requested.

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, thereunto duly authorized on this 9th day of March, 2006.

BIOCRYST PHARMACEUTICALS, INC.

By: /s/ Charles E. Bugg

Charles E. Bugg, Ph.D.
Chairman and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934 this report has been signed by the following persons on behalf of the registrant and in the capacities indicated on March 9, 2006:

Signature	Title(s)
/s/ Charles E. Bugg	Chairman, Chief Executive Officer and Director
(Charles E. Bugg, Ph.D.)	
/s/ J. Claude Bennett	President, Chief Operating Officer, Medical Director and Director
(J. Claude Bennett, M.D.)	
/s/ Michael A. Darwin	Chief Financial Officer (Principal Financial and Accounting Officer), Secretary and Treasurer
(Michael A. Darwin)	
/s/ Stephen R. Biggar	Director
(Stephen R. Biggar, M.D., Ph.D.)	
/s/ William W. Featheringill	Director
(William W. Featheringill)	
/s/ Carl L. Gordon	Director
(Carl L. Gordon, CFA, Ph.D.)	
/s/ John L. Higgins	Director
(John L. Higgins)	
/s/ Zola P. Horovitz	Director
(Zola P. Horovitz, Ph.D.)	
/s/ Beth C. Seidenberg	Director
(Beth C. Seidenberg, M.D.)	
/s/ Joseph H. Sherrill, Jr.	Director
(Joseph H. Sherrill, Jr.)	
/s/ William M. Spencer	Director
(William M. Spencer, III)	
/s/ Randolph C. Steer	Director
(Randolph C. Steer, M.D., Ph.D.)	

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Confidential treatment granted.
& Management contracts.
* Confidential treatment requested.

EXHIBIT 23

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

- Registration Statements (Form S-8 Nos. 333-120345, 333-39484, 333-30751 and 33-95062) pertaining to the BioCryst Pharmaceuticals, Inc. 1991 Stock Option Plan, as amended and restated as of March 8, 2004;
- Registration Statement (Form S-8 No. 333-90582) pertaining to the BioCryst Pharmaceuticals, Inc. Employee Stock Purchase Plan;
- Registration Statement (Form S-3 No. 333-128087) pertaining to the registration of up to $85,000,000, respectively, of BioCryst Pharmaceuticals, Inc. common stock;

of our reports dated March 8, 2006 with respect to the financial statements of BioCryst Pharmaceuticals, Inc., BioCryst Pharmaceuticals, Inc. management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of BioCryst Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2005.

/s/ ERNST & YOUNG LLP

Birmingham, Alabama
March 8, 2006

Exhibit 31.1

CERTIFICATIONS

I, Charles E. Bugg, certify that:

1. I have reviewed this annual report on Form 10-K of BioCryst Pharmaceuticals, 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(s) 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(s) 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.

Date: March 9, 2006

/s/ CHARLES E. BUGG

Charles E. Bugg
Chairman and Chief Executive Officer

Exhibit 31.2

CERTIFICATIONS

I, Michael A. Darwin, certify that:

1. I have reviewed this annual report on Form 10-K of BioCryst Pharmaceuticals, 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(s) 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(s) 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.

Date: March 9, 2006

/s/ MICHAEL A. DARWIN

Michael A. Darwin
Chief Financial Officer and Chief Accounting Officer

Exhibit 32.1

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 of BioCryst Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ending December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Charles E. Bugg, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(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.

/s/ Charles E. Bugg

Charles E. Bugg
Chief Executive Officer
March 9, 2006

This certification is furnished with this Report on Form 10-K pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and shall not, except to the extent required by such Act, be deemed filed by the Company for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.

Exhibit 32.2

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 of BioCryst Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ending December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Michael A. Darwin, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of my knowledge:

(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.

/s/ Michael A. Darwin

Michael A. Darwin
Chief Financial Officer
March 9, 2006

This certification is furnished with this Report on Form 10-K pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and shall not, except to the extent required by such Act, be deemed filed by the Company for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that the Company specifically incorporates it by reference.