BIOCRYST PHARMACEUTICALS INC
Form 10-K
March 06, 2009

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

þ **Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
For the fiscal year ended December 31, 2008

OR

o **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
Common Stock, $.01 Par Value	The NASDAQ Global Market

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

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

Yes o No þ.

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 o No þ.

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 þ No o.

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. o.

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

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

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

The Registrant estimates that the aggregate market value of the Common Stock on June 30, 2008 (based upon the closing price shown on the NASDAQ Global Market[SM] on June 30, 2008) held by non-affiliates was approximately $69,621,854.

The number of shares of Common Stock, par value $.01, of the Registrant outstanding as of February 20, 2009 was 38,331,303 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 2009 Annual Meeting of Stockholders are incorporated by reference into Items 10, 11, 12, 13 and 14 under Part III hereof.

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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 . 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, us, the Company and BioCryst refers to BioCryst Pharmaceuticals, Inc.

Overview

BioCryst Pharmaceuticals, Inc. is a biotechnology company that designs, optimizes and develops novel drugs that block key enzymes involved in cancer, viral infections and autoimmune diseases. 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.

One of our most advanced product candidates, forodesine HCl, is a transition-state analog inhibitor of the target enzyme purine nucleoside phosphorylase (PNP). An oral formulation of the compound is currently in a Phase IIb trial, which is planned to be a pivotal trial, for patients with Cutaneous T-cell Lymphoma (CTCL). The trial is being conducted under a special protocol assessment (SPA) negotiated with the United States Food and Drug Administration (FDA).

Additionally, forodesine HCl is currently being studied in a Phase II trial with an oral formulation in Chronic Lymphocytic Leukemia (CLL). Forodesine HCl has been granted Orphan Drug status by the FDA for three indications: T-cell non-Hodgkin 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-cell acute lymphoblastic leukemia (B-ALL). In December 2007, we announced the presentation of data related to the Phase I/II clinical study of forodesine HCl in subjects with refractory CTCL and a poster detailing the in vitro activity of forodesine HCl as a single agent and the synergistic in vitro activity of forodesine HCl in combination with bendamustine in primary cells from 29 patients with CLL. These data were presented at the 2007 American Society of Hematology meeting. In December 2008, we announced interim data from the ongoing forodesine HCl Phase II program in patients with CLL and data from a healthy subject pharmacokinetic and pharmacodynamic study. The CLL study will continue with an amendment to study a new dosing regimen of oral forodesine, 200 mg twice-daily. An interim analysis was conducted on data from an exploratory Phase II single-arm, open-label program in patients with CLL whose previous treatment had failed. While this analysis showed that no partial or complete responses were observed, five out of 13 patients administered 200 mg of forodesine HCl once-daily had substantial reductions in malignant lymphocytes, and at the time of the analysis, seven patients were still on study. Forodesine HCl was generally safe and well-tolerated at the 200 mg once-daily dose. In a parallel, healthy subject, pharmacokinetic and pharmacodynamic study, we compared the effect of seven days of 200 mg forodesine HCl dosed once-daily with seven days of 200 mg forodesine HCl dosed twice-daily. The study demonstrated substantially increased drug exposure and pharmacodynamic effect in subjects administered forodesine HCl 200 mg twice-daily. Drug exposure, as measured by area under the (plasma-concentration/time) curve (AUC), increased by 63 percent ($P<0.001$) for twice-daily dosing compared to once-daily dosing. Serum uric acid levels were reduced at steady state compared to baseline by 50.0 percent for twice-daily dosing compared to 23.5 percent for once-daily dosing ($p<0.001$), indicating increased PNP enzyme inhibition with twice-daily dosing. Also, use of forodesine HCl is being explored in various cancer settings, and combination studies are being planned. Since February 2006, we have had an exclusive licensing agreement with Mundipharma International Holdings Limited (Mundipharma) to develop and

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commercialize forodesine HCl in markets across the European Union (the EU), Asia and Australia for use in oncology. We have retained full development and commercialization rights in the rest of the world, including North America.

Another one of our most advanced drug candidates is peramivir, an inhibitor of influenza neuraminidase. Peramivir is in development for the treatment of influenza with two parenteral formulations, intramuscular (i.m.) and intravenous (i.v.). We completed a double-blind placebo-controlled Phase II clinical trial with i.m. peramivir testing two different dose levels of peramivir (150 mg and 300 mg) versus placebo in adults with acute uncomplicated influenza. While the trial did not demonstrate statistically significant differences for its primary endpoint of time to alleviation of symptoms, the preliminary analysis of the virologic data indicated that peramivir demonstrated statistically significant reductions in influenza virus shedding in both peramivir treatment groups compared to placebo, with greater reductions in the 300 mg dose. With this information and the additional pharmacokinetic information we have obtained subsequent to the trial, we initiated a Phase II placebo-controlled trial of 600 mg i.m. peramivir for the treatment of seasonal influenza. This trial is ongoing and uses a new, more concentrated 150 mg/ml formulation of peramivir. We expect to have data from this trial sometime in the second quarter of 2009.

In addition, in July 2007, we announced the initiation of a Phase II clinical trial in hospitalized patients using an i.v. formulation of peramivir to compare the efficacy and safety of i.v. peramivir to orally administered oseltamivir in patients who require hospitalization due to acute influenza. In October 2008 we reported results of an exploratory Phase II trial of i.v. peramivir in subjects hospitalized for acute serious or potentially life-threatening influenza. The Phase II trial compared the efficacy and safety of five days of therapy with either 200 mg i.v. peramivir per day, 400 mg i.v. peramivir per day or 75 mg oral oseltamivir twice a day for five days, in subjects who required hospitalization related to influenza. The primary objective of the study was to evaluate a novel composite endpoint, time to clinical stability, which is comprised of normalization of temperature, oxygen saturation, respiratory rate, systolic blood pressure and heart rate. Secondary objectives of the study included evaluation of viral shedding, mortality, clinical relapse and time to resumption of usual activities. As reported in October 2008, there were no statistically significant differences in any of the efficacy endpoints between the three treatment arms, and peramivir was generally safe and well-tolerated at those dose levels. Evaluation of time to clinical stability, the primary endpoint, showed a median of 23.7 hours for peramivir 200mg, 37.0 hours for peramivir 400 mg and 28.1 hours for oseltamivir (p=.306). This exploratory endpoint was driven by resolution of fever. Viral shedding (time weighted change from baseline in viral titer) was reduced by a median of -2.0 logs for peramivir 200mg, -2.1 logs for peramivir 400mg, and -1.9 logs for oseltamivir (p=.908). There was no mortality in the primary efficacy population, and there were no clinical relapses. Patients were discharged from the hospital after a median of 4.0 days for peramivir 200 mg, 3,8 days for peramivir 400 mg, and 4.0 days for oseltamivir (p=0.994). The median number of days required for resumption of usual activities was 8.8 days for peramivir 200 mg, 9.0 days for peramivir 400 mg, and 13.7 days for oseltamivir (p=0.276). BioCryst presented details of this study at the XI International Symposium on Respiratory Viral Infections, held in Bangkok, Thailand in February 2009.

In January 2007, we announced the United States Department of Health and Human Services (HHS), had awarded us a $102.6 million, four-year contract for the advanced development of peramivir. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS

regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

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In March 2007, we announced our collaboration with Shionogi & Co., Ltd. (Shionogi) for the development and commercialization of peramivir in Japan. This exclusive license agreement for Japan included an upfront payment of $14 million and future clinical event milestone payments of up to $21 million. Shionogi recently completed a Phase II study of intravenous (i.v.) peramivir administered via a single dose infusion in the outpatient setting for treatment of seasonal influenza. This trial met its primary endpoint of improvement in the median time to alleviation of symptoms in subjects with confirmed, acute, uncomplicated influenza infection, compared to placebo alone. Time to alleviation of symptoms was 81.8 hours for placebo, 59.1 hours for 300 mg peramivir, and 59.9 hours for 600 mg peramivir. This result was highly statistically significant (p=0.0046) for both the 300 mg dose (p=0.0046) and the 600 mg dose. Further, safety assessments confirmed that i.v. peramivir was generally safe and well-tolerated. Shionogi presented the data at the recent Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/ Infectious Diseases Society of America (IDSA) annual meeting in Washington, D.C. Based on the results from this Phase II study, Shionogi has initiated a Phase III program with i.v. peramivir in the outpatient setting. The Phase III study is a 1,050 subject study and would typically require two seasons to complete. In the event of a very strong flu season it is possible to complete a study of this magnitude in one flu season. Although it has been a strong flu season in Asia, it is not clear at this time if Shionogi will finish in one season or two. It is our understanding that Shionogi plans to complete its studies within this influenza season. In October 2008, the Company and Shionogi amended the license agreement to expand the territory in the agreement to include Taiwan and to provide rights for Shionogi to perform a Phase III clinical trial in Hong Kong.

Our other drug candidate in clinical trials is our second generation PNP inhibitor, BCX-4208. In November 2005, we announced that we were entering into an exclusive worldwide development and commercialization agreement with Roche. In the third quarter of 2007, we announced that Roche had initiated a Phase II clinical trial with oral doses of BCX-4208/R3421, which is designed to evaluate the drug candidate in patients with moderate to severe plaque psoriasis. The efficacy assessment of the study has been completed. Consistent with interim findings we reported in May 2008, the Phase II clinical study of BCX-4208, a potent, rationally designed, orally available PNP inhibitor, met its primary objectives of safety and tolerability. In addition, BCX-4208 displayed dose-dependent reductions in peripheral blood lymphocyte counts, including subsets measuring B cells (CD20), total T cells (CD3), T helper cells (CD4) and T suppressor/cytotoxic cells (CD8). Further, plasma levels of BCX-4208 increased with dose, and plasma uric acid levels showed dose-related reductions with BCX-4208. In addition, consistent with interim results we previously reported, no evidence of clinical efficacy, a secondary objective, was observed in psoriasis patients with doses and duration of administration tested.

In the Phase IIa trial, BCX-4208 was generally safe and well-tolerated at doses up to 120 mg daily. Most adverse events reported were considered mild or moderate, and low in frequency. No opportunistic infections were observed. In addition, detailed laboratory and clinical monitoring did not indicate any patterns suggestive of off-target adverse findings.

Also in May 2008, we announced that we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, we regained worldwide rights to BCX-4208.

BioCryst is a Delaware corporation originally founded in 1986. Our Alabama office is located at 2190 Parkway Lake Drive, Birmingham, Alabama 35244, where the telephone number is (205) 444-4600 and our North Carolina office is located at 2425 Kildaire Farm Road, Cary, North Carolina 27518 where the telephone number is (919) 859-1302. For more information about BioCryst, please visit our website at www.biocryst.com. The information on our website is not incorporated into this Form 10-K.

Our Business Strategy

We design, optimize and develop novel drugs that block key enzymes involved in cancer, viral infections and autoimmune diseases. We integrate 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 business strategy is to maximize sustainable value by moving our drug candidate portfolio through clinical development, registration and ultimately to the market. We believe this is best achieved by retaining full product

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rights to our drug candidates within specialty markets, while relying on collaborative arrangements with third parties for drug candidates within larger markets or outside our area of expertise. Potential third party alliances could include preclinical development, clinical development, regulatory approval, marketing, sales and distribution of our drug candidates. The principal elements of our strategy are:

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.

Select and License Promising Enzyme Targets for the Discovery 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 discovery 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 or niche areas with significant unmet medical need; and

have multiple potential clinical applications.

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.

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 our 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. Many academic institutions 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.

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Developing Drug Candidates or Licensing Them to Other Parties. We generally plan to advance drug candidates through initial and/or early-stage drug development. We prefer to retain full product rights to our drug candidates within specialty markets, while relying on collaborative arrangements with third parties or drug candidates within larger markets or outside our area of expertise. For larger disease indications or those outside our area of expertise, our strategy is to license drug candidates to pharmaceutical or biotechnology partners for collaborative 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 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.

Products in Development

The following table summarizes BioCryst s drug candidates in clinical development as of February 20, 2009:

Program and Candidate Disease Category/Indication	Delivery Form	Development Stage	Worldwide Rights
PNP Inhibitor (forodesine HCl)			BioCryst (U.S.)/Mundipharma (EU, Australia, Asia)
CTCL	Oral	Pivotal	
CLL	Oral	Phase II	
Neuraminidase Inhibitor (peramivir)			BioCryst (Rest of World)/Shionogi (East Asia)/Green Cross (Korea)
Viral	i.v.	Phase II	
Viral	i.m.	Phase II	
Viral	i.v.	Phase III	
PNP Inhibitor (BCX-4208/R3421)			
Psoriasis	Oral	Phase II	BioCryst

Additional Products

In addition to the programs shown above, we also retain exclusive rights to potent inhibitors of parainfluenza neuraminidase, hepatitis C and additional PNP inhibitors. We will continue to evaluate and test each of these compounds to determine which should be taken into clinical testing.

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 primarily suppression of T-cells without significantly impairing the function of other non-lymphoid cells.

Acute Lymphoblastic Leukemia. Acute lymphocytic leukemia (ALL) is a type of blood cancer. Other names for ALL are acute lymphoblastic leukemia and acute lymphoid leukemia. ALL is the most common form of leukemia in children. 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. T-cell lymphoma results when a T-lymphocyte (a type of white blood cell) undergoes a malignant change and begins

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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.

B-cell Related Cancers

Overview. There are two types of lymphocytes in the broadest sense T-cells and B-cells. Although PNP inhibitors were developed specifically to block the T-cells, recent work indicates that the same biochemical event the intracellular accumulation of deoxyguanosine triphosphate (dGTP) also occurs in malignant B-cells. Furthermore, work of Dr. Varsha Gandhi at MD Anderson Cancer Center has shown that PNP inhibitors, when acting *in vitro* on B-cells from patients with CLL induce accumulation of dGTP with resultant apoptosis (cell death).

These studies open the possibility of treating CLL, B-ALL and B-cell non-Hodgkin Lymphoma (NHL) with forodesine HCl. Importantly, B-cell malignancies are considerably more prevalent than are the T-cell leukemias and lymphomas.

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 dGTP. A high concentration of dGTP 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, forodesine HCl, 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 forodesine HCl can modulate T-cell activities. Forodesine HCl is an investigational PNP inhibitor for the potential treatment of T-cell leukemias and lymphomas. In February 2006, we licensed forodesine HCl to Mundipharma to develop and commercialize in markets across Europe, Asia and Australia for use in oncology.

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 forodesine HCl. We completed a Phase I single ascending dose clinical trial and a Phase Ib multi-dose clinical trial, both in healthy volunteers. In November 2005, we licensed BCX-4208 to Roche for the world wide development and commercialization in autoimmune diseases and transplant rejection. We announced termination of the Roche license in 2008 and have regained world wide rights to BCX-4208.

PNP Inhibitor (forodesine HCl)

Overview

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The first clinical trial with an intravenous formulation of forodesine HCl, which began in 2002, was a Phase I clinical trial that enrolled T-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 forodesine HCl 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-ALL by initiating additional clinical trials for refractory patients with B-ALL, CTCL, CLL, and other hematologic malignancies. Based on the encouraging results of these initial studies, we are working with our partner, Mundipharma, to develop a strategy for the simultaneous development of forodesine HCl in multiple indications and in potential combination therapies.

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

Forodesine HCl Clinical Development. Following the completion of a Phase I/II clinical trial in patients with refractory CTCL, in October 2007, we initiated a planned pivotal trial with an oral formulation of forodesine HCl for treatment of patients with CTCL. This trial is being conducted under a SPA agreement negotiated with the FDA and will serve as a basis for a new drug application to the FDA using the oral formulations in patients with relapsed CTCL. This Phase II clinical study has enrolled more than half of the targeted patients.

Based on preclinical studies conducted at the M.D. Anderson Cancer Center which indicated that forodesine HCl induces the same biochemical changes in various other types of leukemia cells that are responsible for the inhibition of T-leukemia cells, we initiated two small clinical studies late in 2005 in B-cell leukemias, which are more prevalent than T-cell leukemias. First, we initiated a Phase II trial with oral forodesine HCl in patients with CLL in an advanced stage and refractory to fludarabine, a current standard therapy. Our initial trial has been amended so that any potential subject who had fludarabine treatment in the past is now eligible. This trial is on-going. In December 2008, we announced interim data from the ongoing forodesine HCl Phase II program in patients with CLL and data from a healthy subject pharmacokinetic and pharmacodynamic study. The CLL study will continue with an amendment to study a new dosing regimen of oral forodesine, 200 mg twice-daily. An interim analysis was conducted on data from an exploratory Phase II single-arm, open-label program in patients with CLL whose previous treatment had failed. While this analysis showed that no partial or complete responses were observed, five out of 13 patients administered 200 mg of forodesine HCl once-daily had substantial reductions in malignant lymphocytes, and at the time of the analysis, seven patients were still on study. Forodesine HCl was generally safe and well-tolerated at the 200 mg once-daily dose. In a parallel, healthy subject, pharmacokinetic and pharmacodynamic study, we compared the effect of seven days of 200 mg forodesine HCl dosed once-daily with seven days of 200 mg forodesine HCl dosed twice-daily. The study demonstrated substantially increased drug exposure and pharmacodynamic effect in subjects administered forodesine HCl 200 mg twice-daily. Drug exposure, as measured by area under the (plasma-concentration/time) curve (AUC), increased by 63 percent ($P<0.001$) for twice-daily dosing compared to once-daily dosing. Serum uric acid levels were reduced at steady state compared to baseline by 50.0 percent for twice-daily dosing compared to 23.5 percent for once-daily dosing ($p<0.001$), indicating increased PNP enzyme inhibition with twice-daily dosing.

We initiated a Phase I/II clinical trial of forodesine HCl to determine the safety of repeat doses of an i.v. formulation of the drug in patients with B-ALL. This trial is completed. Once the data are thoroughly analyzed, we will review the results with Mundipharma to determine the best clinical development strategy going forward.

In January 2007, we initiated a Phase IIb multicenter, open-label, non-randomized repeat-dose registration study to evaluate an intravenous treatment of forodesine HCl followed by an oral treatment of forodesine HCl in patients with relapsed or refractory T-ALL. This study was being conducted under an SPA negotiated with the FDA and was designed to determine the rate of complete remission achieved with forodesine HCl. In March 2007, we announced that as a result of a stability issue with the i.v. formulation, that we were voluntarily placing this Phase IIb clinical trial on hold pending internal review and discussions with our partner, Mundipharma. In December 2007, we announced the formal termination of this study.

In February 2006, we and Mundipharma entered into an exclusive license agreement to develop and commercialize forodesine HCl in markets across Europe, Asia and Australia 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 forodesine HCl in a variety of serious medical conditions potentially including T-cell leukemia, CTCL, CLL, T-cell non-Hodgkin lymphoma and B-cell non-Hodgkin lymphoma.

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PNP Inhibitor (BCX-4208/R3421)

Overview

During 2004, we began clinical development of BCX-4208, another PNP inhibitor, as a drug candidate for the treatment of T-cell mediated autoimmune diseases, including psoriasis, and transplant rejection. Although BCX- 4208 and forodesine HCl are both investigational PNP inhibitors, BCX-4208 differs from forodesine HCl 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 forodesine HCl for the treatment of diseases requiring long-term, chronic administration of a PNP inhibitor. Psoriasis is a chronic and often painful and debilitating disease which affects an estimated 2-3 percent of the world s population, accounting for nearly 125 million persons worldwide. The National Institute of Health estimates that 5.8-7.5 million Americans have psoriasis.

Current Development Strategy

We completed our initial Phase I study, a single dose pharmacokinetic trial in healthy volunteers, early in 2005 and 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. 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 established a joint committee to set the clinical development strategy and the future development program for BCX-4208.

During the third quarter of 2007, we announced that Roche had initiated a Phase IIa clinical trial to evaluate BCX-4208/R3421 in patients with moderate to severe plaque psoriasis. The efficacy assessment of the study has been completed. Consistent with interim findings reported by the Company in May 2008, the Phase II clinical study of BCX-4208, a potent, rationally designed, orally available PNP inhibitor, met its primary objectives of safety and tolerability. In addition, BCX-4208 displayed dose-dependent reductions in peripheral blood lymphocyte counts, including subsets measuring B cells (CD20), total T cells (CD3), T helper cells (CD4) and T suppressor/cytotoxic cells (CD8). Further, plasma levels of BCX-4208 increased with dose, and plasma uric acid levels showed dose-related reductions with BCX-4208. In addition, consistent with interim results previously reported by the Company, no evidence of clinical efficacy, a secondary objective, was observed in psoriasis patients with doses and duration of administration tested.

In the Phase IIa trial, BCX-4208 was generally safe and well-tolerated at doses up to 120 mg daily for six weeks. Most adverse events reported were considered mild or moderate, and low in frequency. No opportunistic infections were observed. In addition, detailed laboratory and clinical monitoring did not indicate any patterns suggestive of off-target adverse findings.

Also in May 2008, we announced that we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, we regained worldwide rights to 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, there are an estimated 200,000 influenza associated hospitalizations, and influenza is responsible for approximately 36,000 deaths annually. 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.

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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 two 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 ranging from those 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 deadly to them. Of the avian influenza viruses that have crossed the species barrier to infect humans, the H5N1 virus has caused the largest number of detected cases of severe disease and death in humans. Thus far, person to person spread of this virus is considered extremely rare, but as influenza A viruses constantly change, they could mutate over time to have the ability to spread rapidly among humans.

Pandemic Influenza. Pandemic influenza 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 20th century.

Influenza 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, drugs in the adamantine class, have been 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. The CDC has recommended against the use of amantadine and rimantadine for the treatment or prophylaxis of influenza in the United States until susceptibility to these antiviral medications has been re-established among circulating influenza A viruses. Osteltamivir and zanamivir, drugs in the neuraminidase inhibitor class, have been used for the treatment of influenza. Recently, the prevalence of resistance to oseltamivir in subtype H1N1 of influenza A has increased, and the CDC has recommended the use of zanamivir or a combination of oseltamivir and rimatadine when influenza A (H1N1) virus infection or exposure is suspected.

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 strain of influenza that circulates is different from that present in the vaccine. In addition, many people decline the required injections. 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 (antigenic drift). 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, peramivir, both Roche, in collaboration with Gilead Sciences, and GlaxoSmithKline (GSK) have neuraminidase inhibitors on the market. 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 and are to be administered for 5 days. Roche s neuraminidase inhibitor is

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also approved for prophylaxis of influenza. In addition to these companies with neuraminidase inhibitors, there are other companies working to develop additional 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.

Government Stockpiling. With the concern of avian influenza and the possible threat of a pandemic, many governments throughout the world have been stockpiling antiviral drugs, such as Roche s neuraminidase inhibitor, oseltamivir. There is interest in many of these governments, including the U.S. government to find additional vaccines and antivirals to address a potential pandemic situation.

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.

Previous development of peramivir in an oral formulation was conducted through a worldwide license agreement between the Company and the R.W. Johnson Pharmaceutical Research Institute and Ortho-McNeil Pharmaceutical Inc. (both Johnson & Johnson companies). Johnson & Johnson made the business decision to terminate this agreement in 2001 and returned all rights to us. In June 2002, we completed an ongoing Phase III clinical trial that had been started by Johnson & Johnson and subsequently terminated development of our oral peramivir program as a result of missing the primary endpoint in the pivotal trial.

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 to oral oseltamivir, or Tamiflu, for addressing a potential pandemic. As a result, we filed an IND in 2005 and re-initiated the clinical development of peramivir during 2006.

Current Development Strategy

Preclinical studies comparing peramivir with other anti-influenza drugs have demonstrated that peramivir has broad-spectrum potency against multiple strains of influenza in the nanomolar or sub-nanomolar range , including the avian strain H5N1. We are currently focusing on injectable formulations of peramivir to achieve high blood levels that may be effective against most strains of influenza, including strains that may be resistant to oseltmivir (Tamiflu). Our investigational new drug application (IND) for i.v. peramivir became effective in December 2005 and for i.m. in December 2006. We received fast track designation from the FDA in January 2006 and initiated a Phase I clinical trial with i.v. peramivir in March 2006. During 2006, we conducted multiple Phase I clinical trials in healthy volunteers in preparation for the Phase II trials to be initiated during the 2006-2007 influenza season, which began with the initiation of a Phase II study with the i.m. formulation in January 2007.

Intramuscular peramivir. We completed a double-blind placebo-controlled Phase II clinical trial with i.m. peramivir testing two different dose levels of peramivir (150 mg and 300 mg) versus placebo in adults with acute uncomplicated influenza. While the trial did not demonstrate statistically significant differences for its primary endpoint of time to alleviation of symptoms, the preliminary analysis of the virologic data indicated that peramivir demonstrated statistically significant reductions in influenza virus shedding in both peramivir treatment groups compared to placebo, with greater reductions in the 300 mg dose. With this information and the additional

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pharmacokinetic information we have obtained subsequent to the trial, we initiated a Phase II placebo-controlled trial of 600 mg i.m. peramivir for the treatment of seasonal influenza. This trial uses a new, more concentrated 150 mg/ml formulation of peramivir. This trial is ongoing.

Intravenous peramivir. In July 2007, we announced the initiation of a Phase II clinical trial of i.v. peramivir to compare the efficacy and safety of i.v. peramivir to orally administered oseltamivir in patients who require hospitalization due to acute influenza. This trial was initiated in the Southern Hemisphere and is currently ongoing in the Northern Hemisphere. On October 27, 2008 the Company announced results of this exploratory Phase II trial. The study compared the efficacy and safety of five days of therapy with either 200 mg i.v. peramivir per day, 400 mg i.v. peramivir per day or 75 mg oral oseltamivir twice a day, in patients who required hospitalization related to influenza. The results were presented at the XI International Symposium on Respiratory Viral Infections in Bangkok, Thailand in February 2009.

Summary. Our plan is to continue developing both injectable formulations in the in-patient and out-patient settings. In addition to the progress made clinically in both programs, we have also made significant progress in the manufacturing and toxicology work required to advance both programs forward toward product approval. 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 injectable formulations of peramivir will have considerable potential for treating patients with seasonal influenza infections, in addition to providing an effective mechanism for treating large numbers of patients rapidly in the event of a flu pandemic.

Congress approved an appropriation of $3.8 billion for 2006 to support the development of various countermeasures for a flu pandemic. The appropriation included funding for the development of new antiviral agents. In January 2007, we announced that HHS had awarded the Company a $102.6 million, four-year contract for the advanced development of peramivir for U.S. licensure. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

In addition to the contract with HHS, we have established collaborative relationships with Shionogi and Green Cross for the development and commercialization in Japan and Taiwan by Shionogi and in Korea by Green Cross. The Shionogi agreement was established in February 2007, which resulted in an upfront payment of $14 million and future clinical event milestone payments of up to $21 million. The Shionogi agreement was amended in 2008 to expand the territory in the agreement to include Taiwan and to provide rights for Shionogi to perform its Phase III clinical trial in Hong Kong. Shionogi recently completed a Phase II study of intravenous (i.v.) peramivir administered via a single dose injection in the outpatient setting for treatment of seasonal influenza. This trial met its primary endpoint of improvement in the median time to alleviation of symptoms in subjects with confirmed, acute, uncomplicated influenza infection, compared to placebo alone. Shionogi commenced a phase III program in East Asia, including Japan, in December 2008.

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

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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. Beginning in June 2006, we began building an internal clinical development and regulatory team, based in Cary, North Carolina to manage the development strategy for our later stage products. During the years ended December 31, 2008, 2007 and 2006, we spent $73.3, $94.1, and $47.1 million, respectively, on 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 entered into two major collaborations for the development and commercialization of our lead PNP inhibitors and two collaborations for the development and commercialization of peramivir in certain countries outside the U.S. In addition, in January 2007, we announced that HHS had awarded the Company a $102.6 million, four-year contract for the advanced development of peramivir for U.S. licensure.

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. For example, our PNP inhibitors were in-licensed from AECOM and IRL in June 2000.

Corporate Alliances

Mundipharma. In February 2006, the Company entered into an exclusive, royalty bearing right and license in the specified territory (primarily Europe, Asia and Australia) with Mundipharma for the development and commercialization of our lead PNP inhibitor, forodesine HCl, for use in oncology. Under the terms of the agreement, Mundipharma obtained oncology rights to forodesine HCl in the specified territory in exchange for a $10 million up-front payment. Mundipharma will share 50% of the documented third party 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 possibility of future event payments totaling $155 million for achieving specified development, regulatory and commercial events (including certain sales level amounts following a product s launch) for certain indications. In addition, the agreement provides that we will receive royalties (ranging from single digits to mid teens) 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

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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.

Within five years of the effective date of the agreement, Mundipharma has a right of first negotiation on existing backup PNP inhibitors we develop through Phase IIb in oncology, but any new PNP inhibitors are exempt from this agreement and we retain all rights to such compounds. We retain the rights to forodesine HCl 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 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.

Shionogi. In March 2007, the Company entered into an exclusive license agreement with Shionogi to develop and commercialize the Company s lead influenza neuraminidase inhibitor, peramivir, in Japan for the treatment of seasonal and potentially life-threatening human influenza. Under the terms of the agreement, Shionogi obtained rights to injectable formulations of peramivir in Japan in exchange for a $14 million up-front payment. The license provides for potential future milestone event payments (up to $21 million) and commercial event milestone payments (up to $95 million) in addition to double digit (between 10 and 20% range) royalty payments on product sales of peramivir. In December 2007, the Company received a $7 million milestone payment from Shionogi for their initiation of a Phase II clinical trial with i.v. peramivir. Generally, all payments under the agreement are nonrefundable and non-creditable, but they are subject to audit. Shionogi will be responsible for all development, regulatory and marketing costs in Japan. The term of the agreement is from February 28, 2007 until terminated by either party in accordance with the license agreement. Either party may terminate in the event of an uncured breach. Shionogi has the right of without cause termination. In the event of termination all license and rights granted to Shionogi shall terminate and shall revert back to the Company. The Company developed peramivir under a license from UAB and will owe sublicense payments to them on the upfront payment and any future event payments and/or royalties received by the Company from Shionogi. In October 2008, the Company and Shionogi amended the license agreement to expand the territory covered by the agreement to include Taiwan and to provide rights for Shionogi to perform a Phase III Clinical Trial in Hong Kong. Shionogi commenced a phase III program in East Asia, including Japan, in December 2008. BioCryst retains all rights to commercialize peramivir in North America, Europe, and other countries outside of Japan, Taiwan and Korea.

Green Cross Corporation (Green Cross). In June 2006, the Company entered into an agreement with Green Cross to develop and commercialize peramivir in Korea. Under the terms of the agreement, Green Cross will be responsible for all development, regulatory, and commercialization costs in Korea. The Company received a one-time license fee of $250,000. Total future milestone payments would be equally modest. The license also provides that the Company will share in profits resulting from the sale of peramivir in Korea, including the sale of peramivir to the Korean government for stockpiling purposes. Furthermore, Green Cross will pay the Company a premium over its cost to supply peramivir for development and any future marketing of peramivir products in Korea. Both parties have the right to terminate in the event of an uncured material breach. In the event of termination all rights, data, materials, products and other information would be transferred to the Company.

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. The license also provided for future milestone event payments for achieving specified development, regulatory and commercial

milestones (including sales level milestones following a product s launch) for certain indications.

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In May 2008 the Company received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. Upon termination during the fourth quarter of 2008, the Company recognized the remaining deferred revenue and deferred expense related to the license agreement, which were $26.5 million and $8.2 million, respectively.

Academic Alliances

Albert Einstein College of Medicine of Yeshiva University and Industrial Research, Ltd, New Zealand (AECOM and IRL respectively) In June 2000, we licensed a series of potent inhibitors of PNP from AECOM and IRL. The lead drug candidates from this collaboration are forodesine HCl and BCX-4208. We have obtained worldwide exclusive rights to develop and ultimately distribute these compounds or any other drug candidates that might arise from research on these inhibitors. We have the option to expand the Agreement to include other inventions in the field made by the investigators or employees of AECOM and IRL. We have agreed to use commercially reasonable efforts to develop these drugs. In addition, we have agreed to pay certain milestone payments for each licensed product (which range in the aggregate from $1.4 million to almost $4 million per indication) for future development of these inhibitors, single digit royalties on net sales of any resulting product made by us, and to share approximately one quarter of future payments received from other third-party partners, if any. In addition, we have agreed to pay annual license fees that can range from $150,000 to $500,000 depending on stage of development of products that are non-refundable, but are creditable against actual royalties and other payments due to AECOM and 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 and/or IRL.

The University of Alabama at Birmingham (UAB). We have had a close relationship with UAB since our formation. Our former Chairman, Dr. Charles E. Bugg, was the previous Director of the UAB Center for Macromolecular Crystallography, and our former Chief Operating Officer, 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 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 single digit royalties on sales of any resulting product and to share in future payments received from other third-party partners. We have completed the research under both the complement and influenza agreements. 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. Upon termination each party shall cease using the other party s proprietary and confidential information and materials, the parties shall jointly own joint inventions and UAB shall resume full ownership of all UAB licensed products. There is currently no activity between us and UAB on these agreements, but when the Company licenses this technology, such as in the case of the Shionogi and Green Cross agreements, or commercialize products related to these programs, we will owe sublicense fees or royalties on amounts we receive.

Emory University (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 single digit royalties on sales of any resulting product and to share in future payments received from other third party partners, if any. We can terminate this agreement at any time by giving 90 days advance notice. Upon termination, BioCryst would cease using the licensed technology.

Government Contracts

In January 2007, we announced that HHS had awarded the Company a $102.6 million, four-year contract for the advanced development of peramivir. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the

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$102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged. HHS has indicated that antiviral drugs are an important element of their pandemic influenza preparedness efforts and that their strategy includes not only stockpiling of existing antiviral drugs but also seeking out new antiviral medications to further broaden their capabilities to treat and prevent all forms of influenza. Peramivir is in the same class of neuraminidase inhibitors as oseltamivir (Tamiflu) and zanamivir (Relenza), all of which are antiviral drugs, but the method of delivery for peramivir will be parenteral (i.m. and i.v.) as compared to the oral Tamiflu or inhaled Relenza. We are committed to working with HHS for the development of these parenteral formulations of peramivir which could be especially useful in hospital settings or pandemic situations due to the ability to achieve high levels of the drug rapidly throughout the body.

This contract is a cost-plus-fixed-fee contract, which is milestone-driven. HHS will make periodic assessments of progress and the continuation of the contract is based on our performance, timeliness and quality of deliverables, and other factors. The government has rights under certain contract clauses to terminate this contract. The contract is terminable by the government at any time for breach or without cause.

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 partners 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, 2009, we have been issued 29 U.S. patents that expire between 2009 and 2025 and that relate to our PNP, serine protease and neuraminidase inhibitor compounds. We have licensed six different class of compounds representing new 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 PCT or 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.

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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 partners to enter into confidentiality agreements, which prohibit the disclosure of confidential information to anyone outside of our company and, where possible, 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 may decide to market, distribute and sell products within specialty markets for use in treatment of various diseases. Our general strategy is to maximize sustainable value by moving our drug candidate portfolio through clinical development, registration and ultimately to the market. We believe that this is best achieved by retaining full product rights to certain drug candidates within specialty markets, while relying on collaborative arrangements with third parties for drug candidates within larger markets or outside our area of expertise. However, in general, we lack experience in marketing, distributing and selling pharmaceutical products. Our strategy includes relying on partners, 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 partners, 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, and inflammatory 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. 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 Eisai s Targretin for CTCL and the current neuraminidase inhibitors marketed by GSK and Roche for influenza. In addition, several pharmaceutical and biotechnology firms, including major pharmaceutical companies, have announced efforts in the field of structure-based drug design and in the therapeutic areas of cancer, infectious disease, autoimmune, and inflammatory disorders, as well as other therapeutic areas where we are focusing our drug discovery efforts.

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;

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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 partners 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 thirteen 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 partners 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 availability of the required number of eligible subjects to be enrolled in a given trial;

the availability of existing or other experimental drugs for the disease we intend to treat;

the willingness of patients to participate; and

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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 partners 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 partners 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 20, 2009, we had 80 employees, of whom 59 were engaged in research and development and 21 were in general and administrative functions. Our research and development staff, 22 of whom hold Ph.D. or M.D. degrees, have diversified experience in biochemistry, pharmacology, X-ray crystallography, synthetic organic chemistry, computational chemistry, and medicinal chemistry, clinical development and regulatory affairs. We consider our relations with our employees to be satisfactory.

Financial Information

For information related to our revenues, profits, net loss and total assets, in addition to other financial information, please refer to the Financial Statement and Notes to Financial Statements contained in this Annual Report.

Available Information

We have available a website on the Internet. Our address is www.biocryst.com. We make available, free of charge, 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. Any amendment to, or waiver from, our code of business conduct will be posted on our website.

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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. To become profitable, we must successfully manufacture and develop drug product candidates, receive regulatory approval, and successfully commercialize or enter into profitable agreements with other parties. 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. 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.

Our success depends upon our ability to advance our products through the various stages of development, especially through the clinical trial process.

To receive the regulatory approvals necessary for the sale of our product candidates, we or our partners must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective. 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 unlikely to show good results in the trials, unlikely to help advance a product to the point of a meaningful collaboration, or unlikely to have a reasonable commercial potential. We may suffer significant setbacks in pivotal clinical trials, even after earlier clinical trials show promising results. Clinical trials may not be adequately designed or executed, which could affect the potential outcome and analysis of study 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 partners, 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 and have acceptable commercial viability.

Our ability to successfully complete clinical trials is dependent upon many factors, including but not limited to:

- our ability to find suitable clinical sites and investigators to enroll patients;
- the availability of and willingness of patients to participate in our clinical trials;
- difficulty in maintaining contact with patients to provide complete data after treatment;
- our product candidates may not prove to be either safe or effective;
- clinical protocols or study procedures may not be adequately designed or followed by the investigators;
- manufacturing or quality problems could affect the supply of drug product for our trials; and
- delays or changes in requirements by governmental agencies.

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Clinical trials are lengthy and expensive. We or our partners 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 partners successfully complete clinical trials for our product candidates, we or our partners might not file the required regulatory submissions in a timely manner and may not receive regulatory approval for the product candidate.

Our later stage clinical trials may not adequately show our drugs are safe or effective.

Progression of our drug products through the clinical development process is dependent upon our trials indicating our drugs have adequate safety profiles and show positive therapeutic effects in the patients being treated by achieving pre-determined endpoints according to the trial protocols. Failure to achieve either of these could result in delays in our trials or even require the performance of additional unplanned trials. This could result in delays in the development of our drug candidates and could result in significant unexpected costs.

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.

As our clinical programs continue to grow and patient enrollment increases, our costs will increase. Our current and planned clinical trials plus the related development, manufacturing, regulatory approval process requirements, and additional personnel resources and testing required for supporting the development of our drug candidates will consume significant capital resources. Our expenses, revenues and burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our collaborative agreements for our drug candidates, the amount of funding we receive from HHS for peramivir, the amount of funding or assistance, if any, we receive from other governmental agencies or other new partnerships with third parties for the development of our drug candidates, the progress and results of our current and proposed clinical trials for our most advanced drug products, the progress made in the manufacturing of our lead products and the progression of our other programs.

We expect that 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, including governmental agencies, in general and from the HHS contract specifically, 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.

If HHS were to eliminate, reduce or delay funding from our contract or dispute some of our incurred costs, this would have a significant negative impact on our revenues, cash flows and the development of peramivir.

Our projections of revenues and incoming cash flows are substantially dependent upon HHS reimbursement for the costs related to our peramivir program. If HHS were to eliminate, reduce or delay the funding for this program or disallow some of our incurred costs, we would have to obtain additional funding for development of this drug candidate or significantly reduce or stop the development effort.

For example, in January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in

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outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, the Company expects to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged. In July 2008, HHS indicated that it does not intend to reimburse us all of the costs incurred related to the terminated Phase III studies. We continue to pursue reimbursement of these costs. During the second quarter of 2008, we recorded a $4.9 million reserve against revenue for amounts we previously expected to receive from HHS related to the costs incurred in this program. Approximately $4.6 million of the reserve relates to revenues recognized in the first quarter of 2008, while approximately $0.3 million of the reserve relates to revenues recognized in 2007.

In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract, which may limit our reimbursement or if we are found to be in violation could result in contract termination. U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion. The U.S. government may terminate its contract with us either for its convenience or if we default by failing to perform in accordance with the contract schedule and terms, which would have a significant negative impact on our cash flows and operations.

Our contract with HHS has special contracting requirements, which create additional risks of reduction or loss of funding.

We have entered into a contract with HHS for the advanced development of our neuraminidase inhibitor, peramivir. In contracting with HHS, we are subject to various U.S. government contract requirements, including general clauses for a cost-reimbursement research and development contract. U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, which subjects us to additional risks. These risks include the ability of the U.S. government to unilaterally:

terminate or reduce the scope of our contract; and

audit and object to our contract-related costs and fees, including allocated indirect costs.

The U.S. government may terminate its contract with us either for its convenience or if we default by failing to perform in accordance with the contract schedule and terms. Termination for convenience provisions generally enable us to recover only our costs incurred or committed, and settlement expenses and profit on the work completed prior to termination. Termination for default provisions does not permit these recoveries.

As a U.S. government contractor, we are required to comply with applicable laws, regulations and standards relating to our accounting practices and are subject to periodic audits and reviews. As part of any such audit or review, the U.S. government may review the adequacy of, and our compliance with, our internal control systems and policies, including those relating to our purchasing, property, estimating, compensation and management information systems. Based on the results of its audits, the U.S. government may adjust our contract-related costs and fees, including allocated indirect costs. In addition, if an audit or review uncovers any improper or illegal activity, we may be subject to civil and criminal penalties and administrative sanctions, including termination of our contracts, forfeiture of profits, suspension of payments, fines and suspension or prohibition from doing business with the U.S. government. We could also suffer serious harm to our reputation if allegations of impropriety were made against us. In addition, under U.S. government purchasing regulations, some of our costs may not be reimbursable or allowed under our contracts. Further, as a U.S. government contractor, we are subject to an increased risk of investigations, criminal prosecution, civil fraud, whistleblower lawsuits and other legal actions and liabilities as compared to private sector commercial companies.

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If we fail to successfully commercialize or establish collaborative relationships to commercialize certain of our drug product candidates or if any partner terminates or fails to perform its obligations under agreements with us, potential revenues from commercialization of our product candidates could be reduced, delayed or eliminated.

Our business strategy is to increase the asset value of our drug candidate portfolio. We believe this is best achieved by retaining full product rights or through collaborative arrangements with third parties as appropriate. As needed, potential third party alliances could include preclinical development, clinical development, regulatory approval, marketing, sales and distribution of our drug product candidates.

Currently, we have established collaborative relationships with certain pharmaceutical companies, Roche (recently terminated), Mundipharma, and both Shionogi and Green Cross for the development and commercialization of BCX-4208, forodesine HCl and peramivir, respectively. The process of establishing and implementing collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- our partners 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 partners and have limited control over their decisions;
- our ability to generate future event payments and royalties from our partners depends upon their 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;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party 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 partner fails to fulfill its responsibilities in a timely manner, or at all, our commercialization efforts related to that collaboration could be reduced, delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our partner. 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.

For example, in May 2008, we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result of the no cause termination by Roche, we regained worldwide rights to BCX-4208.

We are currently in dispute with Mundipharma regarding the contractual obligations of the parties with respect to certain costs related to the manufacturing and development of forodesine HCl. Notwithstanding, we do not believe that we are responsible for any of the disputed amounts. We are engaged in ongoing discussion to resolve this dispute. The maximum potential exposure to us is estimated to be approximately $2.5 million. Because of the preliminary

nature of the discussions, no amounts have been accrued as of December 31, 2008.

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

We have not commercialized any products or technologies, and we may never be able to do so. We currently have no marketing capability and no direct or third-party sales or distribution capabilities and may be unable to establish these capabilities for products we plan to commercialize. In addition, 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 event or other collaborative payments.

Our ability to receive revenue from products we commercialize presents several risks, including:

- we or our collaborators may fail to successfully complete clinical trials sufficient to obtain FDA marketing approval;
- many competitors are more experienced and have significantly more resources and their products could be more cost effective or have a better efficacy or tolerability profile than our product candidates;
- we may fail to employ a comprehensive and effective intellectual property strategy which could result in decreased commercial value of our company and our products;
- we may fail to employ a comprehensive and effective regulatory strategy which could result in a delay or failure in commercialization of our products;
- our ability to successfully commercialize our products are affected by the competitive landscape, which cannot be fully known at this time;
- reimbursement is constantly changing which could greatly affect usage of our products; and
- 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 third parties, such as our development partners and contract research organizations, 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 but not limited to:

- discovery of compounds 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; and
- manufacturing the starting materials and drug substance required to formulate our drug products and the drug products to be used in both our clinical trials and toxicology studies.

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, drug

substance and drug products or manage our regulatory function breached their obligations to us or

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perform their services inconsistent with industry standards and not in accordance with the required regulations, this would delay or prevent the development of our product candidates.

If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to current Good Laboratory Practices (cGLP), current Good Manufacturing Practices (cGMP), or current Good Clinical Practices (cGCP), and similar foreign standards and we do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our product candidates could be delayed.

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

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 but not limited to the following:

- the injectable versions of peramivir are currently in Phase II clinical development and have been tested in a limited number of 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;
- injectable forms of peramivir may not prove to be accepted by patients and physicians as a treatment for seasonal influenza compared to the other currently marketed antiviral drugs, which would limit revenue from non-governmental entities;
- 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 and if we are not successful at marketing peramivir to these entities for any reason, we will not receive substantial revenues from stockpiling orders from these entities.

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

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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 but not limited to problems involving:

- inconsistent production yields;
- product liability claims;
- difficulties in scaling production to commercial and validation sizes;
- 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;
- potential impurities in our drug substance or drug products that could affect availability of product for our clinical trials or future commercialization;
- 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 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.

If we or our partners 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 partners must obtain regulatory approval before marketing or selling our future drug products. If we or our partners 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 process of preparing for and obtaining FDA approval may be lengthy and expensive, and approval is never certain. Products distributed abroad are also subject to foreign government regulation. Neither the FDA nor foreign regulatory agencies have approved any of our drug product candidates. 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

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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, our clinical data and our manufacturing data at our facility. While we do store duplicate copies of most of our clinical data offsite and a significant portion of our data is included in regular backups of our systems, we could lose important 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 partners 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. In November 1995, the FDA issued 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.

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 partners are performing research on or developing products for the treatment of several disorders including T-cell mediated disorders (T-cell cancers, transplant rejection, psoriasis and other autoimmune indications), oncology, influenza, and hepatitis C. 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 Eisai s Targretin for CTCL and the current neuraminidase inhibitors marketed by Glaxo Smith Kline and Roche for influenza. In addition, several pharmaceutical and biotechnology

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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, influenza, hepatitis C, and in other therapeutic areas where we have discovery efforts ongoing. 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 partners to obtain, protect and enforce viable intellectual property rights including but not limited to trade name, trade mark and patent protection for our company and its 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), the Patent Cooperation Treaty offices, nor the courts of the United States and other jurisdictions have consistent policies nor predictable rulings regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology and pharmaceutical patents. The validity, scope, 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 other intellectual property 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 partners 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 partners 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 partners 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 or fail to adequately, initiate, protect, defend or enforce our intellectual property rights in any area of commercial interest or in any part of the world where we wish to seek regulatory approval for our products, methods, processes and other technologies, the value of the drug product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our commercial use of such products, processes, and other technologies, including but not limited to any tradename, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a number of patents for our various

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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 have also filed certain trademark and tradename applications worldwide. 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;
- if patents do issue we can not be sure that we will be able to adequately defend such patents and whether or not we will be able to adequately enforce such patents; or
- whether or not others will obtain patents claiming aspects similar to those covered by our patent applications.

If the USPTO or other foreign patent office 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 or other foreign patent office. 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 partners 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 or commercialize our product candidates and any such events would significantly impair the value of such product candidates.

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 $11 million. 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;

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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 facility incurs damage or power is lost for a significant length of time, our business will suffer.

We currently 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.

In addition, 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.

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.

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, 2008, the 52-week range of the market price of our stock was from $0.85 to $6.53 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;

additional dilution through sales of our common stock or other derivative securities;

status of new or existing licensing or collaborative agreements and government contracts;

announcements relating to the status of our programs;

we or our partners 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;

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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;

purchases or 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.

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.

Information Regarding Forward-Looking Statements

This filing contains forward-looking statements, including statements regarding future results, performance or achievements. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. 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 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, Risk Factors 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 testing, clinical trials, and other research and development efforts;

the potential funding from our contract with HHS for the development of peramivir;

the further preclinical or clinical development and commercialization of our product candidates, including peramivir, forodesine HCl and other PNP inhibitor and hepatitis C development programs;

the implementation of our business model, strategic plans for our business, product candidates and technology;

our ability to establish and maintain collaborations;

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plans, programs, progress and potential success of our collaborations, including Mundipharma for forodesine HCl and Shionogi and Green Cross for peramivir;

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 financial performance; and

competitive companies, technologies and our industry.

These statements reflect our current views with respect to future events and we have no obligation to update or revise the statements. We caution that you should not place undue reliance on these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Risk Factors.

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.

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ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our administrative offices and principal research facilities are located in 50,150 square feet of leased space in Riverchase Industrial/Research Park in Birmingham, Alabama. The lease runs through June 30, 2015 with an option to renew the lease for an additional five years at current market rates. In addition, we currently lease 5,565 square feet of office space in Cary, North Carolina through February 28, 2010 for our clinical and regulatory operation. 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.

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PART II

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

Market Information

Our common stock trades on the NASDAQ Global Market[SM] under the symbol BCRX. The following table sets forth the low and high sales prices of our common stock as reported by NASDAQ Global Market[SM] for each quarter in 2008 and 2007:

	2008		2007	
	Low	**High**	**Low**	**High**
First quarter	$2.81	$6.53	$7.80	$12.50
Second quarter	2.58	4.98	6.57	10.05
Third quarter	2.40	3.60	7.20	13.18
Fourth quarter	.85	3.18	5.68	8.33

The last sale price of the common stock on February 20, 2009 as reported by NASDAQ Global Market[SM] was $1.48 per share.

Holders

As of February 20, 2009, there were approximately 259 holders of record of our common stock.

Dividends

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

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Stock Performance Graph

This performance graph is not soliciting material, is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act of 1933, as amended (the Securities Act), or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The stock price performance shown on the graph is not necessarily indicative of future price performance.

	Beginning Investment 12/31/03	Investment at 12/31/04	Investment at 12/31/05	Investment at 12/31/06	Investment at 12/31/07	Investment at 12/31/08
BioCryst Pharmaceuticals, Inc.	$100.00	$ 84.38	$244.53	$168.76	$ 90.22	$ 20.00
The NASDAQ Stock Market	100.00	108.84	111.16	122.11	132.42	63.80
NASDAQ Pharmaceutical Stocks	100.00	106.51	117.29	114.81	120.74	112.34

The above graph measures the change in a $100 investment in the Company s common stock based on its closing price of $6.85 on December 31, 2003 and its year-end closing price thereafter. The Company s relative performance is then compared with the CRSP Total Return Indexes for the NASDAQ Stock Market (U.S.) and NASDAQ Pharmaceutical Stocks.

Recent Sales of Unregistered Securities

None.

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Issuer Purchases of Equity Securities

We did not repurchase any of our equity securities during the fiscal year ended December 31, 2008.

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ITEM 6. SELECTED FINANCIAL DATA

	Years Ended December 31, (In thousands, except per share data)				
Statement of Operations Data:	**2008**	**2007**	**2006**	**2005**	**2004**
Total revenues	$ 56,561	$ 71,238	$ 6,212	$ 152	$ 337
Research and development expenses	73,327	94,052	47,083	23,642	18,868
Net loss	(24,732)	(29,055)	(43,618)	(26,099)	(21,104)
Amounts per common share:					
Basic and diluted net loss per share	$ (0.65)	$ (0.89)	$ (1.50)	$ (1.01)	$ (1.00)
Weighted average shares outstanding.	38,062	32,771	29,147	25,721	21,165

	December 31, (In thousands)				
Balance Sheet Data:	**2008**	**2007**	**2006**	**2005**	**2004**
Cash, cash equivalents and securities	$ 63,314	$ 85,009	$ 46,236	$ 59,988	$ 28,704
Total assets	84,692	142,717	68,485	99,248	32,469
Long-term deferred revenue	20,937	49,694	36,596	29,426	300
Accumulated deficit	(249,268)	(224,536)	(195,481)	(151,863)	(125,764)
Total stockholders equity	46,426	64,905	21,155	58,440	29,334

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

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.

The following Management s Discussion and Analysis (MD&A) is intended to help the reader understand our results of operations and financial condition. MD&A is provided as a supplement to, and should be read in conjunction with, our audited Financial Statements and the accompanying notes to the financial statements and other disclosures included in this Annual Report on Form 10-K (including the disclosures under Item 1A. Risk Factors).

Overview

2008 Corporate Highlights

Forodesine HCl

Following the completion of a Phase I/II clinical trial of forodesine HCl in patients with refractory CTCL, in October 2007 we initiated a planned pivotal trial with an oral formulation of forodesine HCl for treatment of patients with CTCL. This trial is being conducted under an SPA agreement negotiated with the FDA and will serve as a basis for a new drug application to the FDA using the oral formulations in patients with relapsed CTCL. In February 2007, we announced that the Committee for Orphan Medicinal Products of the European Medicines Agency had granted orphan drug designation to forodesine HCl for the treatment of CTCL. The trial continues to enroll subjects with CTCL stages IIB through IVA who have failed three systemic therapies. Enrollment in the study slowed over the summer of 2008 below our projections. We have taken action to accelerate enrollment and early indications are that these actions are having a positive effect. We have enrolled more than half of the targeted 130 patients in this study and will continue to monitor enrollment going forward.

At the December 2007 meeting of the American Society of Hematology (ASH), Madeline Duvic, M.D., Deputy Chair, Dermatology, The University of Texas M.D. Anderson Cancer Center, presented interim data from the Phase I/II clinical study of oral forodesine HCl in the treatment of subjects with refractory CTCL. The overall response rate for these subjects was 39%, including 2 subjects with complete response (6%) and 12 subjects with partial response (33%). These data indicated that in addition to a good safety profile, forodesine HCl demonstrated clinical activity as a single oral agent in patients with advanced refractory CTCL.

In December 2008, we announced interim data from the ongoing forodesine HCl Phase II program in patients with CLL and data from a healthy subject pharmacokinetic and pharmacodynamic study. The CLL study will continue with an amendment to study a new dosing regimen of oral forodesine, 200 mg twice-daily. An interim analysis was conducted on data from an exploratory Phase II single-arm, open-label program in patients with CLL whose previous treatment had failed. While this analysis showed that no partial or complete responses were observed, five out of 13 patients administered 200 mg of forodesine HCl once-daily had substantial reductions in malignant lymphocytes, and at the time of the analysis, seven patients were still on study. Forodesine HCl was generally safe and well-tolerated at the 200 mg once-daily dose. In a parallel, healthy subject, pharmacokinetic and pharmacodynamic study, we compared the effect of seven days of 200 mg forodesine HCl dosed once-daily with seven days of 200 mg forodesine HCl dosed twice-daily. The study demonstrated substantially increased drug exposure and pharmacodynamic effect in subjects administered forodesine HCl 200 mg twice-daily. Drug exposure, as measured by area under the (plasma-concentration/time) curve (AUC), increased by 63 percent ($P<0.001$) for twice-daily dosing compared to once-daily dosing. Serum uric acid levels were reduced at steady state compared to baseline by 50.0 percent for twice-daily dosing compared to 23.5 percent for once-daily dosing ($p<0.001$), indicating increased PNP enzyme inhibition with twice-daily dosing.

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In January 2007, we initiated a Phase IIb multicenter, open-label, non-randomized repeat-dose registration study to evaluate an intravenous treatment of forodesine HCl followed by an oral treatment of forodesine HCl in patients with relapsed or refractory T-ALL. This study was being conducted under an SPA negotiated with the FDA and was designed to determine the rate of complete remission achieved with forodesine HCl. In March 2007, we announced that as a result of a stability issue with the i.v. formulation, that we were voluntarily placing this Phase IIb clinical trial on hold pending internal review and discussions with the our partner, Mundipharma. In December 2007, we announced the formal termination of this study.

Peramivir

In January 2007, we announced that HHS had awarded the Company a $102.6 million, four-year contract for the advanced development of peramivir. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

In addition to the contract with HHS, in February 2007, we established a collaborative relationship with Shionogi for the development and commercialization of peramivir in Japan. We received an upfront payment of $14 million and the agreement provided for additional future clinical event milestone payments of up to $21 million. Shionogi recently completed a Phase II study of intravenous (i.v.) peramivir administered via a single dose infusion in the outpatient setting for treatment of seasonal influenza. This trial met its primary endpoint of improvement in the median time to alleviation of symptoms in subjects with confirmed, acute, uncomplicated influenza infection, compared to placebo alone. Time to alleviation of symptoms was 81.8 hours for placebo, 59.1 hours for 300 mg peramivir, and 59.9 hours for 600 mg peramivir. This result was highly statistically significant (p=0.0046) for both the 300 mg dose (p=0.0046) and the 600 mg dose. Further, safety assessments confirmed that i.v. peramivir was generally safe and well-tolerated. Shionogi presented the data at the recent Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)/ Infectious Diseases Society of America (IDSA) annual meeting in Washington, D.C. Based on the results from this Phase II study, Shionogi has initiated a Phase III program with i.v. peramivir in the outpatient setting. The Phase III study is a 1,050 subject study and would typically require two seasons to complete. In the event of a very strong flu season it is possible to complete a study of this magnitude in one flu season. Although it has been a strong flu season in Asia, it is not clear at this time if Shionogi will finish in one season or two. It is our understanding that Shionogi plans to complete its studies within this influenza season. In October 2008, the Company and Shionogi amended the license agreement to expand the territory in the agreement to include Taiwan and to provide rights for Shionogi to perform a Phase III clinical trial in Hong Kong.

Intramuscular peramivir. We completed a double-blind placebo-controlled Phase II clinical trial with i.m. peramivir testing two different dose levels of peramivir (150 mg and 300 mg) versus placebo in adults with acute uncomplicated influenza. While the trial did not demonstrate statistically significant differences for its primary endpoint of time to alleviation of symptoms, the preliminary analysis of the virologic data indicated that peramivir demonstrated statistically significant reductions in influenza virus shedding in both peramivir treatment groups compared to placebo, with greater reductions in the 300 mg dose group. With this information and the additional pharmacokinetic information we have obtained subsequent to the trial, we initiated a Phase II placebo-controlled trial

of 600 mg i.m. peramivir for the treatment of seasonal influenza. This trial uses a new, more concentrated 150 mg/ml formulation of peramivir. This trial is ongoing in the Northern Hemisphere and we expect results sometime in the second quarter of 2009.

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Intravenous peramivir In July 2007, we announced the initiation of a Phase II clinical trial of i.v. peramivir to compare the efficacy and safety of i.v. peramivir to orally administered oseltamivir in patients who require hospitalization due to acute influenza.

The primary objective of the study was to evaluate time to clinical stability, which is a composite endpoint comprised of normalization of temperature, oxygen saturation, respiratory rate, systolic blood pressure and heart rate. This type of endpoint has previously been used in pneumonia studies, but not in influenza. Secondary objectives of the study included evaluation of viral shedding, mortality, clinical relapse and time to resumption of usual activities.

The multicenter, randomized, double-blind, double-dummy, active-controlled, Phase II Study enrolled 137 patients, who tested positive by rapid antigen test (RAT) for influenza and had one or more criteria for hospitalization, namely: age > 60 years, chronic lung disease, congestive heart failure, diabetes mellitus, low oxygen saturation, low blood pressure, or severity of illness requiring supportive care. Of the 137 patients randomized, 122 age 19 to 101 years had influenza confirmed by polymerase chain reaction (PCR) testing and were included in the intent-to-treat infected (ITTI) patient population; 41 patients received oseltamivir 75 mg orally twice-daily, 41 patients received 200 mg i.v. peramivir once-daily and 40 patients received 400 mg i.v. peramivir once-daily. As reported in October 2008, there were no statistically significant differences in any of the efficacy endpoints between the three treatment arms, and peramivir was generally safe and well-tolerated at those dose levels. Evaluation of time to clinical stability, the primary endpoint, showed a median of 23.7 hours for peramivir 200mg, 37.0 hours for peramivir 400 mg and 28.1 hours for oseltamivir (p=.306). This exploratory endpoint was driven by resolution of fever. Viral shedding (time weighted change from baseline in viral titer) was reduced by a median of -2.0 logs for peramivir 200mg, -2.1 logs for peramivir 400mg, and -1.9 logs for oseltamivir (p=.908). There was no mortality in the primary efficacy population, and there were no clinical relapses. Patients were discharged from the hospital after a median of 4.0 days for peramivir 200 mg, 3,8 days for peramivir 400 mg, and 4.0 days for oseltamivir (p=0.994). The median number of days required for resumption of usual activities was 8.8 days for peramivir 200 mg, 9.0 days for peramivir 400 mg, and 13.7 days for oseltamivir (p=0.276). The Company presented the results at the XI International Symposium on Respiratory Viral Infection being held in Bangkok, Thailand in February 2009.

BCX-4208/R3421

During the third quarter of 2007, we announced that Roche had initiated a Phase IIa clinical trial to evaluate oral doses of BCX-4208/R3421 in patients with moderate to severe plaque psoriasis. The efficacy assessment of the study has been completed. Consistent with interim findings reported by the Company in May 2008, the Phase II clinical study of BCX-4208, a potent, rationally designed, orally available PNP inhibitor, met its primary objectives of safety and tolerability. In addition, BCX-4208 displayed dose-dependent reductions in peripheral blood lymphocyte counts, including subsets measuring B cells (CD20), total T cells (CD3), T helper cells (CD4) and T suppressor/cytotoxic cells (CD8). Further, plasma levels of BCX-4208 increased with dose, and plasma uric acid levels showed dose-related reductions with BCX-4208. In addition, consistent with interim results previously reported by the Company, no evidence of clinical efficacy, a secondary objective, was observed in psoriasis patients with doses and duration of administration tested.

In the Phase IIa trial, BCX-4208 was generally safe and well-tolerated at doses up to 120 mg daily for six (6) weeks. Most adverse events reported were considered mild or moderate, and low in frequency. No opportunistic infections were observed. In addition, detailed laboratory and clinical monitoring did not indicate any patterns suggestive of off-target adverse findings.

Also in May 2008, we announced that we received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, we regained worldwide rights to BCX-4208.

Results of Operations

Year Ended December 31, 2008 Compared with the Year Ended December 31, 2007

Collaborative and other research and development revenues were $56.6 million for the year ended December 31, 2008, compared to $71.2 million for the year ended December 31, 2007. This decrease was partially driven by a reduction of $33.7 million in revenue from the contract with HHS for the development of peramivir, which includes the establishment of a $4.9 million reserve recorded by the Company during the second quarter of 2008 for amounts

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that were previously expected to be received from HHS related to costs incurred in the Phase III program of intramuscular (i.m.) peramivir for outpatient influenza. The Company initiated this program and voluntarily discontinued it following a decision to pursue higher doses in the ongoing Phase II study. Reimbursement of these costs is under discussion with HHS. Further contributing to the decrease in collaborative and other R&D revenues from 2007 to 2008 was the prior year receipt of a $7.0 million milestone payment from Shionogi. This was offset by the recognition of $26.5 million of previously deferred revenue related to the termination of the Company s collaboration with Roche in the fourth quarter of 2008.

Research and development expenses were $73.3 million for the year ended December 31, 2008, compared to $94.1 million for the year ended December 31, 2007. The decrease in R&D expenses was due to a reduction in the clinical development costs of $16.3 million and toxicology costs of $1.6 million associated with the peramivir program, a reduction in manufacturing costs of $10.3 million and $6.4 million associated with the peramivir and Forodesine HCl programs, respectively, and a reduction in costs incurred on the Company s pre-clinical compounds of $0.9 million. These reductions were offset by an increase in the Company s clinical development costs of $2.6 million for Forodesine HCl, the recognition of $8.2 million of previously deferred expense related to the termination of the Company s collaboration with Roche, and increases of $4.2 million in personnel related costs, consulting fees, and operating costs.

General and administrative expenses were $10.4 million for the year ended December 31, 2008, compared to $9.5 million for the year ended December 31, 2007. The higher expenses were primarily due to increases in professional fees and operating costs.

The net loss for the year ended December 31, 2008 was $24.7 million, or $0.65 per share, compared to a net loss for the year ended December 31, 2007 of $29.1 million, or $0.89 per share.

Year Ended December 31, 2007 Compared with the Year Ended December 31, 2006

Collaborative and other research and development revenue was $71.2 million for the year compared to $6.2 million for 2006. The increase for 2007 was primarily due to revenue from HHS related to our contract for the development of peramivir. In addition, we received a $7.0 million milestone payment from Shionogi in December 2007 for their initiation of a Phase II clinical trial, and there was an increase of $3.1 million in amortization of deferred revenue compared to 2006 on the continuing amortization of the upfront payments from the Roche, Shionogi and Mundipharma agreements. These increases in revenue were partially offset by a decrease of $1.5 million in reimbursement from Mundipharma for our clinical trial costs compared to 2006.

Research and development expenses for 2007 were $94.1 million, a 100.0% increase from 2006 expenses of $47.1 million, primarily attributable to the clinical and manufacturing costs of our expanded peramivir and forodesine HCl programs, increases in personnel and related costs to support the advanced development of our pipeline, and increases in consulting and toxicology. Included in R&D expenses for 2007 is approximately $2.3 million of pre-contract costs directly related to the Phase II trials for both the i.v. and i.m. peramivir products. These costs were incurred during 2006 in anticipation of a contract award from HHS and were required to meet the delivery schedule of the proposed contract. In accordance with the provisions of Federal Acquisition Regulation 31.205-32, the costs were included in the Company s request for proposal and were eligible for reimbursement from HHS. The $2.3 million of costs incurred prior to the contract award date were deferred and included in other current assets on the Company s balance sheet at December 31, 2006. In the first quarter of 2007, the $2.3 million in costs were billed and expensed. Concurrently, revenue was recognized for these costs plus the applicable fixed fee.

General and administrative expenses for 2007 were $9.5 million, an increase of 55.7% over the 2006 expense of $6.1 million, primarily due to additional compensation, which also included an increase of $1.2 million non-cash share-based compensation charge related to Statement of Financial Accounting Standards No. 123 (revised 2004), *Share Based Payment* (Statement No. 123R). In addition, there was an increase in professional fees, including legal, which were partially offset by an increase in costs allocated to R&D.

The net loss for the year ended December 31, 2007 was $29.1 million, or $0.89 per share, compared to a net loss of $43.6 million, or $1.50 per share in 2006.

Liquidity and Capital Resources

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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 and cash from collaborative and other research and development agreements, including government contracts, and to a lesser extent interest. For example, during 2008, we received cash from collaborative and other research and development agreements and government contracts (primarily HHS, Mundipharma, and Shionogi,) of approximately $52.9 million and on August 9, 2007, we announced the closing of a $65.3 million private placement of common stock to certain existing stockholders. As of December 31, 2008, we have approximately $12.0 million due from our collaborators, primarily HHS. Other sources of funding have included the following:

other collaborative and other research and development agreements;

government grants and contracts;

equipment lease financing;

facility leases;

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 for the continuation of the validation process. 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 by policy, limit the amount of credit exposure at any one institution. These investments are generally not collateralized and mature within two years. We have not realized any significant losses from such investments.

On August 7, 2007, we amended our lease for our current Birmingham facilities, consisting of 50,150 square feet, through June 30, 2015. We have an option to renew the lease for an additional five years at the current market rate in effect on June 30, 2015. The lease requires us to pay monthly rent currently at $40,273 per month in December 2008 and escalates annually to a minimum of $48,072 per month in the final year, plus our pro rata share of operating expenses and real estate taxes in excess of base year amounts. In addition, the most recent lease amendment provided an allowance of $300,000 for our use in making certain improvements to the premises.

In August 2006, we opened an office in Cary, North Carolina for the establishment of our clinical and regulatory operation. We currently have 5,565 square feet under lease through February 28, 2010. This lease currently requires us to pay $7,881 per month and escalates annually to $8,118 per month in the final year.

During 2008, we incurred capital costs of approximately $1.2 million, while we incurred capital costs of approximately $3.3 million in 2007. Included in 2007 capital costs were amounts related to a renovation of our facility to build additional laboratory space. The cost of this expansion was partially funded by a $300,000 tenant allowance in our 2007 lease amendment.

At December 31, 2008, we had long-term operating lease obligations, which provide for aggregate minimum payments of $641,323 in 2009, $575,246 in 2010, and $551,744 in 2011. These obligations include the future rental of our operating facilities.

We plan to finance our needs principally from the following:

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payments under our contract with HHS;

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.

In March 2007, we announced a collaborative agreement with Shionogi for rights to peramivir in Japan. This agreement required an upfront payment of $14 million that was received in April 2007. In December 2007, we received a $7 million milestone payment from Shionogi for their initiation of a Phase II clinical trial with i.v. peramivir. In October 2008, the Company and Shionogi amended the license agreement to expand the territory covered by the agreement to include Taiwan and to provide rights for Shionogi to perform a Phase III Clinical Trial in Hong Kong. Shionogi initiated a Phase III study in December 2008.

In January 2007, we announced that HHS had awarded the Company a $102.6 million, four-year contract for the advanced development of peramivir. The contract is a standard cost plus fixed fee contract, which we expect will continue to have a significant positive impact on our financial position and cash flow. We bill our incurred costs to HHS on a monthly basis. Any significant delays in payment, rejection of significant costs by HHS or cancellation of this contract by HHS would have a significant negative effect on our financial position. In January 2008, we announced that the development plan for peramivir had changed and that we would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January, we announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

In February 2006, we licensed forodesine HCl to Mundipharma for the development and commercialization of this drug in Europe, Asia and Australasia. In addition to the upfront payment of $10 million, which was received in February 2006, Mundipharma is paying 50% of the clinical development costs we are incurring for forodesine HCl 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. In January 2007, we initiated our pivotal study with forodesine HCl in T-cell leukemia patients under an SPA negotiated with the FDA, which triggered a $5 million event payment from Mundipharma. Subsequently, in March 2007, the Company made a decision to put this trial on voluntary hold to investigate particulates that were found in some batches of i.v. formulation. In December 2007, we announced the termination of our development in T-ALL with forodesine HCl. In July 2007, we announced the Company had received an SPA for a pivotal trial of forodesine HCl in CTCL patients. The trial is a multicenter, multinational, open-label, single-arm, repeat dose pivotal trial which began enrollment during October 2007. The trial continues to enroll subjects with CTCL stages IIB through IVA who have failed three systemic therapies. Enrollment in the study slowed over the summer of 2008 below our projections. We have taken action to accelerate enrollment and early indications are that these actions are having a positive effect. We will continue to monitor enrollment going forward.

The collaboration with Roche for the worldwide development and commercialization of BCX-4208 in November 2005 provided an upfront payment of $30 million, which was received in 2006. In May 2008, we announced that we

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received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. As a result, we regained worldwide rights to BCX-4208.

For the year, our cash, cash equivalents and marketable securities balance has decreased from $85.0 million as of December 31, 2007 to $63.3 million as of December 31, 2008. This decrease was primarily due to cash used for operations, partially offset by reimbursement from collaborators. As a result, our net cash burn rate for 2008 was approximately $1.8 million per month. We caution that our revenues, our expenses, and our cash flows will vary significantly from quarter to quarter throughout 2009 due to the nature of the trials in influenza and the reimbursement from HHS. We are projecting our 2009 net cash use to be $30 to $38 million, dependent on the achievement of certain milestones. Our actual burn rate could vary significantly from the projection above depending on the timing of Company expenses and the related reimbursement from our collaborators.

As our clinical programs continue to progress and patient enrollment increases, our costs will increase. Our current and planned clinical trials plus the related development, manufacturing, regulatory approval process requirements and additional personnel resources and testing required for the continuing development of our drug candidates will consume significant capital resources and will increase our expenses. Our expenses, revenues and burn rate could vary significantly depending on many factors, including our ability to raise additional capital, the development progress of our collaborative agreements for our drug candidates, the amount and timing of funding we receive from HHS for peramivir, the amount of funding or assistance, if any, we receive from other governmental agencies or other new partnerships with third parties for the development of our drug candidates, the progress and results of our current and proposed clinical trials for our most advanced drug products, the progress made in the manufacturing of our lead products and the progression of our other programs.

As of December 31, 2008, we had $63.3 million in cash, cash equivalents and marketable securities. With our currently available funds and the amounts to be received from HHS, Shionogi and our other collaborators, we believe these resources will be sufficient to fund our operations for at least the next twelve months. 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:

- our ability to perform under the contract with HHS and receive reimbursement;
- the progress and magnitude of our research, drug discovery and development programs;
- changes in existing collaborative relationships or government contracts;
- 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 partners, 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 certain drug candidates; or a decision to build or expand internal development and commercial capabilities;
- successful commercialization of marketed products by either us or a partner;
- the scope and results of preclinical studies and clinical trials to identify and evaluate drug candidates;
- our ability to engage sites and enroll subjects in our clinical trials;
- the scope of manufacturing of our drug candidates to support our preclinical research and clinical trials;

increases in personnel and related costs to support the development of our drug candidates;

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the scope of 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; and

the costs involved in all aspects of intellectual property strategy and protection including the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims.

We expect that 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, including governmental agencies in general and from the HHS contract specifically, 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, 2008, 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, 2008. 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.

		Payments due by period			
Contractual Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Operating Lease Obligations	$ 3,738,049	$ 641,323	$ 1,126,990	$ 1,112,846	$ 856,890
Purchase Obligations (1)	15,872,895	14,942,895	310,000	310,000	310,000
Total	$ 19,610,944	$ 15,584,218	$ 1,436,990	$ 1,422,846	$ 1,166,890

(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

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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 in this Annual Report on Form 10-K for the year ended December 31, 2008, 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, event payments, research and development fees, government contracts, and interest income. Revenue is recognized in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* and Emerging Issues Task Force Issue 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF Issue 00-21). License fees, event 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 Mundipharma license agreement, we deferred the upfront payment over the remaining life of the patent, which is 2017. 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.

Under the guidance of EITF Emerging Issues Task Force Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent* and Emerging Issues Task Force Issue 01-14, *Income Statement Characterization of Reimbursements Received for Out-of-Pocket Expenses*, 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. For example, the amounts received from our collaboration with Mundipharma for the reimbursement of clinical trial costs and the costs received from HHS for reimbursement will be recorded as revenue in the period the related costs were recorded.

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.

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.

Research and Development Expenses

In accordance with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs*, we expense research and development costs as incurred. Prior to January 1, 2008, we also expensed nonrefundable advance payments for goods and services received in connection with research and development activities. Effective January 1, 2008, we adopted the consensus in Emerging Issues Task Force Issue 07-3, *Accounting for Nonrefundable Advance Payments for Goods and Services Received for Use in Future Research and Development Activities* (EITF Issue 07-3). EITF 07-3 requires that these payments be deferred and recognized as an expense as the related goods are delivered or the related services are performed. We applied the new guidance to all advance payments made during 2008 for contracts executed after the effective date of this consensus.

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Research and development expenses include, among other items, 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. Most of our manufacturing and clinical and preclinical studies are performed by third-party CRO s. Costs for studies performed by CRO s are accrued by us over the service periods specified in the contracts and estimates are adjusted, if required, based upon our on-going review of the level of services actually performed.

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

Our accounting for deferred sublicense payments related to revenues that have been deferred is based on the guidance in SAB No. 104, which states that the incremental direct costs incurred related to the acquisition or origination of a contract in a transaction that results in the deferral of revenue may either be expensed as incurred or accounted for in accordance with paragraph 4 of Financial Accounting Standards Board (FASB) Technical Bulletin 90-1, *Accounting for Separately Priced Extended Warranty and Product Maintenance Costs* (FTB 90-1). Sublicense payments are paid to our academic partners upon receipt of consideration from various commercial partners. These deferred expenses would not have been incurred without receipt of such payments from our commercial partners and are being expensed in proportion to the related revenue being recognized. We believe that this accounting treatment appropriately matches expenses with the associated revenue.

We group our R&D expenses into two major categories: direct external expenses and all other R&D expenses. Direct external expenses consist of costs of outside parties to conduct laboratory studies, to develop manufacturing processes and manufacture the product candidate, to conduct and manage clinical trials and similar costs related to our clinical and preclinical studies. These costs are accumulated and tracked by program. All other R&D expenses consist of costs to compensate personnel, to purchase lab supplies and services, to maintain our facility, equipment and overhead and similar costs of our research and development efforts. These costs apply to work on our clinical and preclinical candidates as well as our discovery research efforts. These costs have not been charged directly to each program historically because the number of product candidates and projects in research and development may vary from period to period and because we utilize internal resources across multiple projects at the same time.

The following table summarizes our R&D expenses for the periods indicated:

	Year ended December 31,		
	2008	**2007**	**2006**
Direct external R&D expenses by program:			
PNP Inhibitor (forodesine HCl)	$ 15,918,040	$ 19,351,789	$ 17,667,599
PNP Inhibitor (BCX-4208)	8,974,238	211,923	643,605
Neuraminidase Inhibitor (peramivir)	21,473,202	50,302,010	11,352,737
Hepatitis C Polymerase Inhibitor	471,824	951,207	1,673,480
Other	1,599,826	2,503,514	206,176
All other R&D expenses:			
Compensation and fringe benefits	12,935,679	11,357,030	6,870,194
Supplies and services	2,871,803	1,888,552	3,366,683
Maintenance, depreciation, and amortization	2,169,027	1,391,730	975,790
Overhead allocation and other	6,912,995	6,094,241	4,327,108
Total R&D expenses	$ 73,326,634	$ 94,051,996	$ 47,083,372

At this time, due to the risks inherent in the clinical trial process and given the stages of our various product development programs, we are unable to estimate with any certainty the costs we will incur in the continued development of our drug candidates for potential commercialization. While we are currently focused on advancing each of our development programs, our future R&D expenses will depend on the determinations we make as to the scientific and clinical success of each drug candidate, as well as ongoing assessments as to each drug candidate s commercial potential. As such, we are unable to predict how we will allocate available resources among our product

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development programs in the future. In addition, we cannot forecast with any degree of certainty the development progress of our existing partnerships for our drug candidates, which drug candidates will be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

The successful development of our drug candidates is uncertain and subject to a number of risks. We cannot be certain that any of our drug candidates will prove to be safe and effective or will meet all of the applicable regulatory requirements needed to receive and maintain marketing approval. Data from preclinical studies and clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory clearance. We, the FDA, or other regulatory authorities may suspend clinical trials at any time if we or they believe that the subjects participating in such trials are being exposed to unacceptable risks or if such regulatory agencies find deficiencies in the conduct of the trials or other problems with our products under development. Delays or rejections may be encountered based on additional governmental regulation, legislation, administrative action or changes in FDA or other regulatory policy during development or the review process. Other risks associated with our product development programs are described in Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K, as updated from time to time in our subsequent periodic reports and current reports filed with the SEC. Due to these uncertainties, accurate and meaningful estimates of the ultimate cost to bring a product to market, the timing of completion of any of our product development programs and the period in which material net cash inflows from any of our product development programs will commence are unavailable.

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, there have been no material changes to our estimates. 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. To date, there have been no material changes to our estimates. 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

At December 31, 2008, we have two stock-based employee compensation plans, the Stock Incentive Plan and the Employee Stock Purchase Plan. Prior to January 1, 2006, we accounted for these plans under the recognition and

measurement provisions of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and other related Interpretations, as permitted by Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* (Statement No. 123). No stock-based compensation cost related to our employees

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was recognized in the Statements of Operations for any period ending prior to January 1, 2006, as all options granted to our employees had exercise prices equal to the market value of the underlying common stock on the date of grant. Effective January 1, 2006, we adopted the fair value recognition provisions of Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (Statement No. 123R), using the modified prospective transition method. Results for prior periods have not been restated.

Under the fair value recognition provisions of Statement No. 123R, stock-based compensation cost is estimated at the grant date based on the fair value of the award and is recognized as expense over the requisite service period of the award. Consistent with the valuation method we used for disclosure-only purposes under the provisions of Statement No. 123, we use the Black-Scholes option pricing model to estimate fair value under Statement No. 123R. Determining the appropriate fair value model and the related assumptions for the model requires judgment, including estimating the life of an award, the stock price volatility, and the expected term. Compensation cost is recognized on a straight-line basis over the requisite service period.

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 our excess cash principally in U.S. marketable securities from a diversified portfolio of institutions with strong credit ratings 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 market risk arising from our investments. Therefore, no quantitative tabular disclosure is provided.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA
BioCryst Pharmaceuticals, Inc.
BALANCE SHEETS

	December 31, 2008	December 31, 2007
Assets		
Cash and cash equivalents	$ 22,342,058	$ 31,155,320
Marketable securities	39,186,404	19,542,193
Receivables from collaborations	11,982,430	39,127,676
Prepaid expenses and other current assets	1,136,842	948,440
Deferred collaboration expense	376,972	931,023
Total current assets	75,024,706	91,704,652
Marketable securities	1,786,034	34,310,988
Furniture and equipment, net	4,880,475	5,294,079
Deferred collaboration expense	3,000,462	11,407,120
Total assets	$ 84,691,677	$ 142,716,839
Liabilities and Stockholders Equity		
Accounts payable	$ 5,265,947	$ 19,771,375
Accrued expenses	8,442,398	2,863,815
Accrued vacation	794,375	824,143
Deferred rent	40,000	
Deferred revenue	2,565,285	4,658,266
Total current liabilities	17,108,005	28,117,599
Deferred rent	220,000	
Deferred revenue	20,937,445	49,694,186
Stockholders equity:		
Preferred stock: shares authorized 5,000,000 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 95,000,000; shares issued and outstanding 38,275,167 in 2008 and 37,967,254 in 2007	382,751	379,672
Additional paid-in capital	295,207,583	288,683,369
Accumulated other comprehensive income	103,507	378,057
Accumulated deficit	(249,267,614)	(224,536,044)
Total stockholders equity	46,426,227	64,905,054
Total liabilities and stockholders equity	$ 84,691,677	$ 142,716,839

See accompanying notes to financial statements.

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BioCryst Pharmaceuticals, Inc.
STATEMENTS OF OPERATIONS

	Years Ended December 31,		
	2008	**2007**	**2006**
Revenues			
Collaborative and other research and development	$ 56,561,369	$ 71,237,901	$ 6,211,936
Expenses			
Research and development	73,326,634	94,051,996	47,083,372
General and administrative	10,399,227	9,465,962	6,108,373
Total expenses	83,725,861	103,517,958	53,191,745
Loss from operations	(27,164,492)	(32,280,057)	(46,979,809)
Interest and other income	2,432,922	3,224,533	3,361,956
Net loss	$ (24,731,570)	$ (29,055,524)	$ (43,617,853)
Basic and diluted net loss per common share	$ (0.65)	$ (0.89)	$ (1.50)
Weighted average shares outstanding	38,062,131	32,770,923	29,147,397

See accompanying notes to financial statements.

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BioCryst Pharmaceuticals, Inc.
STATEMENTS OF STOCKHOLDERS EQUITY

	Common Stock	Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stock-holders' Equity	Comprehensive Loss
Balance at December 31, 2005	$ **288,135**	$ **210,014,946**	$	**$ (151,862,667)**	$ **58,440,414**	
Net loss				(43,617,853)	(43,617,853)	$ (43,617,853)
Unrealized gain on marketable securities available-for-sale			32,463		32,463	32,463
Comprehensive loss						$ (43,585,390)
Exercise of stock options, 409,328 shares, net	4,093	2,765,801			2,769,894	
Employee stock purchase plan sales, 25,988 shares	260	191,070			191,330	
Stock-based compensation expense		3,338,761			3,338,761	
Balance at December 31, 2006	**292,488**	**216,310,578**	**32,463**	**(195,480,520)**	**21,155,009**	
Net loss				(29,055,524)	(29,055,524)	$ (29,055,524)
Unrealized gain on marketable securities available-for-sale			345,594		345,594	345,594
Comprehensive loss						$ (28,709,930)
Issue of restricted common stock, 60,000 shares	600	(600)				
Sale of common stock, 8,315,513 shares, net	83,155	65,034,937			65,118,092	
Exercise of stock options, 308,037 shares, net	3,080	1,378,098			1,381,178	
Employee stock purchase plan sales, 34,855 shares	349	269,328			269,677	
Stock-based compensation		5,691,028			5,691,028	

expense						
Balance at December 31, 2007	**379,672**	**288,683,369**	**378,057**	**(224,536,044)**	**64,905,054**	
Net loss				(24,731,570)	(24,731,570)	$ (24,731,570)
Unrealized loss on marketable securities available-for-sale			(274,550)		(274,550)	(274,550)
Comprehensive loss						$ (25,006,120)
Issue of restricted common stock, 76,536 shares	765	(765)				
Exercise of stock options, 146,470 shares, net	1,465	397,634			399,099	
Employee stock purchase plan sales, 84,907 shares	849	266,691			267,540	
Stock-based compensation expense		5,860,654			5,860,654	
Balance at December 31, 2008	$ **382,751**	$ **295,207,583**	**$ 103,507**	**$ (249,267,614)**	$ **46,426,227**	

See accompanying notes to financial statements.

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BioCryst Pharmaceuticals, Inc.
STATEMENTS OF CASH FLOWS

	Years Ended December 31,		
	2008	**2007**	**2006**
Operating activities			
Net loss	$ (24,731,570)	$ (29,055,524)	$ (43,617,853)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization, and impairment	1,625,878	1,369,713	810,310
Stock-based compensation expense	5,860,654	5,691,028	3,338,761
Changes in operating assets and liabilities:			
Receivables from collaborations	27,145,246	(34,571,531)	25,443,855
Prepaid expenses and other current assets	(188,402)	(274,682)	(173,071)
Deferred collaboration expense	8,960,709	1,361,824	(7,535,749)
Accounts payable and accrued expenses	(8,956,613)	15,424,180	(2,472,827)
Deferred rent	260,000		
Deferred collaboration revenue	(30,849,722)	15,057,193	8,995,259
Net cash used in operating activities	**(20,873,820)**	**(24,997,799)**	**(15,211,315)**
Investing activities			
Acquisitions of furniture and equipment	(1,212,274)	(3,343,827)	(1,398,314)
Purchases of patents and licenses			(136,372)
Purchases of marketable securities	(124,459,834)	(62,907,146)	(42,870,522)
Sales and maturities of marketable securities	137,066,027	51,217,617	31,916,000
Net cash provided by (used in) investing activities	**11,393,919**	**(15,033,356)**	**(12,489,208)**
Financing activities			
Sale of common stock, net of issuance costs		65,118,092	
Exercise of stock options	399,099	1,381,178	2,769,894
Employee stock purchase plan sales	267,540	269,677	191,330
Net cash provided by financing activities	**666,639**	**66,768,947**	**2,961,224**
(Decrease) increase in cash and cash equivalents	(8,813,262)	26,737,792	(24,739,299)
Cash and cash equivalents at beginning of year	31,155,320	4,417,528	29,156,827
Cash and cash equivalents at end of year	**$ 22,342,058**	**$ 31,155,320**	**$ 4,417,528**

See accompanying notes to financial statements.

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BioCryst Pharmaceuticals, Inc.
NOTES TO FINANCIAL STATEMENTS

Note 1 Significant Accounting Policies

The Company

BioCryst Pharmaceuticals, Inc. (the Company), a Delaware corporation, 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 multiple research projects in different stages of development from early discovery to a pivotal Phase II trial of the Company s most advanced drug candidate, forodesine HCl. 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*.

Marketable Securities

In accordance with Statement of Financial Accounting Standards No. 115, *Accounting for Certain Investments in Debt and Equity Securities*, the Company is required to classify securities as trading, available-for-sale, or held-to-maturity. The appropriateness of each classification is assessed at the time of purchase and at each reporting date. Unrealized gains and losses on securities available-for-sale are recognized in other comprehensive income, unless an unrealized loss is considered to be other than temporary, in which case the unrealized loss is charged to operations.

Effective January 1, 2008, the Company adopted Statement of Financial Accounting Standards No. 157, *Fair Value Measurements* (Statement No. 157), for financial assets and liabilities and any other assets and liabilities carried at fair value. This pronouncement defines fair value, establishes a framework for measuring fair value, and expands disclosures about fair value measurements. While this standard applies whenever other standards require (or permit) assets or liabilities to be measured at fair value, it does not expand the use of fair value in any new circumstances. The adoption of Statement No. 157 did not have a significant impact on the Company s financial statements.

Effective January 1, 2008, the Company also adopted Statement of Financial Accounting Standards No. 159, *The Fair Value Option for Financial Assets and Liabilities* (Statement No. 159), but did not elect to apply fair value accounting to any financial instruments that were not already accounted for at fair value under existing guidance. As a result, the adoption of Statement No. 159 did not have a significant impact on the Company s financial statements.

At December 31, 2007, the Company had $53,853,181 of marketable securities, of which $43,770,636 was classified as available-for-sale and $10,082,545 was classified as held-to-maturity. Securities available-for-sale consisted primarily of U.S. Agency securities carried at estimated fair values. At December 31, 2007, the amortized cost of securities available-for-sale was $42,918,200. At December 31, 2007, gross unrealized gains on securities available-for-sale were $378,057. There were no gross unrealized losses on securities available-for-sale at December 31, 2007. Securities held-to-maturity consisted primarily of U.S. Agency securities carried at amortized cost. The estimated fair value of securities held-to-maturity at December 31, 2007 was $10,096,160 based on independent quoted market prices. At December 31, 2007, gross unrecognized holding gains on securities held-to-maturity were $16,131, while gross unrecognized losses on securities held-to-maturity at December 31, 2007 were $2,516.

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During 2008, in an effort to minimize investment risk in light of the current economic environment, the Company sold two securities previously classified as held-to-maturity. The carrying amount of these securities was $3,469,506, which represented amortized cost. The proceeds from the sale of these securities was $3,458,814.

At December 31, 2008, the Company had $40,972,438 of marketable securities, all of which were classified as available-for-sale. These securities consisted of U.S. Treasury bills and notes carried at estimated fair values. The estimated fair value of these securities was based on independent quoted market prices and represents the highest priority of Level 1 in the fair value hierarchy as defined in Statement No. 157. The following table summarizes by year the scheduled maturity for the securities available-for-sale at December 31, 2008 and includes accrued interest of $265,172.

2009	$ 39,186,404
2010	1,786,034
	$ 40,972,438

At December 31, 2008, the amortized cost of securities available-for-sale, including accrued interest, was $40,868,931. At December 31, 2008, gross unrealized gains on securities available-for-sale were $103,507. There were no gross unrealized losses on securities available-for-sale at December 31, 2008.

Receivables from Collaborations

Receivables are recorded for amounts due to the Company related to reimbursable research and development costs and event payments. These receivables are evaluated to determine if any reserve or allowance should be established at each reporting date. At December 31, 2008, the Company had the following receivables from collaborations.

	Billed	Unbilled	Total
U.S. Department of Health and Human Services	$ 2,337,442	$ 8,574,717	$ 10,912,159
Mundipharma		1,070,271	1,070,271
Total	$ 2,337,442	$ 9,644,988	$ 11,982,430

Unbilled receivables from the U.S. Department of Health and Human Services (HHS) are net of a reserve for costs and fees of $4,918,849 at December 31, 2008 that are uncertain of recovery and related to the voluntarily terminated Phase III studies of the peramivir intramuscular (i.m.) program. The Company is in discussions with HHS regarding the reimbursement of these costs and fees. To the extent that any additional recoveries are realized or become probable of realization, the reserve will be adjusted in a future period(s). Any such adjustments could have a material impact on future operating results.

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, 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 less. In accordance with Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, the Company periodically reviews its furniture and equipment 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. Furniture and equipment to be disposed of are reported at the lower of carrying amount or fair value less cost to sell.

Patents and Licenses

The Company seeks patent protection on all internally developed processes and products. All patent related costs are expensed to general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

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Accrued Expenses

The Company records all expenses in the period incurred. In addition to recording expenses for invoices received, the Company estimates the cost of services provided by third parties or materials purchased for which no invoices have been received as of each balance sheet date. Accrued expenses as of December 31, 2008 and 2007 consisted primarily of development and clinical trial expenses payable to contract research organizations in connection with the Company s research and development programs.

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.

Effective January 1, 2007, the Company adopted the provisions of Financial Accounting Standards Board Interpretation No. 48, *Accounting for Uncertainty in Income Taxes, an interpretation of FASB Statement No. 109* (FIN No. 48). FIN No. 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise s financial statements in accordance with Statement No. 109, and prescribes a recognition threshold and measurement process for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return.

Accumulated Other Comprehensive Income

Accumulated other comprehensive income is comprised of unrealized gains and losses on securities available-for-sale and is disclosed as a separate component of stockholders equity.

Revenue Recognition

The Company s revenues have generally been limited to license fees, event payments, research and development fees, government contracts, 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, 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 over an estimated period determined by management based on the terms of the agreements and the products licensed. 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.

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.

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.

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

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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.

The Company recorded the following revenues from collaborations for the years ended December 31:

	2008	2007	2006
U.S. Department of Health and Human Services	$ 21,779,745	$ 55,449,095	$
Mundipharma	4,615,448	5,298,271	5,086,928
Roche	27,783,252	1,898,403	1,093,758
Shionogi	2,007,924	8,515,714	
Other	375,000	76,418	31,250
Total	$ 56,561,369	$ 71,237,901	$ 6,211,936

Revenues from the contract with HHS for the year ended December 31, 2008 are shown net of a provision for costs and fees of $4,918,849 (or $0.13 per share), of which $4,567,604 relates to revenues recognized in the three months ended March 31, 2008 and $351,245 relates to revenues recognized in 2007. These costs and fees are uncertain of recovery and related to the voluntarily terminated Phase III studies of the peramivir i.m. program.

Research and Development Expenses

In accordance with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs*, the Company expenses research and development costs as incurred. Prior to January 1, 2008, the Company also expensed nonrefundable advance payments for goods and services received in connection with research and development activities. Effective January 1, 2008, the Company adopted the consensus in Emerging Issues Task Force Issue 07-3, *Accounting for Nonrefundable Advance Payments for Goods and Services Received for Use in Future Research and Development Activities* (EITF Issue 07-3). EITF 07-3 requires that these payments be deferred and recognized as an expense as the related goods are delivered or the related services are performed. The Company applied the new guidance to all advance payments made during 2008 for contracts executed after the effective date of this consensus. As a result, approximately $295,000 (or $0.01 per share) of advanced payments have been capitalized at December 31, 2008 that would have been expensed under the Company s former accounting policy.

Research and development expenses include, among other items, 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. Most of the Company s manufacturing and clinical and preclinical studies are performed by third-party CRO s. Costs for studies performed by CRO s are accrued by the Company over the service periods specified in the contracts and estimates are adjusted, if required, based upon the Company s on-going review of the level of services actually performed.

Additionally, the Company has license agreements with third parties, such as Albert Einstein College of Medicine of Yeshiva University (AECOM), Industrial Research, Ltd. (IRL), and the University of Alabama at Birmingham (UAB), which require fees related to sublicense agreements or maintenance fees. The Company expenses sublicense payments as incurred unless they are related to revenues that have been deferred, in which case the expenses are deferred and recognized over the related revenue recognition period. The Company expenses maintenance payments as incurred.

The Company s accounting for deferred sublicense payments related to revenues that have been deferred is based on the guidance in SAB No. 104, which states that the incremental direct costs incurred related to the acquisition or origination of a contract in a transaction that results in the deferral of revenue may either be expensed as incurred or accounted for in accordance with paragraph 4 of Financial Accounting Standards Board (FASB) Technical Bulletin 90-1, *Accounting for Separately Priced Extended Warranty and Product Maintenance Costs* (FTB 90-1). At December 31, 2008, the Company had deferred collaboration expenses of $3,377,434. These deferred expenses were sub-license payments, paid to the Company s academic partners upon receipt of consideration from various commercial partners. These deferred expenses would not have been incurred without receipt of such payments from

the Company s commercial partners and are being expensed in proportion to the

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related revenue being recognized. The Company believes that this accounting treatment appropriately matches expenses with the associated revenue.

Stock-Based Compensation

In accordance with Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (Statement No. 123R), all share-based payments, including grants of stock option awards and restricted stock awards, are recognized in the Company s income statement based on their fair values. Statement No. 123R was adopted by the Company on January 1, 2006 using the modified prospective transition method. Under the fair value recognition provisions of Statement No. 123R, stock-based compensation cost is estimated at the grant date based on the fair value of the award and is recognized as expense on a straight-line basis over the requisite service period of the award.

As of December 31, 2008, the Company had two stock-based employee compensation plans, the Stock Incentive Plan (Incentive Plan) and the Employee Stock Purchase Plan (ESPP). In addition, during 2007, the Company made an inducement grant outside of the Incentive Plan and ESPP to recruit a new employee to a key position within the Company. Prior to January 1, 2006, the Company accounted for all share-based payments under the recognition and measurement provisions of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB Opinion No. 25), and other related interpretations, as permitted by Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation*. No stock-based compensation cost related to the Company s employees was recognized in the Statements of Operations for any period ending prior to January 1, 2006. Stock-based compensation expense of $5,860,654 ($5,545,458 of expense related to the Incentive Plan, $165,492 of expense related to the ESPP, and $149,704 of expense related to the inducement grant) was recognized during 2008, while $5,691,028 ($5,428,505 of expense related to the Incentive Plan, $150,245 of expense related to the ESPP, and $112,278 of expense related to the inducement grant) was recognized during 2007 and $3,338,761 ($3,243,751 of expense related to the Plan and $95,010 of expense related to the ESPP) was recognized during 2006.

As of December 31, 2008, there was approximately $9,155,261 of total unrecognized compensation cost related to non-vested employee stock option awards and restricted stock awards granted by the Company. That cost is expected to be recognized as follows: $4,676,499 in 2009, $3,430,204 in 2010, $958,675 in 2011, and $89,883 in 2012.

Statement 123R also requires that the benefits from tax deductions in excess of recognized compensation cost should be reported as a financing cash flow rather than as an operating cash flow. The Company has never recognized any benefits from such tax deductions, as the Company has always maintained a loss position.

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, outstanding warrants, and common shares expected to be issued under the Company s employee stock purchase plan were anti-dilutive.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires the Company 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 2007 and 2006 financial statements have been reclassified to conform to the 2008 financial statement presentation. The changes had no effect on the results of operations previously reported.

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Note 2 Furniture and Equipment

Furniture and equipment consisted of the following at December 31:

	2008	2007
Furniture and fixtures	$ 535,994	$ 491,827
Office equipment	1,126,282	907,389
Software	1,116,661	1,015,062
Laboratory equipment	6,973,158	6,361,495
Leased equipment	62,712	62,712
Leasehold improvements	6,100,516	5,082,554
Construction-in-progress		883,779
	15,915,323	14,804,818
Less accumulated depreciation and amortization	(11,034,848)	(9,510,739)
Furniture and equipment, net	$ 4,880,475	$ 5,294,079

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 by policy, limits the amount of credit exposure at any one institution. These investments are generally not collateralized and mature within less than two years. The Company has not realized any significant losses from such investments.

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:

	2008	2007
Accrued research and clinical expenses	$ 6,479,546	$ 1,675,665
Accrued professional fees	486,047	126,500
Stock purchase plan withholdings	138,237	167,365
Accrued bonus	1,011,739	756,534
Other	326,829	137,751
Accrued expenses	$ 8,442,398	$ 2,863,815

Note 5 Lease Obligations and Other Contingencies

The Company has the following lease obligations at December 31, 2008:

	Operating Leases
2009	$ 641,323
2010	575,246
2011	551,744
2012	560,383
2013	552,463
Thereafter	856,890

Total minimum payments	$ 3,738,049

Rent expense for operating leases was $636,819, $575,538, and $566,524 in 2008, 2007, and 2006, respectively. The commitment for operating leases is primarily related to building leases in Birmingham, Alabama and Cary, North Carolina. The lease for the building in Birmingham, Alabama expires June 30, 2015. This lease, as amended effective August 7, 2007 for an increase in occupied space and lease term, currently requires monthly rents of

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$40,273 in December 2008 and escalates annually to a minimum of $48,072 per month in the final year. The Company has an option to renew the Birmingham, Alabama lease for an additional five years at the current market rate on the date of termination. The lease for the building in Cary, North Carolina expires February 28, 2010. This lease, as amended effective August 9, 2007 for an increase in occupied space, currently requires monthly rents of $7,881 in December 2008 and escalates to a minimum of $8,118 per month in the final year. The Company has an option to twice renew the Cary, North Carolina lease for an additional three years at the current market rate prior to lease termination.

Note 6 Income Taxes

Effective January 1, 2007, the Company adopted the provisions of FIN No. 48, which clarifies the accounting for uncertainty in income taxes recognized in an enterprise s financial statements in accordance with Statement No. 109 and prescribes a recognition threshold and measurement process for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The Company has concluded that there were no significant uncertain tax positions requiring recognition in its financial statements. Tax years 2005-2007 remain open to examination by the major taxing jurisdictions to which the Company is subject. Additionally, years prior to 2005 are also open to examination to the extent of loss and credit carryforwards from those years.

As of December 31, 2008, 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 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.

The Company will recognize interest and penalties accrued related to unrecognized tax benefits as components of its income tax provision. The Company did not have any interest and penalties accrued upon the adoption of FIN No. 48 and as of December 31, 2008, the Company does not have any interest and penalties accrued related to unrecognized tax benefits.

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:

	2008	2007	2006
Federal tax benefit at statutory rate on income before income taxes	$ (8,656,050)	$ (10,169,433)	$ (15,266,249)
State tax benefit, net of federal income tax effect	(1,868,186)	(1,231,316)	(1,931,360)
Increase in valuation allowance	8,476,111	16,143,862	21,011,952
Permanent items (federal effect)	1,484,952	3,333,875	2,338,857
R&D credit	(1,242,788)	(9,214,625)	(6,561,953)
Expiration of net operating losses and credits	2,228,949	1,640,467	461,678
Other-net	(422,988)	(502,830)	(52,925)
Total tax expense	$	$	$

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:

	2008	2007
Deferred tax assets:		
Net operating losses	$ 68,863,295	$ 61,544,215
General business credits	32,972,811	32,067,935
Fixed assets	1,101,002	845,621
Accrued expenses	813,383	433,093

Deferred revenue	8,097,958	9,827,259
Stock-based compensation	3,079,952	1,734,167
Total deferred tax assets	114,928,401	106,452,290
Total deferred tax liabilities		

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	2008	2007
Net deferred tax asset	114,928,401	106,452,290
Valuation allowance	(114,928,401)	(106,452,290)
Net deferred tax assets	$	$

As of December 31, 2008, the Company had net operating loss and research and development credit carryforwards of approximately $175,589,000 and $32,973,000 respectively, which expire at various dates from 2009 through 2027.

Note 7 Stockholders Equity

On August 6, 2007, the Company entered into a Stock and Warrant Purchase Agreement with a group of existing stockholders for the private placement of 8,315,513 shares of the Company s common stock at a purchase price of $7.80 per share and warrants to purchase 3,159,895 shares of the Company s common stock at a purchase price of $0.125 per warrant. The aggregate proceeds from the sale were approximately $65.3 million. The exercise price of the warrants is $10.25 per share. The participants in the transaction include funds managed by Baker Brothers Investments, Kleiner Perkins Caufield & Byers, EHS Holdings, OrbiMed Advisors, Texas Pacific Group Ventures, and Stephens Investment Management, all of whom are current shareholders in the Company. The Company has registered the shares and warrants under the Securities Act of 1933, as amended (the Securities Act), for resale.

On May 16, 2007, the stockholders approved an amendment to the Company s third restated certificate of incorporation to increase the number of shares of common stock authorized to issue from 45,000,000 to 95,000,000. All shares of the Company s common stock, including the additional shares authorized by the amendment, are equal in rank and have the same voting, dividend, and liquidation rights.

In June 2002, the Company s 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 10.1% as of August 15, 2007, 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. In August 2007, this plan was amended for a transaction involving funds managed by or affiliated with Baker Brother Investments such that they could purchase up to 25% without triggering the Rights. After closing of our August 2007 private placement, such group owns approximately 19.0% of our stock. 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, the Company increased the authorized shares available under these rights to 45,000 to match the authorized common shares of 45,000,000 at that time. In addition, the Board of Directors has the authority to issue up to 4,955,000 shares of undesignated preferred stock and to determine the rights, preferences, privileges and restrictions of those shares without further vote or action by the Company s stockholders.

Note 8 Stock-Based Compensation

Stock Incentive Plan

The Company grants stock option awards and restricted stock awards to its employees, directors, and consultants under the Stock Incentive Plan (Incentive Plan), as amended and restated in February 2008. The Incentive Plan was

approved by the Company s stockholders in May 2008. Under the Incentive Plan, stock option awards are granted with an exercise price equal to the market price of the Company s stock at the date of grant. Stock option

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awards granted to employees 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. Stock option awards granted to non-employee directors of the Company generally vest over one year. All stock option awards have contractual terms of 10 years. The vesting exercise provisions of all awards granted under the Incentive Plan are subject to acceleration in the event of certain stockholder-approved transactions, or upon the occurrence of a change in control as defined in the Incentive Plan.

Related activity under the Incentive Plan is as follows:

	Awards Available	Options Outstanding	Weighted Average Exercise Price
Balance December 31, 2005	443,047	3,241,351	$ 7.60
Plan amendment	1,500,000		
Stock option awards granted	(1,222,154)	1,222,154	12.35
Stock option awards exercised		(411,076)	6.82
Stock option awards canceled	99,861	(99,861)	15.91
Balance December 31, 2006	820,754	3,952,568	8.94
Plan amendment	1,200,000		
Stock option awards granted	(1,721,706)	1,721,706	9.51
Restricted stock awards granted	(50,000)		
Stock option awards exercised		(308,037)	4.48
Stock option awards canceled	342,979	(342,979)	12.02
Balance December 31, 2007	592,027	5,023,258	9.20
Plan amendment	1,200,000		
Stock option awards granted	(1,060,005)	1,060,005	3.38
Restricted stock awards granted	(76,536)		
Stock option awards exercised		(146,470)	2.72
Stock option awards canceled	459,144	(459,144)	8.53
Balance December 31, 2008	1,114,630	5,477,649	8.30

For stock option awards granted under the Incentive Plan during 2008, 2007, and 2006, the fair value was estimated on the date of grant using a Black-Scholes option pricing model and the assumptions noted in the table below. The weighted average grant date fair value of these awards granted during 2008, 2007, and 2006 was $2.16, $6.16 and $8.64, respectively. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method. The following explanations describe the assumptions used by the Company to value the stock option awards granted during 2008. The expected life is based on the average of the assumption that all outstanding stock option awards will be exercised at full vesting and the assumption that all outstanding stock option awards will be exercised at the midpoint of the current date (if already vested) or at full vesting (if not yet vested) and the full contractual term. The expected volatility represents an average of the implied volatility on the Company s publicly traded options, the volatility over the most recent period corresponding with the expected life, and the Company s long-term reversion volatility. The Company has assumed no expected dividend yield, as dividends have never been paid to stock or option holders and will not be for the foreseeable future. The weighted average risk-free interest rate is the implied yield currently available on zero-coupon government issues with a remaining term equal to the expected term.

Weighted Average Assumptions for Stock Option Awards Granted under the Incentive Plan

	2008	2007	2006
Expected Life	5.5	5.7	5.9
Expected Volatility	78.4%	74.5%	82.6%
Expected Dividend Yield	0.0%	0.0%	0.0%
Risk-Free Interest Rate	2.8%	4.6%	5.0%

The total intrinsic value of stock option awards exercised under the Incentive Plan was $223,369 during 2008, $1,347,010 during 2007, and $4,697,366 during 2006. The intrinsic value represents the total proceeds (fair market value at the date of exercise, less the exercise price, times the number of stock option awards exercised) received by all individuals who exercised stock option awards during the period.

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The following table summarizes, at December 31, 2008, by price range: (1) for stock option awards outstanding under the Incentive Plan, the number of stock option awards outstanding, their weighted average remaining life and their weighted average exercise price; and (2) for stock option awards exercisable under the Plan, the number of stock option awards exercisable and their weighted average exercise price:

	Outstanding			Exercisable	
Range	Number	Weighted Average Remaining Life	Weighted Average Exercise Price	Number	Weighted Average Exercise Price
$0 to 3	496,233	6.4	$ 1.82	278,400	$ 1.27
3 to 6	1,298,702	7.3	3.67	628,840	4.06
6 to 9	1,710,911	6.2	8.02	1,194,362	8.16
9 to 12	893,163	8.1	11.37	413,673	11.34
12 to 15	850,231	7.1	12.55	599,831	12.52
15 to 18	5,771	6.3	15.74	5,416	15.72
18 to 21	3,998	3.5	19.27	3,456	19.32
21 to 24	199,020	0.9	22.84	199,020	22.84
24 to 27	13,620	1.3	25.75	13,620	25.75
27 to 30	6,000	1.4	29.29	6,000	29.29
$0 to 30	5,477,649	6.7	8.30	3,342,618	9.00

The weighted average remaining contractual life of stock option awards exercisable under the Incentive Plan at December 31, 2008 was 5.5 years.

The aggregate intrinsic value of stock option awards outstanding and exercisable under the Incentive Plan at December 31, 2008 was $89,016. The aggregate intrinsic value represents the value (the period s closing market price, less the exercise price, times the number of in-the-money stock option awards) that would have been received by all stock option award holders under the Incentive Plan had they exercised their stock option awards at the end of the year.

The total fair value of the stock option awards vested under the Incentive Plan was $6,928,011 during 2008, $5,613,761 during 2007, and $2,473,986 during 2006.

As of December 31, 2008, the number of stock option awards vested and expected to vest under the Incentive Plan is 5,047,571. The weighted average exercise price of these stock option awards is $8.28 and their weighted average remaining contractual life is 6.8 years.

During 2007, the Company granted 50,000 restricted stock awards under the Incentive Plan with a grant date fair value of $11.81. During the second quarter of 2008, the Company also granted 76,536 restricted stock awards under the Incentive Plan with a grant date fair value of $3.12. None of the restricted stock awards granted under the Incentive Plan have vested as of December 31, 2008.

Employee Stock Purchase Plan

The ESPP was originally approved by the Company s stockholders in May 1995 and the most recent amendment was approved in May 2008. The Company has reserved a total of 600,000 shares of common stock to be purchased under the ESPP, of which 179,851 shares remain available for purchase at December 31, 2008. 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 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 84,907, 34,855, and 25,988 shares of common stock purchased under the ESPP in 2008, 2007, and 2006, respectively, at a weighted average price per share of $3.15, $7.74, and $7.36, respectively. Expense of

$165,492, $150,245, and $95,010 related to the ESPP was recognized during 2008, 2007, and 2006, respectively. For all periods, expense was determined using a Black-Scholes option pricing model. The weighted average grant

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date fair values of shares granted under the ESPP during 2008, 2007, and 2006 were $1.34, $2.98, and $4.57, respectively.

Stock Inducement Grant

In March 2007, the Company s Board of Directors approved a stock inducement grant of 110,000 stock option awards and 10,000 restricted stock awards to recruit a new employee to a key position within the Company. The stock option awards were granted in April 2007 with an exercise price equal to the market price of the Company s stock at the date of grant. The awards vest 25% after one year and monthly thereafter on a pro rata basis over the next three years until fully vested after four years. The stock option awards have contractual terms of 10 years. The vesting exercise provisions of both the stock option awards and the restricted stock awards granted under the inducement grant are subject to acceleration in the event of certain stockholder-approved transactions, or upon the occurrence of a change in control as defined in the respective agreements.

For the stock option awards granted under the inducement grant, the fair value was estimated on the date of grant using a Black-Scholes option pricing model and the following assumptions: expected life of 5.7 years, expected volatility of 72.9%, expected dividend yield of 0.0%, and risk-free interest rate of 4.6%. The weighted average grant date fair value of these stock option awards was $5.25. The fair value of the stock option awards is amortized to expense over the vesting periods using a straight-line expense attribution method. The expected life is based on the average of the assumption that all outstanding stock option awards will be exercised at full vesting and the assumption that all outstanding stock option awards will be exercised at the midpoint of the current date (if already vested) or at full vesting (if not yet vested) and the full contractual term. The expected volatility represents an average of the implied volatility on the Company s publicly traded stock options, the volatility over the most recent period corresponding with the expected life, and the Company s long-term reversion volatility. The Company has assumed no expected dividend yield, as dividends have never been paid to stock or option holders and will not be for the foreseeable future. The weighted average risk-free interest rate is the implied yield currently available on zero-coupon government issues with a remaining term equal to the expected term.

The exercise price of the stock option awards and the grant date fair value of the restricted stock awards granted under the inducement grant was $8.20. As of December 31, 2008, 4,166 of these restricted stock awards have vested.

Note 9 Employee Benefit Plans

In January 1991, the Company adopted an employee retirement plan (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 $418,215, $330,559, and $252,735 in 2008, 2007, and 2006, respectively.

Note 10 Collaborative and Other Research and Development Contracts

Shionogi & Co., Ltd. (Shionogi). In March 2007, the Company entered into an exclusive license agreement with Shionogi to develop and commercialize the Company s lead influenza neuraminidase inhibitor, peramivir, in Japan for the treatment of seasonal and potentially life-threatening human influenza. Under the terms of the agreement, Shionogi obtained rights to injectable formulations of peramivir in Japan in exchange for a $14 million up-front payment. The license provides for potential future milestone event payments (up to $21 million) and commercial event milestone payments (up to $95 million) in addition to double digit (between 10 and 20% range) royalty payments on product sales of peramivir. Generally, all payments under the agreement are nonrefundable and non-creditable, but they are subject to audit. Shionogi will be responsible for all development, regulatory and marketing costs in Japan. The term of the agreement is from February 28, 2007 until terminated by either party in accordance with the license agreement. Either party may terminate in the event of an uncured breach. Shionogi has the right of without cause termination. In the event of termination all license and rights granted to Shionogi shall terminate and shall revert back to the Company. The Company developed peramivir under a license from UAB and will owe sublicense payments to them on the upfront payment and any future event payments and/or royalties received by the Company from Shionogi. In October 2008, the Company and Shionogi amended the license agreement to expand the territory covered by the agreement to include Taiwan and to provide rights for Shionogi to

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perform a Phase III clinical trial in Hong Kong. In December, 2008 Shionogi initiated its phase III trial. BioCryst retains all rights to commercialize peramivir in North America, Europe, and other countries outside of Japan, Taiwan, and Korea. In accordance with SAB No. 104 and EITF Issue 00-21, the Company deferred the $14 million up-front payment that was received from Shionogi. This deferred revenue began to be amortized to revenue in April 2007 and will continue through December 2018. In December 2007, the Company received a $7 million milestone payment from Shionogi for their initiation of a Phase II clinical trial with i.v. peramivir.

U.S. Department of Health and Human Services (HHS). In January 2007, the Company was awarded a four-year contract from HHS to develop its influenza neuraminidase inhibitor, peramivir, for the treatment of seasonal and life-threatening influenza, including avian flu. The contract commits $102.6 million to support manufacturing, process validation, clinical studies, and other product approval requirements for peramivir. The contract with HHS is defined as a standard cost-plus-fixed-fee contract. That is, the Company is entitled to receive reimbursement for all costs incurred in accordance with the contract provisions that are related to the development of peramivir plus a fixed fee, or profit. HHS will make periodic assessments of progress and the continuation of the contract is based on the Company s performance, timeliness and quality of deliverables, and other factors. The government has rights under certain contract clauses to terminate this contract. The contract is terminable by the government at any time for breach or without cause.

In January 2008, the Company announced that the development plan for peramivir had changed and that it would no longer pursue the Phase III i.m. program in peramivir for the current influenza season, but would move forward in evaluating higher doses than used in previous studies. Also in January 2008, the Company announced that the program would cost in excess of the $102.6 million contract and that any funding above the $102.6 million may be the responsibility of the Company. Since then, HHS and the Company have been working in collaboration through various contract modifications to maximize resources by stopping work on some projects (e.g. the Phase III i.m. program) and capping expenditures on other projects in order to maximize remaining funds. HHS and the Company executed a contract modification that fully funds the Company through the completion of both the phase II studies in outpatients treated with intramuscular peramivir, the phase II study in hospitalized patients with intravenous peramivir, and certain manufacturing and toxicology components of the program. The modification also allows the Company and HHS to agree on additional development activities for peramivir within the confirmed $102.6 million funding. All temporary restraints, effected through a stop work order, have now been removed. Following completion of the phase II studies, we expect to continue the dialogue with HHS regarding additional funding beyond the $102.6 million for peramivir development through U.S. licensure. The original contract of $102.6 million and the four year term remain unchanged.

Green Cross Corporation (Green Cross). In June 2006, the Company entered into an agreement with Green Cross to develop and commercialize peramivir in Korea. Under the terms of the agreement, Green Cross will be responsible for all development, regulatory, and commercialization costs in Korea. The Company received a one-time license fee of $250,000. The agreement also provides for relatively insignificant future milestone payments. The license also provides that the Company will share in profits resulting from the sale of peramivir in Korea, including the sale of peramivir to the Korean government for stockpiling purposes. Furthermore, Green Cross will pay the Company a premium over its cost to supply peramivir for development and any future marketing of peramivir products in Korea. Both parties have the right to terminate in the event of an uncured material breach. In the event of termination all rights, data, materials, products and other information would be transferred to the Company. In accordance with SAB No. 104 and EITF Issue 00-21, the Company deferred the up-front payment that was received from Green Cross. This deferred revenue began to be amortized to revenue August 2006 and will continue through November 2009.

Mundipharma International Holdings Limited (Mundipharma). In February 2006, the Company entered into an exclusive, royalty bearing right and license agreement with Mundipharma for the development and commercialization of the Company s lead PNP inhibitor, forodesine HCl, for use in oncology. Under the terms of the agreement, Mundipharma obtained rights to forodesine HCl 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. The Company has incurred approximately $21.9 million of costs related to these trials since inception of the agreement (approximately $7.5 million of these costs were incurred during 2008). In addition, Mundipharma will conduct additional clinical trials at their own cost up to a maximum of $15 million. The license provides for possibility of

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future event payments totaling $155 million for achieving specified development, regulatory and commercial events (including certain sales level amounts following a product s launch) for certain indications. In addition, the agreement provides that the Company will receive royalties (ranging from single digits to mid teens) 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 forodesine HCl and other PNP inhibitors from AECOM and IRL and will owe sublicense payments to these third parties on the upfront payment, 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 forodesine HCl 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 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 deferred the $10 million up-front payment that was received from Mundipharma in February 2006. This deferred revenue began to be amortized to revenue February 2006 and will end 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 forodesine HCl are recorded as revenue when the expense is incurred up to the $10 million limit stipulated in the agreement.

The Company is currently in dispute with Mundipharma regarding the contractual obligations of the parties with respect to certain costs related to the manufacturing and development of forodesine HCL. Notwithstanding, the Company does not believe that it is responsible for any of the disputed amounts. The Company is engaged in ongoing discussion to resolve this dispute. The maximum potential exposure to the Company is estimated to be approximately $2.5 million. Because of the preliminary nature of the discussions, no amounts have been accrued as of December 31, 2008.

F.Hoffmann-La Roche Ltd. and Hoffman-La Roche Inc. (Roche). In November 2005, the Company entered into an exclusive license with Roche for the development and commercialization of the Company s 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 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.

In 2005, the Company recorded deferred revenue of $30 million related to the Roche collaboration in accordance with SAB No. 104 and EITF Issue 00-21. This deferred revenue began to be amortized to revenue in October 2006, when the IND was transferred to Roche, and was to continue through August 2023, which is the date of expiration for the last-to-expire patent covered by the agreement. However, in May 2008 the Company received notice that Roche was exercising the no cause termination right under the license agreement for BCX-4208. Upon termination during the fourth quarter of 2008, the Company recognized the remaining deferred revenue and deferred expense related to the license agreement, which was $26.5 million and $8.2 million, respectively.

Albert Einstein College of Medicine of Yeshiva University and Industrial Research, Ltd.(AECOM and IRL respectively). 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 Forodesine HCl 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 the option to expand the Agreement to include other inventions

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in the field made by the investigators or employees of AECOM and IRL. The Company has agreed to use commercially reasonable efforts to develop these drugs. In addition, the Company has agreed to pay certain milestone payments for each licensed product (which range in the aggregate from $1.4 million to almost $4 million per indication) for future development of these inhibitors, single digit royalties on net sales of any resulting product made by the Company, and to share approximately one quarter of future payments received from other third-party partners, if any. In addition, the Company has agreed to pay annual license fees, which can range from $150,000 to $500,000, that are 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.

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 single digit royalties on sales of any resulting product and to share in future payments received from other third-party partners. The Company has completed the research under the UAB agreements. 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. Upon termination both parties shall cease using the other parties proprietary and confidential information and materials, the parties shall jointly own joint inventions and UAB shall resume full ownership of all UAB licensed products. There is currently no activity between the Company and UAB on these agreements, but when the Company licenses this technology, such as in the case of the Shionogi and Green Cross agreements, or commercialize products related to these programs, we will 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 single digit royalties on sales of any resulting product and to share in future payments received from other third party partners, if any. The Company can terminate this agreement at any time by giving 90 days advance notice. Upon termination, the Company would cease using the licensed technology.

Note 11 Recent Accounting Pronouncements

In May 2008, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 162, *The Hierarchy of Generally Accepted Accounting Principles* (Statement No. 162). Statement No. 162 identifies the sources of accounting principles and the framework for selecting the principles to be used in the preparation of financial statements that are presented in conformity with generally accepted accounting principles. Statement No. 162 was effective in November 2008 and had no impact on the Company s financial statements.

In December 2007, the FASB issued Statement No. 160, *Non-controlling Interests in Consolidated Financial Statements* (Statement No. 160). Statement No. 160 establishes accounting and reporting standards that require the ownership interests in subsidiaries non-parent owners be clearly presented in the equity section of the balance sheet; requires the amount of consolidated net income attributable to the parent and to the non-controlling interest be clearly identified and presented on the face of the consolidated statement of income; requires that changes in a parent s ownership interest while the parent retains its controlling financial interest in its subsidiary be accounted for consistently; requires that when a subsidiary is deconsolidated, any retained non-controlling equity investment in the former subsidiary be initially measured at fair value and the gain or loss on the deconsolidation of the subsidiary be measured using the fair value of any non-controlling equity; and requires that entities provide disclosures that clearly identify the interests of the parent and the interests of the non-controlling owners. Statement No. 160 is effective as of the beginning of an entity s first fiscal year that begins after December 15, 2008. The Company has not determined the impact, if any, this statement will have on its financial statements.

In December 2007, the FASB issued Statement of Financial Accounting Standards No. 141 (revised 2007), *Business Combinations* (Statement No. 141R). In Statement No. 141R, the FASB retained the fundamental

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requirements of Statement No. 141 to account for all business combinations using the acquisition method (formerly the purchase method) and for an acquiring entity to be identified in all business combinations. However, the new standard requires the acquiring entity in a business combination to recognize all (and only) the assets acquired and liabilities assumed in the transaction; establishes the acquisition-date fair value as the measurement objective for all assets acquired and liabilities assumed; and requires the acquirer to disclose to investors and other users all of the information they need to evaluate and understand the nature and financial effect of the business combination. Statement No. 141R is effective for annual periods beginning on or after December 15, 2008. The Company has not yet determined the impact, if any, that Statement No. 141R will have on its financial statements.

In November 2007, a final consensus was reached on Emerging Issues Task Force Issue 07-1, *Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property* (EITF Issue 07-1). EITF Issue 07-1 will require the Company to disclose the nature and purpose of its collaborative arrangements in its annual financial statements, its rights and obligations under the collaborative arrangements, the stage of the underlying endeavors life cycle, the Company s accounting policies for the arrangements and the income statement classification and amount of significant financial statement amounts related to the collaborative arrangements. EITF Issue 07-1 will be effective for fiscal years beginning after December 15, 2008 and will require the Company to apply it as a change in accounting principle through retrospective application to all prior periods for all collaborative arrangements existing as of the effective date. The Company is currently assessing the impact of EITF 07-1 on its financial statements.

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

	First	Second	Third	Fourth
2008 Quarters				
Revenues	$ 10,768	$ 2,659	$ 8,894	$34,240
Net (loss) income	(13,098)	(12,709)	(8,995)	10,070
Net (loss) income per share	(.34)	(.33)	(.24)	.26
2007 Quarters				
Revenues	$ 9,159	$ 13,444	$ 20,463	$28,172
Net loss	(8,825)	(6,963)	(10,984)	(2,284)
Net loss per share	(.30)	(.24)	(.32)	(.06)

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

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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, 2008 and 2007, and the related statements of operations, stockholders equity and cash flows for each of the three years in the period ended December 31, 2008. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of BioCryst Pharmaceuticals, Inc. at December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, 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), BioCryst Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2008, 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 6, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
Birmingham, Alabama
March 6, 2009

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Report of Independent Registered Public Accounting Firm on Internal Control

The Board of Directors and Shareholders
BioCryst Pharmaceuticals, Inc.

We have audited BioCryst Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2008, 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 included in the accompanying Management s Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on 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, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, 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, BioCryst Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria**.**

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of BioCryst Pharmaceuticals, Inc. as of December 31, 2008 and 2007, and the related statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2008 of BioCryst Pharmaceuticals, Inc. and our report dated March 6, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
Birmingham, Alabama
March 6, 2009

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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 of 1934, as amended (the Exchange Act), is recorded, processed, summarized and reported in a timely manner under the Exchange Act of 1934. We carried out an evaluation as required by paragraph (b) of Rule 13a-15 or Rule 15d-15 under the Exchange Act,, 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 (as defined in Rule 13a-15(e) or Rule 15d-15 under the Exchange Act). Based upon that evaluation, the Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2008, our disclosure controls and procedures are effective. The Company believes that its disclosure controls and procedures will ensure that information required to be disclosed in the reports filed or submitted by it under the Exchange Act 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, 2008, 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, 2008, our internal control over financial reporting was effective. Management believes our internal control over financial reporting will 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.

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Ernst & Young LLP, the independent registered public accounting firm that audited our financial statements included in this report, has issued an attestation report on the Company s internal control over financial reporting, a copy of which appears on page 70 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, 2008 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT

The information required by this item is set forth under the captions *Items to be Voted on 1. Election of Directors, Executive Officers, Section 16(a) Beneficial Ownership Reporting Compliance* and *Corporate Governance* in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is set forth under the caption *Executive Compensation* in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this item is set forth under the captions *Equity Compensation Plan Information* and *Security Ownership of Certain Beneficial Owners and Management* in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this item is set forth under the captions *Certain Relationships and Related Transactions* and *Corporate Governance* in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders and incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item is set forth under the caption *Items to be Voted on 2. Ratification of Appointment of Independent Registered Public Accountants* in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders and incorporated herein by reference.

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PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) Financial Statements

	Page in Form 10-K
The following financial statements appear in Item 8 of this Form 10-K:	
Balance Sheets at December 31, 2008 and 2007	50
Statements of Operations for the years ended December 31, 2008, 2007 and 2006	51
Statements of Stockholders Equity for the years ended December 31, 2008, 2007 and 2006	52
Statements of Cash Flows for the years ended December 31, 2008, 2007 and 2006	53
Notes to Financial Statements	54
Report of Independent Registered Public Accounting Firm on Financial Statements	69
Report of Independent Registered Public Accounting Firm on Internal Control	70

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. See Index of Exhibits.

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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 March 6, 2009.

BIOCRYST PHARMACEUTICALS, INC.

By: /s/ Jon P. Stonehouse
Jon P. Stonehouse
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 6, 2009:

Signature	Title(s)
/s/ Jon P. Stonehouse	President, Chief Executive Officer and Director
(Jon P. Stonehouse)	
/s/ Stuart Grant	Senior Vice President and Chief Financial Officer and Treasurer
(Stuart Grant)	
/s/ J. Michael Mills	Controller and Principal Accounting Officer
(J. Michael Mills)	
/s/ Stephen R. Biggar	Director
(Stephen R. Biggar, M.D., Ph.D.)	
	Director
(Stanley C. Erck)	
/s/ William W. Featheringill	Director
(William W. Featheringill)	
	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/ Randolph C. Steer Director

(Randolph C. Steer, M.D., Ph.D.)

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INDEX TO EXHIBITS

Number	Description
3.1	Third Restated Certificate of Incorporation of Registrant. Incorporated by reference to Exhibit 3.1 to the Company s Form 8-K filed December 22, 2006.
3.2	Certificate of Amendment to the Third Restated Certificate of Incorporation of Registrant. Incorporated by reference to Exhibit 3.1 to the Company s Form 8-K filed July 24, 2007.
3.3	Certificate of Increase of Authorized Number of Shares of Series B Junior Participating Preferred Stock. Incorporated by reference to Exhibit 3.1 to the Company s Form 8-K filed November 4, 2008.
3.4	Amended and Restated Bylaws of Registrant effective October 29, 2008. Incorporated by reference to Exhibit 3.2 to the Company s Form 8-K filed November 4, 2008.
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 filed June 17, 2002.
4.2	Amendment to Rights Agreement, dated as of August 5, 2007. Incorporated by reference to Exhibit 4.2 of the Company s Form 10-Q filed August 9, 2007.
10.1&	Stock Incentive Plan, as amended and restated effective February 28, 2008. Incorporated by reference to Appendix A to the Company s Definitive Proxy Statement, filed April 16, 2008.
10.2&	Employee Stock Purchase Plan, as amended and restated effective February 28, 2008. Incorporated by reference to Appendix B to the Company s Definitive Proxy Statement, filed April 16, 2008.
10.3&	Retention Bonus Agreement between BioCryst Pharmaceuticals, Inc. and Stuart Grant dated May 21, 2008. Incorporated by reference to Exhibit 10.25 of the Company s Form 10-Q filed August 8, 2008.
10.4&	Retention Bonus Agreement between BioCryst Pharmaceuticals, Inc. and David McCullough dated May 21, 2008. Incorporated by reference to Exhibit 10.26 of the Company s Form 10-Q filed August 8, 2008.
10.5&	Employment Letter Agreement between BioCryst Pharmaceuticals, Inc. and William P. Sheridan dated June 12, 2008. Incorporated by reference to Exhibit 10.27 of the Company s Form 10-Q filed August 8, 2008.
10.6&	Consulting Agreement between BioCryst Pharmaceuticals, Inc. and J. Claude Bennett, M.D. dated June 13, 2008. Incorporated by reference to Exhibit 10.28 of the Company s Form 10-Q filed August 8, 2008.
10.7#	Agreement dated January 3, 2007, between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services, as amended by Amendment number 1 dated January 3, 2007 and Amendment number 2 dated May 11, 2007. Incorporated by reference to Exhibit 10.3 to the Company s Form 10-Q filed August 9, 2007.

10.8	Amendment #3 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services, dated October 2, 2007. Incorporated by reference to Exhibit 10.6 of the Company s Form 10-K filed March 4, 2008.
10.9	Amendment #4 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services dated April 3, 2008. Incorporated by reference to Exhibit 10.29 of the Company s Form 10-Q filed August 8, 2008.
10.10	Amendment #5 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services dated July 2, 2008. Incorporated by reference to Exhibit 10.30 of the Company s Form 10-Q filed August 8, 2008.
10.11	Amendment #6 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services dated August 18, 2008. Incorporated by reference to Exhibit 10.1 of the Company s Form 8-K filed November 7, 2008.
(10.12)	Amendment #7 to the Agreement between BioCryst Pharmaceuticals, Inc. and the Department of Health and Human Services dated November 17, 2008.

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Number	Description
10.13&	Annual Incentive Plan. Incorporated by reference to Exhibit 10.1 of the Company s Form 10-K filed March 4, 2008.
10.14&	Executive Relocation Policy. Incorporated by reference to Exhibit 10.2 of the Company s Form 10-K filed March 4, 2008.
10.15&	Amendment to Employment Letter Agreement for Stuart Grant Dated July 23, 2007. Incorporated by reference to Exhibit 10.3 of the Company s Form 10-K filed March 4, 2008.
10.16&	Form of Notice of Grant of Non-Employee Director Automatic Stock Option and Stock Option Agreement. Incorporated by reference to Exhibit 10.4 of the Company s Form 10-K filed March 4, 2008.
10.17&	Form of Notice of Grant of Stock Option and Stock Option Agreement. Incorporated by reference to Exhibit 10.5 of the Company s Form 10-K filed March 4, 2008.
10.18#	License, Development and Commercialization Agreement dated as of February 28, 2007, by and between the Company and Shionogi & Co., Ltd. Incorporated by reference to Exhibit 10.4 to the Company s Form 10-Q filed May 10, 2007.
(10.19*)	First Amendment to License, Development and Commercialization Agreement, effective as of September 30, 2008, between the Company and Shionogi & Co., Ltd.
10.20&	Employment Letter Agreement dated April 2, 2007, by and between the Company and David McCullough. Incorporated by reference to Exhibit 10.5 to the Company s Form 10-Q filed May 10, 2007.
10.21&	Amended and Restated Employment Letter Agreement dated February 14, 2007, by and between the Company and Jon P. Stonehouse. Incorporated by reference to Exhibit 10.12 to the Company s Form 10-K for the year ended December 31, 2006, filed March 14, 2007.
10.22	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 filed August 8, 2000.
10.23	Third Amendment to Lease Agreement dated August 7, 2007, by and between Riverchase Capital LLC, a Florida limited liability company, Stow Riverchase, LLC, a Florida limited liability company, as successor landlord to RBP, LLC and the Company. Incorporated by reference to Exhibit 10.4 of the Company s Form 10-Q filed August 9, 2007.
10.24	Stock and Warrant Purchase Agreement dated as of August 6, 2007, by and among BioCryst Pharmaceuticals, Inc. and each of the Investors identified on the signature pages thereto. Incorporated by reference to Exhibit 4.1 of the Company s Form 8-K filed August 7, 2007.
10.25&	Employment letter agreement between BioCryst Pharmaceuticals, Inc. and Stuart Grant dated July 23, 2007. Incorporated by reference to Exhibit 10.1 of the Company s Form 8-K filed July 26, 2007.
10.26	

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 filed February 17, 2005.

10.27# Development and License Agreement dated as of February 1, 2006, by and between BioCryst Pharmaceuticals, Inc. and Mundipharma International Holdings Limited (Portions omitted pursuant to request for confidential treatment.) Incorporated by reference to Exhibit 10.2 to the Company s Form 8-K/A filed May 2, 2006.

10.28# 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 filed November 30, 2005.

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Number	Description
10.29#	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 filed December 22, 2005.
10.30	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 filed December 16, 2005.
10.31	Nomination and Observer Agreement, dated as of December 16, 2005, by and between BioCryst Pharmaceuticals, Inc. and Kleiner Perkins Caufield & Byers. Incorporated by reference to Exhibit 4.2 to the Company s Form 8-K filed December 16, 2005.
(10.32&)	Severance Agreement and General Release between Michael Darwin and BioCryst Pharmaceuticals, Inc., dated December 31, 2008.
(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 requested.

\# Confidential treatment granted.

& Management contracts.

( ) Filed herewith.