Pharmasset Inc
Form 10-K
December 11, 2008
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

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

For the Fiscal Year Ended September 30, 2008

or

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

For the transition period from to

Commission file number 1-33428

Pharmasset, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**98-0406340**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
303-A College Road East	**08540**

Princeton, New Jersey
(Address of principal executive offices) **(Zip Code)**
Registrant s telephone number, including area code (609) 613-4100

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 Par Value Per Share	The NASDAQ Stock Market LLC

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, 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.

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

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

The aggregate market value of the registrant s common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) based on the last reported sale price of the common stock on March 31, 2008 was $341.5 million.

As of November 30, 2008, the registrant had 23,384,029 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2009 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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The Company, Pharmasset, we and us as used in this Annual Report on Form 10-K, refer to Pharmasset, Inc., a Delaware corporation. Pharmasset and our logo are our trademarks, and Racivir is our registered trademark. Other trademarks mentioned in this Annual Report on Form 10-K are the property of their respective owners.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. The forward-looking statements are principally contained in the sections entitled Business, Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations. These statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. For this purpose, any statement that is not a statement of historical fact should be considered a forward-looking statement. We may, in some cases, use words such as project, believe, anticipate, plan, expect, estimate, intend, potential, or other words that convey uncertainty of future outcomes to identify these forward-looking statements. These forward-looking statements include statements about the following:

- our product development efforts, in particular with respect to the clinical trial results and regulatory approval of clevudine, Racivir , R7128, PSI-7851 and DFC;
- the initiation, completion or success of preclinical studies and clinical trials;
- clinical trial initiation and completion dates, anticipated regulatory filing dates and regulatory approval for our product candidates;
- the commercialization of our product candidates;
- our collaboration agreement with F. Hoffmann-LaRoche Ltd. and Hoffmann- La Roche Inc. (collectively, Roche), including potential milestone or royalty payments thereunder;
- our intentions regarding the establishment of collaborations or the licensing of product candidates or intellectual property;
- our intentions to expand our capabilities and hire additional employees;
- anticipated operating losses, future revenues, research and development expenses, and the need for additional financing; and
- our financial performance.

Forward-looking statements reflect our current views with respect to future events and are subject to risks and uncertainties. We discuss many of the risks and uncertainties associated with our business in greater detail under the heading Risk Factors. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. All forward-looking statements represent our estimates and assumptions only as of the date of this Annual Report on Form 10-K.

You should read this Annual Report on Form 10-K and the documents that we reference in it completely and with the understanding that our actual future results may be materially different from what we expect. Our business, financial condition, results of operations, and prospects may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the federal securities laws to update and disclose material developments related to previously disclosed information. The forward-looking statements contained in this Annual Report on Form 10-K are subject to the safe-harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act).

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PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Our primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus, or HBV, hepatitis C virus, or HCV, and human immunodeficiency virus, or HIV. Our research and development efforts focus on a class of compounds known as nucleoside analogs, which act to inhibit the natural enzymes required for viral replication. We currently have three clinical-stage product candidates, two of which we are developing ourselves and one of which we are developing with a strategic partner:

- Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America (the Americas) and Europe;
- R7128, a pro-drug of PSI-6130 for the treatment of HCV, has completed Phase 1 clinical trials in combination with Pegasys® plus Copegus® through a strategic collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche); and
- Racivir, for the treatment of HIV, has completed a Phase 2 clinical trial.

We are developing clevudine and Racivir ourselves, and we have a strategic collaboration with Roche for the development of PSI-6130 and its pro-drugs, including R7128. Under the collaboration, Roche pays all development costs and provides us with potential income from milestone payments that can be used to fund the advancement of our proprietary product candidates. We have also identified proprietary, next generation HCV development candidates that are being evaluated for advancement into clinical development. One of these compounds, PSI-7851, was recently nominated as a lead candidate and is being advanced into Good Laboratory Practice (GLP) toxicity studies required for submission of an Investigational New Drug (IND) application with the United States Food and Drug Administration (FDA) or an equivalent foreign regulatory filing.

Although there are many currently approved antiviral drugs, there are unmet medical needs in HCV, HBV and HIV. In the treatment of HCV, pegylated interferon in combination with ribavirin is the standard of care and has demonstrated, for some patients, the ability to offer a sustained virologic response, or SVR, defined as a virus that is undetectable by a standard test utilizing polymerase chain reaction, or PCR, six months after discontinuation of therapy. However, pegylated interferon is injectable and has side effects, including fatigue, bone marrow suppression, anemia and neuropsychiatric effects. In the treatment of HCV, we believe there is an unmet medical need for drugs that offer an improved SVR rate with fewer side effects. In the treatment of HBV, interferon is not widely used because it produces an SVR in too few patients to justify its side effects. For HBV patients, treatment involves a chronic regimen of antiviral drugs to keep their viral load as low as possible. We believe that there is an unmet medical need for an HBV product which has a limited treatment period and SVR, similar to that of pegylated interferon, coupled with the fewer side effects and greater convenience of orally administered small molecule drugs. For HIV patients, treatment also involves a chronic regimen of antiviral drugs. During such prolonged treatment, viral mutations occur that make the viruses resistant to the drugs being used. We believe there is an unmet medical need for new HIV drugs that are effective against resistant viruses and can replace existing therapies that have lost effectiveness.

We believe nucleoside analogs are well suited to treat viral diseases because they can be designed to be highly specific and potent, are relatively simple to manufacture, and have the potential for oral administration. Nucleoside analog drugs have demonstrated a higher barrier to viral resistance than non-nucleoside and protease inhibitor drugs, and have a well-established development and regulatory history. There are 14 nucleoside analogs for the treatment of HBV, HCV or HIV that have been approved by the FDA and additional nucleoside analogs have been approved by the FDA for the treatment of cytomegalovirus and herpes simplex virus. In addition to

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clevudine, R7128, and Racivir, we also have discovery programs focused on other nucleoside analogs for HCV and HIV. Our scientific team of virologists, biologists and nucleoside chemists has experience discovering and developing nucleoside analog drugs for antiviral indications. Collectively, our management team s product development experience includes 40 therapeutic and diagnostic product approvals. Our discovery platform includes a library of nucleoside analogs and a collection of viral and cellular assays that we use to evaluate new product candidates.

We were initially incorporated as Pharmasset, Ltd. on May 29, 1998 under the laws of Barbados. We redomiciled under the laws of Delaware on June 8, 2004 as Pharmasset, Inc., and Pharmasset, Ltd. was dissolved on June 21, 2004. Pharmasset, Inc., then-existing as a Georgia corporation, incorporated on June 5, 1998 and our only subsidiary of Pharmasset, Ltd., was merged with and into us on July 23, 2004.

Strategy

Our primary objective is to become a leader in discovering, developing and commercializing novel antiviral therapeutics that provide a competitive advantage and address unmet medical needs. Our primary focus is on the development of oral therapeutics for the treatment of HBV, HCV and HIV. To achieve this goal, we are pursuing the following strategies:

Focus on developing our current clinical-stage product candidates and advancing them toward marketing approval. We are increasing our internal clinical development capabilities to enhance our ability to advance these product candidates. Our development team is responsible for planning and managing our clinical trials and supporting our partner, Roche, in its future clinical trials of R7128.

Maintain a broad pipeline of potential product candidates to diversify commercial opportunities and reduce our dependence on any one product candidate s clinical or commercial success. Our development capabilities not only advance our clinical-stage product candidates, but also can be used to evaluate product opportunities from sources outside our company. We intend to leverage our research and development capabilities to evaluate external opportunities and may in-license products or technologies that we believe will complement our antiviral therapeutic focus. By maintaining a broad pipeline, we hope to create a portfolio of products that reduces our dependence on any one product and creates synergy within our pipeline through potential combination products.

Leverage our core competency in nucleoside chemistry for research innovation and the discovery of additional product candidates. Our core competency is the discovery and development of nucleoside analogs for use as antiviral therapeutics. We believe our nucleoside chemistry expertise and our nucleoside library provide us with a strong foundation from which to identify additional product candidates. We intend to continue to invest in our nucleoside research capabilities and expand our nucleoside analog library.

Commercialize our products ourselves or through collaborations, where appropriate, to optimize economic returns while managing financial risk. We allocate our limited resources to efforts that we believe will provide the greatest returns. Accordingly, we enter into collaborations to leverage our development capabilities and capitalize on commercialization opportunities that we cannot accomplish by ourselves. We believe this strategy will enable us to obtain the greatest returns from our antiviral discovery and development efforts.

Background on Viral Disease

A virus is a cellular parasite that cannot reproduce by itself and therefore must infect a susceptible host cell to replicate. A viral infection begins when the virus encounters a susceptible host cell and attaches to the cell membrane. The virus then enters the host cell and directs the host cell s metabolic machinery to participate in copying the viral genetic information, which is either RNA or DNA, and to produce the proteins encoded by that genetic information. This viral genetic information is packaged within a shell of newly produced viral proteins, forming an immature virus. In the case of HBV, HCV or HIV, this immature virus then acquires a coating or

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envelope of specific viral proteins and cellular lipids, forming a mature virus particle that is capable of infecting other cells. There are a wide variety of viruses, some of which are associated with a low rate of mortality, such as viruses causing the common cold, while others, including HBV, HCV and HIV, are associated with higher mortality rates.

The challenge in developing antiviral therapies is to inhibit viral replication without injuring the host cell. For many years, it appeared that the development of safe and effective antiviral therapies would not be possible because the processes of viral replication were so intertwined with the cell s metabolic processes that the inhibition of viral functions would result in cell death. A breakthrough occurred with the identification of viral enzymes, such as viral polymerases, which are required for viral replication. These enzymes differ enough from cellular enzymes to permit their selective inhibition and thus prevent viral replication without harming the cell. HBV, a DNA virus, has one polymerase enzyme with two activities: a reverse transcriptase which makes one strand of viral DNA from an RNA template; and a DNA polymerase, which makes a second strand of viral DNA from a DNA template, whose activity is the primary target for the treatment of HBV. HCV, an RNA virus, has an RNA polymerase which makes new viral RNA strands from an RNA template. HIV, an RNA virus, has a reverse transcriptase which makes viral DNA from an RNA template.

A major challenge of antiviral therapy is the emergence of viral mutations that result in forms of the virus that are resistant to current therapies. Viral mutations result from mistakes that occur during the natural viral replication process when the genetic information is copied. The mutated form of the virus infects other cells and replicates in its mutated form. Some mutations make the virus resistant to certain types of antiviral medications. When a drug-resistant form of virus first arises, it usually comprises a very small percentage of the virus circulating within the blood. As the original or wild-type virus continues to be suppressed by antiviral therapy and the drug-resistant virus continues to replicate, the mutated virus eventually becomes the dominant virus type. To reduce the likelihood of a dominant drug-resistant mutation, patients must comply with their treatment regimens; however, current studies show that at any given time only approximately 70% of patients strictly adhere to their therapy. Each of the FDA-approved oral viral therapies is susceptible to a mutation that confers drug resistance. New drug-resistant forms of virus continue to emerge, and as a result, new therapies to fight drug-resistant virus will continue to be needed.

HBV, HCV and HIV patients are classified as treatment-naïve or treatment-experienced. Treatment-naïve patients have not been exposed to antiviral therapies. Once viral mutations begin to occur and the virus develops resistance to the therapy, physicians either switch treatment regimens or add new drugs to existing regimens for the now treatment-experienced patients.

Our Product Candidates

Our research and development programs are focused on developing drugs that treat HBV, HCV and HIV infections. Our product candidates are nucleoside analogs that we believe have potential competitive advantages with respect to safety, efficacy, resistance profile and/or convenience of dosing as compared to currently approved drugs and other investigational agents. The following table summarizes the three product candidates on which we are focusing:

Product Candidate	Indication	Status	Next Expected Milestone	Commercialization Partners
Clevudine	HBV	Enrolling Phase 3 registration clinical trial	Complete full enrollment in Phase 3 registration studies during the first calendar quarter of 2009	
R7128	HCV	Completed Phase 1	Begin Phase 2b study during the first calendar quarter of 2009	Roche
Racivir	HIV	Completed Phase 2	Complete evaluation of clinical data and engage a development partner for a combination drug study	

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Clevudine for the Treatment of HBV

HBV Background

Hepatitis B viruses can cause liver disease leading to significant morbidity and death. HBV can cause either acute or chronic (lifelong) infection. The World Health Organization, or WHO, has reported that approximately 350 million people worldwide have chronic HBV infection, including approximately 4.4 million people in the United States, Italy, Spain, Germany, the United Kingdom and France. According to the Centers for Disease Control and Prevention, or CDC, approximately 1.25 million people in the United States are chronically infected with HBV, and approximately 5,000 people in the United States die each year from chronic liver disease related to HBV infection. In addition, the Hepatitis B Foundation reports that 100,000 people will become infected with HBV this year. In the United States, about half, or 680,000, of the chronic HBV carriers have been diagnosed, and about 300,000 of these are under a physician s care, and only approximately 34,000, or 11.3%, of these patients are currently prescribed oral HBV drugs, according to estimates by independent third-party sources. We believe this poor use of oral antiviral drugs indicates an unmet medical need in the treatment of HBV. At present, treating physicians are more likely to monitor a patient and delay use of pegylated interferon or an oral HBV drug. Our market research suggests that many hepatologists delay or avoid HBV treatment with pegylated interferon due to adverse events, such as fatigue, bone marrow suppression and neuropsychiatric effects and delay or avoid HBV treatment with small molecule drugs due to the cost of therapy or a preference to delay the initiation of chronic therapy. Accordingly, we believe that there is an unmet medical need for an HBV product which has a limited treatment period and SVR of pegylated interferon coupled with the fewer side effects and greater convenience, resulting in improved patient compliance with dosing schedules, of orally administered small molecule drugs. We believe this medical need is unmet due to the lack of sustained antiviral response after stopping therapy with currently approved drugs, which results in chronic, lifetime use of these drugs once treatment with them is begun. Worldwide HBV therapeutic sales were approximately $1.1 billion in 2007.

Acute asymptomatic infection, which is the most common type of HBV infection, lasts several weeks with few, if any, detectible symptoms. Acute symptomatic infection is more serious, and is associated with more severe symptoms such as flu-like illness and mild jaundice. In rare circumstances, acute symptomatic infection can lead to nonfatal hepatic necrosis or fatal fulminant hepatitis. In both symptomatic and asymptomatic acute HBV infection, an individual s broad-based immune responses develop and can clear the virus. If this occurs, immunity usually remains with the patient for the rest of the patient s life.

When HBV develops into a chronic infection, infected individuals cannot clear the virus with their immune system. A person is considered to have chronic HBV infection based on the presence of hepatitis B surface antigen for more than six consecutive months in the blood. This chronic state is typically marked by both replicative and non-replicative phases of disease progression, which are further characterized by four primary markers in the blood: elevated liver enzymes, viral DNA load, viral antigens and virus-specific antibodies. The relative level of these blood markers indicates whether the disease presents in either active or inactive form. Chronic hepatitis B patients are classified into two groups: e-antigen positive individuals are those in whom the e-antigen is present and e-antigen negative persons are those in whom the e-antigen is not present. The e-antigen is a viral protein that indicates active replication of HBV or a persistent disease carrier state. A carrier is an infected individual who does not develop the disease, but can transmit the virus to others. The e-antigen negative form of the disease has been more difficult to treat effectively than the e-antigen positive form. Chronic hepatitis, left untreated, can result in cirrhosis of the liver, liver cancer, liver failure or death.

HBV uses human cellular machinery to replicate and spread the virus throughout the body. When an individual is exposed to HBV, the virus infects human liver cells and its DNA is transported to the cell nucleus. Subsequently, the partially circular viral DNA is converted to covalently closed circular DNA (cccDNA), which serves as a template for transcription of messenger RNA and the synthesis of the viral proteins that are required for replication. Newly synthesized RNA can be used to direct the synthesis of several viral proteins or is packaged into immature virus particles where it is converted into viral DNA by the process of reverse transcription (similar to HIV). Synthesis of viral DNA is performed by a DNA polymerase that is specific to

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HBV. Because the HBV polymerase is required for the virus to replicate, its activity is the primary target for the treatment of HBV. Mature DNA-containing viruses are assembled with envelopes of viral proteins and cellular lipids and transported out of the cell, which completes the replication process. A reservoir of cccDNA remains inside the infected cell, from which additional copies of the virus are made in a continuing cycle. Despite the reduction in HBV viral load levels resulting from currently approved therapies, these drugs have little effect on cccDNA and cannot truly resolve the infection. Since cccDNA is the reservoir responsible for persistent infection and long-term latency, any attempts to eradicate HBV have become increasingly focused on eradicating the cccDNA form of the virus.

A safe and effective vaccine against HBV has been available since 1982, and the WHO guidelines recommend this vaccination for all newborns universally. According to the WHO, however, only 153 countries had introduced the hepatitis B vaccine in routine infant immunization as of the end of 2003. Moreover, the vaccine only benefits those not yet infected with HBV. In the United States, five oral nucleoside analogs, lamivudine, adefovir dipivoxil (adefovir), telbivudine, entecavir, and tenofovir disoproxil fumarate (tenofovir), and one injectable protein, alpha interferon, which is available in standard and pegylated forms, have been approved for the treatment of HBV. While these products have demonstrated some patient benefits, we believe there is a market opportunity for new antiviral HBV therapies with different mechanisms of action that provide sustained viral response, improved potency, efficacy in patients with drug-resistance, and reduced side effects.

Long-term therapy with nucleoside analog anti-HBV drugs has led to the development of drug-resistant strains of the virus that reduce the efficacy of the therapy. Since HBV is so prolific, producing 10 billion to 1 trillion virions per day, a large number of spontaneous mutations could potentially be generated at every site in the HBV genome per day. The combination of a rapid virus replication cycle coupled with a relatively long half-life of infected cells suggests the need for prolonged antiviral therapy to eradicate HBV with currently approved drugs. The longer the treatment period, however, the greater likelihood that mutations will arise and resistance will develop. This has been demonstrated by mutations found in the HBV polymerase following lamivudine, adefovir, entecavir and telbivudine therapy. Clinical studies have reported the emergence of resistance to lamivudine, adefovir, entecavir and telbivudine.

As a result of drug resistance, HBV therapeutic trends with currently approved drugs have become similar to HIV treatment regimens, whereby patients who no longer receive benefit from their original therapy change prescriptions to a new therapeutic alternative. This has been demonstrated by patients who begin to use adefovir or entecavir, after resistance to lamivudine arises and treatment becomes less efficacious. In addition to the five approved nucleoside analogs for HBV, there are a number of therapeutics in development or seeking regulatory approval. As more data and more drug products become available for HBV, there is a high likelihood that physicians may begin to prescribe combination therapy for HBV. We also believe that a combination of two therapies may delay the onset of drug-resistant virus. In addition, individuals co-infected with HIV and HBV may become candidates for combination therapy.

Clevudine

Clevudine is an oral, once-daily pyrimidine nucleoside analog that we are developing for the treatment of HBV. Clevudine has been studied in 14 completed clinical trials in a total of more than 800 patients. We licensed clevudine from Bukwang Pharm. Co., Ltd., or Bukwang, a Korean pharmaceutical company. Bukwang completed two Korean Phase 3 clinical trials, Studies 301 and 302, in which clevudine demonstrated the ability to significantly reduce HBV viral load in 337 patients. Based on the results of these trials, Bukwang received Korean approval in November 2006. Bukwang initiated the commercial launch of clevudine in the Korean market in February 2007 under the brand name Levovir.

We believe there is an unmet medical need for HBV drugs that offer an SVR without serious side effects. Physician surveys, our discussions with key opinion leaders in HBV, and the history of the HBV drug market lead us to believe that the global market for HBV therapeutics may grow significantly from its current level of

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approximately $1.1 billion when an HBV drug becomes available that provides an SVR in a significant percentage of patients without serious side effects. The only approved HBV therapy that offers an SVR is pegylated interferon, which is an injectable drug and is not well tolerated by patients. However, pegylated interferon is not widely used to treat HBV because it produces an SVR in too few patients to offset its side effects. Clevudine has the potential to provide a significant SVR without the side effects of pegylated interferon. In Study 302, clevudine sustained, for 24 weeks, a viral load that was undetectable by PCR in 16% of e-antigen negative HBV patients following 24 weeks of therapy. In clevudine Study 303, 80% of e-antigen negative HBV patients had a viral load that was undetectable by PCR 12 weeks after following a 48 week course of therapy.

For the many HBV patients that do not achieve an SVR, treatment is a chronic regimen of antiviral drugs to keep their viral load as low as possible. During such prolonged treatment, viral mutations occur that make the viruses resistant to the drugs being used. Treatment with several drugs at once in combination may slow the rate of mutation and the rise of the related drug resistance. Clevudine has the potential to be used in combination with other HBV therapies because its mechanism of action is different from that of other nucleoside analogs. Clevudine inhibits viral replication by primarily acting on the HBV polymerase enzyme to reduce its ability to incorporate nucleosides into a new viral DNA chain. In contrast, other nucleoside analog inhibitors currently in use or in development for the treatment of HBV, including lamivudine, adefovir, entecavir, telbivudine and tenofovir, act by competing with natural nucleosides for incorporation into the growing HBV DNA chain, causing the premature termination of the viral DNA chain and halting viral replication. Laboratory data suggests that clevudine may be additive or synergistic when used in combination with existing therapies. As such, we believe clevudine s mechanism of action is complementary to that of other HBV drugs and could be used either as a single agent for treatment-naïve patients or in combination with existing HBV therapies for treatment-experienced patients.

As part of our agreement with Bukwang, we have the exclusive rights to commercialize clevudine in the Americas, the Caribbean, Europe and Israel. Bukwang has retained rights to the rest of the world, excluding those Asian territories that were licensed to Eisai Pharmaceuticals (Eisai) in November 2004. Under the agreement, we have the right to use the clinical data generated by Bukwang or Eisai, as well as all historical data collected by Triangle Pharmaceuticals (acquired by Gilead Sciences in 2003) and Gilead Sciences, the prior licensee of clevudine, for regulatory and other cross-filing needs.

If clevudine receives marketing approval in the United States, we intend to commercialize clevudine ourselves with a sales force of approximately 40 to 45 employees. We believe this sales force size is comparable to those for competing HBV products in the United States. If clevudine receives marketing approval in Europe, we may commercialize clevudine ourselves or we may engage a marketing partner.

Clinical Development. We intend to seek regulatory approval for clevudine in North, Central and South America and Europe. Marketing approval by the FDA and European regulatory authorities will be based primarily on the data resulting from our two 48 week Phase 3 registration studies, one in approximately 376 e-antigen positive patients, Study 305, and one in approximately 480 e-antigen negative patients, Study 306, each comparing clevudine treatment to the approved HBV antiviral adefovir. In these trials, which commenced dosing patients in October 2007, patients will be randomized and will receive either adefovir or 30 mg of clevudine once-daily for the 48-week duration of the studies. The primary endpoint of these registration studies is a composite endpoint measuring the percentage of patients with undetectable HBV DNA (less than 300 copies/ml) and the normalization of liver enzyme levels at the 48th week on therapy. The registration studies will also assess improvement in liver histology, hepatitis B e-antigen (eAg) seroconversion (which is the loss of eAg together with an undetectable level of HBV DNA and normalized levels of liver enzyme), decreases in the reservoir of HBV hepatic cccDNA, and quantitative eAg and surface antigen (sAg). These trials are designed to test the superiority of clevudine over adefovir on these endpoints. We will continue these studies from week 48 to week 96. The number of patients to be enrolled in the e-antigen positive and e-antigen negative studies are intended to provide sufficient statistical support to detect a 20% and a 19% difference, respectively, between clevudine and adefovir for the primary endpoint with a 95% confidence level.

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Both Study 305 and Study 306 will continue for an additional 48 weeks after the registration data has been obtained to gather additional safety and efficacy data through week 96, as well as to assess clevudine s SVR rate. We expect that a portion of the e-antigen negative patients treated with clevudine will continue to be evaluated against adefovir through week 96. We expect that the remaining clevudine e-antigen negative patients, if they continue to meet the primary composite endpoint, will be taken off clevudine therapy at week 72 to measure SVR at week 96 after 24 weeks without treatment. Additionally, we expect that a portion of the e-antigen positive patients treated with clevudine will continue to be evaluated against a portion of the e-antigen positive patients treated with adefovir through week 96. We expect the remaining e-antigen positive patients treated with clevudine and adefovir, if they meet certain criteria, will be taken off therapy at week 72. These criteria include undetectable HBV DNA, alanine aminotransferase, or ALT, normalization and the loss of e-antigen and the presence of anti-HBV e antibody. We will then measure SVR in these e-antigen positive patients for clevudine and adefovir at week 96, 24 weeks after stopping treatment. There can be no assurances as to the results of these planned registration and continuation studies or as to any particular patient s response to clevudine.

Bukwang received marketing approval for clevudine from the Korean equivalent of the FDA based on two placebo-controlled, double-blinded, randomized, multi-center Korean Phase 3 clinical trials, Study 301 and Study 302, designed to determine the efficacy of clevudine over a 24-week period. Patients were evaluated for an additional 24 weeks of follow-up care without treatment. Study 301 enrolled e-antigen positive hepatitis B patients, and Study 302 enrolled e-antigen negative hepatitis B patients.

Study 301 involved 248 e-antigen positive patients who received 30 mg of clevudine or a placebo once daily. At week 24, 59% of patients receiving clevudine in this study had HBV DNA levels below those detectable by a PCR test, indicating very low viral infection or clearance of the virus from the body versus 0% of patients receiving placebo. Furthermore, 68% of e-antigen positive patients had normalized liver enzyme levels. Study 302 comprised 89 e-antigen negative patients who received 30 mg of clevudine or a placebo once daily. At week 24, 92% of patients receiving clevudine in this study had undetectable HBV DNA levels, versus 0% of patients receiving placebo. Furthermore, 75% of e-antigen negative patients had normalized liver enzyme levels. These viral load reductions were statistically significant when compared to the placebo groups. Clevudine s effect on viral load observed after 24 weeks of treatment in Study 301 and Study 302 was comparable to the effect observed in independent clinical studies after 48 or 52 weeks of treatment with other HBV drugs that are currently available or in development based on historical data for those therapies.

In Study 301, 24 weeks after the cessation of therapy, average HBV DNA levels in patients who received clevudine remained lower than baseline by 2.02 log (99.1% reduction) compared to patients who received placebo, whose average HBV DNA levels were lower than baseline by only 0.68 log (79.1% reduction), a statistically significant difference. In Study 302, 24 weeks after the cessation of therapy, the reduction in HBV DNA levels was 3.11 log (99.9% reduction) for treated patients versus 0.66 log (78.1% reduction) for the placebo group, a statistically significant difference. Furthermore, in Study 302, 24 weeks after the cessation of treatment, 16% of the patients who had received clevudine had an SVR versus 0% of the patients who had received placebo. We believe that patients whose viral load remains undetectable after 24 weeks off-treatment demonstrate the potential for a limited duration of therapy.

In March 2006, Bukwang completed Study 303, a Korean follow-on study of clevudine Studies 301 and 302. The goal of Study 303 was to evaluate the safety, antiviral activity, biochemical improvement, and serologic response in patients treated with clevudine for a total of 48 weeks. This open label follow-on study enrolled 55 treatment-naïve patients (40 e-antigen positive patients and 15 e-antigen negative patients) who were receiving placebo in Studies 301 and 302. Although, based on the results of the prior Phase 1 and Phase 2 dose-ranging studies, we expect clevudine s commercial dosing regimen to be 30 mg per day for the entire duration of treatment, Study 303 used a dosing regimen of 30 mg of clevudine for 24 weeks followed by a maintenance dose for an additional 24 weeks of 10 mg of clevudine, a dose which has previously been shown to be suboptimal. Results show that, at week 48, 63% of e-antigen positive patients and 87% of e-antigen negative patients had HBV DNA levels below those detectable by PCR tests. Furthermore, 83% of e-antigen positive patients and 87%

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of e-antigen negative patients had normalized liver enzyme levels. No serious adverse events were observed, and all adverse events were mild and transient. At week 60, twelve weeks after stopping treatment, the viral load had been sustained at undetectable levels in 28% of e-antigen positive patients and 80% of e-antigen negative patients. To our knowledge, no other HBV oral therapeutic has demonstrated this sustained antiviral effect.

The table below summarizes historical data for approved HBV nucleoside therapies. This historical data was derived from independent clinical trials reported in patient information inserts, New Drug Application, or NDA filings, medical journals and company reports and presentations. We have not conducted any clinical trials comparing clevudine to any of these other therapies.

Results from Independent Clinical Trials of Approved Nucleoside HBV Therapies	e-Antigen Positive Patients	e-Antigen Negative Patients
At 24 Weeks on Treatment		
Patients with Undetectable Virus (PCR Negative)		
clevudine	59%	92%
entecavir	45%	76%
telbivudine	44%	80%
lamivudine	32%	64%
adefovir	12%	36%
tenofovir	49%	85%
At 48 or 52 Weeks on Treatment		
Patients with Undetectable Virus (PCR Negative)		
clevudine	63%	87%
entecavir	67%	90%
telbivudine	60%	88%
lamivudine	36%	72%
adefovir	21%	52%
tenofovir	76%	93%
Patients with Normalized Liver Enzyme Levels		
clevudine	83%	87%
entecavir	68%	78%
telbivudine	77%	74%
lamivudine	60%	71%
adefovir	48%	72%
tenofovir	68%	76%
Patients with SVR, or Undetectable Virus (PCR Negative)		
24 Weeks After Stopping 48 or 52 Weeks of Therapy		
All approved nucleoside HBV therapies		3-7%
12 Weeks After Stopping 48 Weeks of Therapy		
clevudine 303 study		80%
24 Weeks After Stopping 24 Weeks of Therapy		
clevudine 302 study		16%

In Study 302, 16% of e-antigen negative patients sustained a viral load that was undetectable by PCR 24 weeks after completing the 24-week course of therapy. In Study 303, 80% of e-antigen negative patients receiving clevudine sustained a viral load that was undetectable by PCR 12 weeks after completing the 48-week course of therapy. This compares to one year of pegylated interferon therapy, which produces a viral load that is undetectable by PCR 6 months after stopping therapy in 19% of e-antigen negative patients, and other nucleoside HBV treatments that have reported viral load undetectable by PCR in approximately 3% to 7% of e-antigen negative patients, 24 weeks after completing a one year course of therapy. We note that while these results are

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not directly comparable because the clevudine data represents viral load 12 weeks after completing therapy, while the data for the competing products represents viral load 24 weeks after completing therapy, we believe the results indicate the potential for a higher rate of SVR with clevudine.

Overall, clevudine was generally well-tolerated by patients with chronic hepatitis due to HBV. Serious adverse events during treatment in Studies 301 and 302 and during follow-up indicated that a higher percentage of placebo-treated patients had seriously elevated ALT levels or flares. ALT (also called alanine aminotransferase) is an enzyme found mainly in the liver. High levels of ALT in the bloodstream mean that the liver may be damaged or diseased. Otherwise, there was no meaningful difference between clevudine and placebo in the incidence of serious adverse events.

Clevudine has been the subject of six completed Phase 2 studies. Three of these studies were conducted by Bukwang in Korea. In Study 201, 99 patients with chronic hepatitis B received either placebo, 30 mg, or 50 mg of clevudine each day for 12 weeks with a follow-up period of 12 weeks. At the end of the trial, 63% of patients receiving 30 mg and 52% of patients receiving 50 mg had HBV below measurable levels compared to 0% of patients in the placebo group. Positive results were also observed in the other two trials conducted by Bukwang, Study 203 and Study 204. In addition, Gilead Sciences conducted a trial with 163 patients testing a 10 mg dose of clevudine in combination with 200 mg of emtricitabine versus 200 mg of emtricitabine alone over a 24-week period. Although 10 mg of clevudine has been shown to be a suboptimal dose in previous clinical trials, treatment-naïve e-antigen negative patients experienced a statistically significant improvement of an endpoint that combined reduction of HBV DNA levels with a normalization of liver enzyme levels when taking clevudine in addition to emtricitabine versus emtricitabine alone. Based on these studies, we believe that clevudine may be complementary to existing HBV treatments and could therefore be used as either a single agent or in combination with existing therapies.

Clevudine was also the subject of four completed Phase 1 trials designed to test the safety, tolerability and pharmacokinetic profile of the drug at various doses. In these Phase 1 trials and all other trials to date, clevudine has been generally well-tolerated.

Mechanism of Action. We believe clevudine inhibits viral replication by inhibiting the HBV polymerase enzyme through a mechanism of action that may or may not prevent the binding of other nucleoside inhibitors of the HBV polymerase enzyme. Unlike several other nucleoside analogs in development for the treatment of HBV, clevudine is not incorporated into normal human cellular DNA, and therefore is unlikely to interfere with cellular replication. Cell-based assays of clevudine in combination with other nucleoside analogs demonstrated that clevudine was not antagonistic with certain nucleoside analogs and may be active in combination with lamivudine, adefovir and emtricitabine. Laboratory data show clevudine to be additive or synergistic when used in combination with existing therapies. In vitro resistance studies showed that the HBV mutation, M204V, which confers resistance to lamivudine, was not resistant to clevudine, however, the M204I mutation was resistant to clevudine.

In woodchucks infected with woodchuck hepatitis virus, a common animal model for human HBV, clevudine demonstrated a significant reduction of the cccDNA form of the virus after treatment with clevudine. The cccDNA form of the viral genome is believed to be responsible for the persistence of chronic HBV infection and for reactivation of hepatitis B after stopping therapy.

Product Candidates for the Treatment of HCV

HCV Background

HCV is a leading cause of chronic liver disease and liver transplants. The WHO estimates that nearly 180 million people worldwide, or approximately 3% of the world s population, are infected with HCV. 130 million of these individuals are chronic HCV carriers who are at increased risk of developing liver cirrhosis or liver cancer, approximately 15 million of whom are in the United States, Europe and Japan. The CDC has

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reported that 4.1 million people in the United States have been infected with HCV, of whom 3.2 million were chronically infected. Approximately 2.2%, or 71,000, of these HCV patients are treated each year, and there are an estimated 400,000 treatment-experienced patients who were unable to obtain an SVR. Although chronic HCV infection varies greatly in its course and outcomes, 70% of chronically infected patients develop some form of chronic liver disease, including, in some cases, cirrhosis or liver cancer. Worldwide sales of HCV drugs in 2005 were approximately $2.2 billion, and are forecasted to reach more than $4.0 billion by 2010 and more than $8.0 billion in 2015. We believe that historical sales of HCV drugs increased as new therapies that improved the SVR rate were introduced. For example, when adding ribavirin to interferon in 1998 increased the SVR rate from a range of about 13% to 19% to a range of about 38% to 43%, sales of HCV drugs increased significantly from approximately $400 million in 1996 to approximately $600 million in 1998. Additionally, when the replacement of interferon with pegylated interferon in 2000 further increased the SVR rate to a range of about 47% to 54%, sales of HCV drugs again increased significantly from more than $1.3 billion in 2000 to more than $2.0 billion in 2002.

In the United States, the current standard of care for the treatment of HCV is a combination of pegylated interferon and a nucleoside analog named ribavirin. Pegylated interferon is a modified version of alpha interferon, a protein that occurs naturally in the human body and boosts the immune system s ability to fight viral infections. Patients treated with a combination of ribavirin and interferon respond better than those treated with interferon alone. According to the WHO, treatment with interferon in combination with ribavirin is effective in 30% to 50% of patients, while interferon alone is effective in approximately 10% to 20% of patients. In HCV genotypes 1a and 1b, which account for over 70% of HCV infections in the United States, less than 50% of patients respond to standard therapy consisting of pegylated interferon plus ribavirin. In addition, these therapies have side effects that include fatigue, bone marrow suppression, anemia and neuropsychiatric effects. As a result of the limited benefits and side effects of existing therapies, we believe treatment rates remain low and there are significant opportunities for new antiviral therapies to fight HCV.

HCV s inherent ability to mutate enables the virus to generate every possible genetic mutation twice each day, although not all mutated viruses are viable. Amino acid changes that occur at the active sites of essential viral enzymes may not allow the viral enzymes to function while changes at other locations on these viral enzymes are generally tolerated. Genes that give rise to components of the active sites of essential viral enzymes are much more highly conserved, that is, mutations of these genes are less likely to be found, since they reduce the activity of the enzymes needed to produce viable viruses. Genes that give rise to the components of non-active sites of viral enzymes are less conserved, since mutations at these sites do not generally reduce the activity of the enzymes needed to produce viable viruses. When a patient is exposed to a new anti-HCV drug that inhibits a specific viral function, the ability of that virus to reproduce is reduced or stopped. If the site of action of a drug is in one of the more conserved locations on the viral enzyme then the drug will inhibit more of the virus since there will be less chance that it will encounter an amino acid change that would reduce its activity, giving rise to drug resistance. On the other hand, if the drug acts on a region of the protein that is less well conserved and which can tolerate multiple changes, the drug will have a higher probability of encountering an amino acid change that either reduces or prevents its activity.

There are currently two approaches to inhibiting the activity of the HCV polymerase. One is the use of nucleoside analogs that mimic the nucleotides normally recognized by the enzyme as it builds a new copy of the viral genome. These nucleoside analogs take advantage of the fact that the virus can tolerate few mutations in their active sites. Any amino acid changes that might occur which would reduce the ability of the nucleoside analog to bind may also reduce the ability of the polymerase to bind the normal nucleotides. The other approach involves non-nucleoside molecules that can bind to various regions on the polymerase away from the active site. This kind of binding generally prevents the polymerase from assuming the correct configuration and in turn either reduces or prevents its activity. Since these regions can tolerate more changes, many of the differences seen in the genomes of the different variants of HCV can be found in these regions. The activity of these non-nucleoside drugs depends on their ability to bind relatively tightly to specific amino acid sequences and often involves multiple molecular interactions. If any of these interactions are missing due to a change in the

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polymerase sequence then binding can not occur properly. The chances of this happening are much greater with non-nucleoside drugs than with nucleoside analog drugs that act at more conserved sites. Another way of describing this is referred to as the genetic barrier to developing resistance to a drug. A site of inhibition that is naturally conserved would have a higher genetic barrier than one that is naturally variable or polymorphic.

Early clinical trials with nucleoside analog drug candidates and non-nucleoside drug candidates have demonstrated this phenomenon. In monotherapy studies with the nucleoside analogs NM283 and R1626 over 14 days, viral breakthrough or viral rebound while on therapy did not occur. On the other hand, in studies with the non-nucleoside inhibitors HCV-796 and A-837093 in humans and chimpanzees infected with HCV, viral breakthrough or viral rebound was seen as early as 3 to 4 days into the 14-day treatment period. Analysis of the virus that appeared showed single amino acid changes that prevented or significantly reduced the binding of these non-nucleoside inhibitors. The rapidity of the rebound strongly suggested that these variant viruses existed in the patient prior to drug exposure and that the presence of the drug did not prevent these viruses from replicating and becoming the predominant variant in the patient. It is likely that resistance will arise with most if not all anti-HCV drugs, but the rapidity with which this occurs will likely have significant consequences for the patient.

Recent clinical studies have demonstrated the development of drug-resistant mutations in HCV. As such, the practice of using combination therapies may be applicable to the treatment of HCV infections. We also believe that a combination of HCV therapies may delay the onset of drug-resistant virus.

R7128

Roche and we are developing R7128 for the treatment of HCV. Roche is a market leader in HCV therapy through their FDA-approved products, Pegasys (pegylated interferon) and Copegus (ribavirin). We believe R7128 represents an HCV product candidate that could complement Roche s expanding HCV franchise. R7128 is a pro-drug of a molecule we discovered named PSI-6130, an oral cytidine nucleoside analog. A pro-drug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. PSI-6130 is the active component of R7128. At low concentrations, PSI-6130 was shown to be an inhibitor of HCV replication, specifically targeting the HCV RNA polymerase.

In October 2004, we entered into a collaboration with Roche for the development and commercialization of PSI-6130 and related compounds. In exchange for these rights, Roche agreed to make milestone payments upon the achievement of predetermined clinical or regulatory events and pay royalties on sales of the products arising from the collaboration. Under this collaboration, Roche agreed to reimburse us for all expected external expenses (up to an agreed-upon amount) associated with, and we have been responsible for, certain preclinical work, the IND filing and the Phase 1 clinical trials. Roche will fund all of the expenses of, and be responsible for, other preclinical studies, future clinical development and commercialization of R7128. We will continue to develop and retain worldwide rights to ongoing and future HCV programs unrelated to the PSI-6130 series of nucleoside polymerase inhibitors.

Clinical Development. During September 2008, we completed the clinical activities in Part 3 of a Phase 1 clinical trial with R7128 that was initiated by Roche and us in October 2006 under an IND filing. This expanded Phase 1 trial was a multiple center, observer-blinded, randomized and placebo-controlled study designed to investigate the pharmacokinetics, pharmacodynamics, safety, tolerability and food effect of R7128 in healthy volunteers and in patients chronically infected with HCV genotype 1, 2 or 3. This Phase 1 trial also provided antiviral potency data over 14 and 28 days in patients chronically infected with HCV genotype 1 and following 28 days of treatment in patients chronically-infected with HCV genotypes 2 or 3. This adaptive Phase 1 study was comprised of three parts:

Part 1 was a single ascending dose study conducted in 46 healthy volunteers. The primary objective of Part 1 was to assess the safety, tolerability and pharmacokinetics of R7128 following single ascending doses under fasting conditions. The secondary objective of Part 1 was to explore the effect of food on the pharmacokinetics of R7128. Single oral doses of R7128 were administered to 46 healthy volunteers

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in five sequential dose groups (500 mg, 1500 mg, 4500 mg, 6000 mg and 9000 mg) and one food effect group (1500 mg). Results from the single ascending dose portion of the study indicated:

- All doses of R7128 studied (500 mg to 9000 mg) were generally safe and well-tolerated.
- All patients completed the study, and none experienced gastrointestinal adverse events or serious adverse events during the study.
- No hematologic or other safety laboratory abnormalities of clinical significance were noted.
- No maximum tolerated dose was identified.

Part 2 was a multiple ascending dose study conducted in 40 patients chronically infected with HCV genotype 1 who had previously failed interferon therapy. The primary objective of Part 2 was to assess the safety, tolerability and pharmacokinetics of R7128 after once-daily (QD) or twice-daily (BID) dosing for 14 days. The secondary objective was to assess antiviral efficacy by measuring the change in HCV RNA. Results from the multiple ascending dose portion of the study indicated:

- R7128 demonstrated potent, dose-dependent antiviral activity in four patient cohorts (8 active, 2 placebo per cohort) receiving 750 mg or 1500 mg administered either QD or BID for 14 days as monotherapy. The maximum decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg BID. R7128 demonstrated mean HCV RNA decreases from baseline of 0.9 log (87.4% reduction), 1.5 log (96.8% reduction), 2.1 log (99.2% reduction) and 2.7 log (99.8% reduction) in patients receiving 750 mg QD, 1500 mg QD, 750 mg BID and 1500 mg BID, respectively. Based on the mean data, all four dose groups reached nadir values at Day 15. A maximum 4.2 log (99.9% reduction) HCV RNA decrease was demonstrated in a patient following 14 days of monotherapy with 1500 mg BID of R7128, a value also below the level of detection, which was less than 15 International Units per milliliter (IU/ml).
- There was no evidence of viral rebound in any dose cohort during the 14 days of dosing.
- R7128 was generally safe and well tolerated over 14 days of treatment of patients chronically infected with HCV genotype 1 who had previously failed interferon therapy. There were no serious adverse events, no adverse events requiring dose modification, and no dose-related gastrointestinal adverse events.

Part 3 was a 4-week study of R7128 in combination with the current standard of care for chronic HCV infection, Pegasys (pegylated interferon) plus Copegus (ribavirin) in 81 treatment-naïve patients chronically infected with HCV genotype 1, and additionally, in 25 prior treatment non-responders, or patients who did not achieve an SVR with previous interferon-based therapy, who were chronically infected with HCV genotypes 2 or 3. The primary objective of this study was to assess the safety, tolerability, and pharmacokinetics of R7128 in the clinically-relevant setting of combination therapy with the current standard of care for chronic HCV infection. The secondary objective of Part 3 was to evaluate the short-term change in HCV RNA. The study included three oral dose regimens of R7128 (500 mg, 1500 mg and 1000 mg cohorts 1,2 and 3, respectively) in patients chronically infected with HCV genotype 1 and one oral dose regimen of R7128 (1500 mg cohort 4) in patients chronically infected with HCV genotypes 2 or 3. All four dose regimens were administered twice-daily with Pegasys plus Copegus for 4 weeks. Dose cohorts 1, 2 and 4 enrolled 25 patients, with 20 patients randomized to receive R7128 and five patients randomized to receive placebo, and cohort 3 enrolled 31 patients, with 25 patients randomized to receive R7128 and six patients randomized to receive placebo, all administered in combination with standard of care. After completing four weeks of the triple combination regimen and a follow-up of four weeks of Pegasys plus Copegus, all patients are scheduled to receive up to 40 weeks of open-label standard of care dosing under a separate

protocol.

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Results from cohorts 1, 2 and 3 in 81 treatment-naïve patients chronically infected with HCV genotype 1 indicated:

Following 4 weeks of treatment with R7128 500mg BID with Pegasys plus Copegus (cohort 1), patients achieved a mean 3.8 log10 IU/mL decrease in HCV RNA and 30% (6 of 20) achieved undetectable levels of HCV RNA (<15 IU/ml), or rapid virologic response (RVR).

Following 4 weeks of treatment with R7128 1500mg BID with Pegasys plus Copegus (cohort 2), patients achieved a mean 5.1 log10 IU/mL decrease in HCV RNA and 85% (17 of 20) achieved RVR.

Following 4 weeks of treatment with R7128 1000mg BID with Pegasys plus Copegus (cohort 3), preliminary results indicated patients achieved a mean 5.1 log10 IU/mL decrease in HCV RNA and 88% (22 of 25) patients achieved RVR.

Following 4 weeks of treatment with placebo with Pegasys plus Copegus, patients achieved a mean 2.9 log10 IU/mL decrease in HCV RNA and 18.75% (3 of 16) achieved RVR.

For cohorts 1, 2 and 3 in treatment-naïve genotype 1 patients, safety and tolerability for the 4-week treatment period were similar for R7128 with Pegasys plus Copegus compared to placebo with Pegasys plus Copegus. There were no serious adverse events reported during the 4-week treatment periods of triple therapy, and most of the adverse events reported were of mild to moderate intensity. Headache and fatigue were the most frequently reported adverse events in patients who received active R7128 plus Pegasys plus Copegus, with an overall frequency of 66% and 42% reporting at least one of these events, respectively. These events were also the most frequently reported adverse events in patients who received placebo with Pegasys and Copegus. In general, the adverse events reported were consistent with the clinical safety profile for Pegasys and Copegus, including the frequency and severity of these adverse events, as well as any general body system observations. Grade 3/4 neutropenia was observed in 31% of the placebo patients and in 12% to 30% of the R7128 patients in each active dosing cohort. Grade 3 changes in hemoglobin were observed in 19% of the placebo patients and in 31% of the R7128 patients. There were no clinically significant changes in hepatic, renal, or other safety laboratory parameters, vital signs, or electrocardiograms. Overall, there was no clinical evidence of any major organ toxicities related to R7128. One patient in the active treatment group discontinued the study during the 4 week treatment period due to lower-gastrointestinal adverse events. At the time of study discontinuation, this patient had undetectable HCV RNA. R7128 was generally safe and well-tolerated when administered for 4 weeks in combinations with Pegasus plus Copegus in patients with HCV genotype 1.

Results from the 1500 mg dose cohort (cohort 4) in 25 prior treatment non-responders, or patients who did not achieve an SVR with previous interferon-based therapy, and who were chronically infected with HCV genotypes 2 or 3 indicated:

Following 4 weeks of treatment with R7128 1500mg BID with Pegasys plus Copegus (cohort 4), preliminary results indicated patients achieved a mean 5.0 $\log_{10}$ IU/mL decrease in HCV RNA and 90% (18 of 20) patients achieved RVR.

Following 4 weeks of treatment with placebo with Pegasys plus Copegus, patients achieved a mean 3.7 $\log_{10}$ IU/mL decrease in HCV RNA and 60.0% (3 of 5) achieved RVR.

For cohort 4, safety and tolerability during the 4-week treatment period were similar for R7128 with Pegasys plus Copegus compared to placebo with Pegasys plus Copegus. There were no serious adverse events reported during the 4-week treatment period, and most of the adverse events reported were of mild to moderate intensity. One subject discontinued R7128, Pegasys and Copegus due to protocol specified stopping criteria (not treatment-emergent), and ECG changes. Adverse events reported in cohort 4 were similar to those reported in Cohorts 1-3. Grade 3/4

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neutropenia was observed in 0% of the 5 placebo patients and in 20% of the 20 R7128 patients in the active dosing cohort. Grade 3 changes in hemoglobin were observed in 20% of the placebo patients and in 25% of the R7128 patients. There were no clinically significant changes in hepatic, renal, or other safety laboratory parameters, vital signs, or electrocardiograms. As seen in the patients infected with HCV genotype 1, there was no clinical evidence of any major organ toxicities related to R7128. R7128 was generally safe and well-tolerated when administered for 4 weeks in combination with Pegasus plus Copegus in patients with HCV genotypes 2 and 3.

We cannot guarantee that the final results of this study or any future study of R7128 will corroborate earlier results, and further testing will be required to provide sufficient evidence regarding safety and efficacy to support an NDA filing with the FDA in the future. We and Roche expect to meet with the FDA during January 2009 to discuss a Phase 2b study plan, as well as additional studies to support desired product label claims.

On October 12, 2007, we were informed by the FDA that R7128 received fast track designation.

Mechanism of Action. In a study evaluating the mechanism of action of PSI-6130, the compound was found to be active against the HCV RNA polymerase by terminating HCV RNA synthesis.

Preclinical Development. We and Roche have performed and will continue to perform in vitro and animal studies to determine the preclinical pharmacokinetics and safety of PSI-6130 administered as its pro-drug, R7128. PSI-6130 did not cause genetic mutations or cellular damage in preclinical models. The goal of longer-term animal studies is to identify the potential target organs and to determine the reversibility and monitorability of changes to their function and physical structure. In general, following single and repeated doses, R7128 was well tolerated in mice (up to 13 weeks), rats (up to 6 months), and dogs (up to 4 weeks) up to the highest doses tested (2000 mg/kg/day) for repeat dose studies. Manifestations of toxicity in monkeys, the most sensitive species tested, appeared to be time and dose dependent, causing significant changes in the kidney.

Oral administration of R7128 at doses of 200, 600 and 2000 mg/kg/day in monkeys, in a study designed to be six months but stopped at 13 weeks, did not establish a No Observed Adverse Effect Level (NOAEL) dose. A thorough examination of the monkeys tissues in every organ system determined that the only significant treatment-related pathology changes were confined to the glomeruli of the kidney. We believe these changes were dose-related, appearing in all animals in the high and middle dose groups and one animal in the low dose group, in which the glomerulopathy appeared in a much milder form. No scarring was observed, so changes were considered likely to be reversible.

A second long-term R7128 safety study in monkeys began in April 2008 at doses of 10, 40, 100, and 600 mg/kg/day, administered for 13 weeks in preparation for the start of a Phase 2b study in which humans are expected to receive R7128 for up to 12 weeks. Histopathology data confirmed the glomerulopathy findings from the previous study and confirmed the lack of progression to scarring or fibrosis. In addition, in animals that had been followed for an additional 8 weeks after treatment was stopped, renal function had returned to normal and histopathology revealed reversing (inactive) glomerular lesions without progression or scarring. Therefore, we believe the changes in kidney function observed in monkeys are both reversible and monitorable. In this study, we established a NOAEL dose in monkeys over 13 weeks.

In January 2008, Roche completed the dosing portion of a six month safety study of R7128 in rats. The results of this study revealed no toxicities at any dose level tested, which were 200, 600 and 2000 mg/kg/day.

In 2008, Roche completed a 13 week safety study of R7128 in mice. The results of this study showed that the drug was well tolerated with no observable toxicities at any dose level tested, which were 200, 600 and 2000 mg/kg/day.

Species-specific differences in drug metabolism and excretion that may render the monkey more susceptible to the pathology changes observed with R7128 than the rat or humans continue to be under review.

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PSI-7851

We are developing PSI-7851 for the treatment of HCV. PSI-7851 was nominated as a lead candidate and has advanced into preclinical safety studies required for submission of an IND application with the FDA or an equivalent foreign regulatory filing. This pyrimidine nucleotide analog is being investigated as part of our research and development efforts to identify another compound that might be used in a proprietary combination treatment for HCV.

In vitro antiviral testing has shown that this compound is approximately 20 fold more potent than PSI-6130. In animal studies following oral dosing, PSI-7851 preferentially localizes in liver cells where it is efficiently converted to the active triphosphate form. The rapid and efficient delivery to liver cells and the improved in vitro potency observed in our early preclinical studies may allow for lower and less frequent dosing in the clinic. We anticipate filing an IND with the FDA during the first calendar quarter of 2009.

Purine Research

We are researching a third generation of nucleosides and nucleotides utilizing a purine base with the goal of generating a product candidate that has comparable activity to PSI-7851 and a resistance profile that is complementary to PSI-7851 to enable a proprietary fixed-dose combination that has the potential to eliminate or reduce the use of interferon for the treatment of HCV.

Product Candidates for the Treatment of HIV

HIV Background

HIV destroys the body s ability to fight infections by attacking cells of the immune system. In 1981, the first cases of Acquired Immunodeficiency Syndrome, or AIDS, were documented, and in 1983, HIV was identified as the cause of AIDS. According to a 2007 AIDS epidemic update by UNAIDS and the WHO, over 33 million people worldwide are living with HIV, and at least 25 million people worldwide have died from AIDS since the epidemic began. In the United States, the CDC has reported that the HIV mortality rate has steadily declined since the mid-to-late 1990s, while the incidence of infection continues to rise. This decrease in mortality can be attributed, in part, to the increased availability of HIV therapeutics used in the long-term treatment of HIV. According to a 2007 UNAIDS/WHO report, by the end of 2007, approximately 1.3 million people in North America and 760,000 people in Western and Central Europe were living with HIV and an additional 46,000 new patients in North America and 31,000 new patients in Western and Central Europe are diagnosed each year. The current market for HIV therapeutics is approximately $6.5 billion and is estimated to reach $10.0 billion by 2010.

The FDA has approved 32 single agents and six fixed-dose combination therapies for the treatment of HIV. The single agents are classified as nucleoside reverse transcriptase inhibitors, or NRTIs, non-nucleoside reverse transcriptase inhibitors, or NNRTIs, protease inhibitors, or PIs, integrase inhibitors and entry inhibitors. Both NRTIs and NNRTIs target the reverse transcriptase enzyme, while PIs, integrase inhibitors and entry inhibitors target other viral proteins.

NRTIs mimic natural nucleosides and are commonly referred to as nucleoside analogs. Each NRTI is an analog of one of the following naturally occurring nucleosides: 2 deoxycytidine (cytidine), 2 deoxythymidine (thymidine), 2 deoxyadenosine (adenosine) or 2 deoxyguanosine (guano In the body, NRTIs block viral replication by interfering with the ability of reverse transcriptase to make a DNA copy of HIV RNA. This occurs because this enzyme incorporates the nucleoside analogs instead of the natural nucleosides into newly synthesized viral DNA, causing the premature termination of the DNA chain. This impairs either the synthesis or the functionality of the new viral genome, thereby suppressing viral replication. There are eight NRTIs approved by the FDA for the treatment of HIV.

NNRTIs are composed of a diverse group of compounds unrelated to nucleosides that also directly target reverse transcriptase. These drugs bind to the enzyme, causing a change in the shape of the enzyme that makes it less efficient in producing DNA. There are three NNRTIs approved by the FDA for the treatment of HIV.

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PIs, integrase inhibitors and entry inhibitors are the other three classes of approved HIV therapeutics. The HIV protease is an enzyme that is required to make fully mature and infectious virus. This enzyme processes the viral proteins required to create a protective protein shell that surrounds the HIV RNA. The protease inhibitor class of compounds prevents the HIV protease from making mature virus capable of infecting other cells. Integrase inhibitors represent the newest class of HIV drugs to be approved by the FDA. These drugs prevent the integrase enzyme from integrating the viral genetic material into human chromosomes, a critical step in the pathogenesis of HIV. Entry inhibitors work outside the cell by inhibiting a virus from entering and infecting the cell. There are 10 PIs, one integrase inhibitor, and two entry inhibitors approved by the FDA for the treatment of HIV.

The standard treatment for HIV infection, as recommended by the U.S. Department of Health and Human Services, includes two NRTIs combined with a third drug from another class, either an NNRTI or a PI, to form a triple combination therapy known as Highly Active Anti-Retroviral Therapy, or HAART. The two NRTIs in HAART are usually analogs of different nucleosides. Typically, a cytidine analog is paired with a thymidine or an adenosine analog in an effort to ensure the broadest activity against viral mutations and delay the onset of drug resistance. Racivir is a cytidine analog. It has been estimated that lamivudine and emtricitabine currently are the most commonly prescribed cytidine analogs, alone or as components of fixed dose combination products.

NRTIs, NNRTIs and PIs are generally administered orally as a tablet or capsule. In addition, several of the drugs in these classes are effective when taken only once each day. In treatment-naïve individuals, a once-daily therapy has been shown to improve compliance with the prescribed treatment regimen, which leads to better treatment outcomes. To provide additional convenience, companies have developed combination therapies that combine two or more NRTIs into a single tablet or capsule. These fixed-dose combination therapies have become leaders in the HIV marketplace. We believe that the most commonly prescribed combination therapies are Combivir, which combines lamivudine and zidovudine, and Truvada, which combines emtricitabine and tenofovir disoproxil fumarate (tenofovir). In 2006, a triple-combination called Atripla was approved by the FDA, which combines tenofovir, emtricitabine and efavirenz. In the near future, we anticipate that Altripla could become the most commonly prescribed combination therapy due to its ease of compliance as a once-daily triple combination. As patients develop resistance to their therapies, they are switched to other treatments. Increasingly, potency against drug-resistant virus becomes more important than convenience in treatment-experienced patients.

In HIV there is a class of mutations called thymidine analog mutations, or TAMs. These mutations typically confer resistance to thymidine nucleoside analogs such as zidovudine and stavudine. In addition to TAMs, other mutations include M184V, which typically confers resistance to cytidine analogs such as lamivudine and emtricitabine; K65R, which typically is associated with resistance to tenofovir; L74V, which is associated with resistance to abacavir, didanosine, and zalcitabine; and K103N, which is associated with resistance to efavirenz.

The following table describes the approved NRTIs for the treatment of HIV and their primary resistance mutations:

				Primary Resistance
Brand Names	**Generic Name**	**Chemical Name Abbreviation**	**Analog Type**	**Mutations**
Epivir	lamivudine	3TC	cytidine	M184V
Emtriva	emtricitabine	FTC	cytidine	M184V
Retrovir	zidovudine	AZT	thymidine	TAMs
Zerit	stavudine	d4T	thymidine	TAMs
Viread	tenofovir	TDF	adenosine	K65R, three or more TAMs
Videx/Videx EC	didanosine	ddI	adenosine	TAMs, K65R, L74V, M184V
Ziagen	abacavir	ABC	guanosine	TAMs, K65R, L74V, M184V
Hivid	zalcitabine	ddC	cytidine	TAMs, K65R, L74V, M184V

HIV s inherent ability to mutate results in the occurrence of about one mutation in every new virus particle produced. With over ten million virus particles produced within a 24-hour period, it is possible to observe every

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conceivable genetic mutation each day, although not all mutated viruses are viable. When a drug-resistant form of HIV first arises, it usually comprises a very small percentage of the HIV circulating within the blood. As the original or wild-type virus continues to be suppressed by antiviral therapy and the drug-resistant HIV continues to replicate, the mutated virus eventually becomes the dominant virus type. To reduce the likelihood of a dominant drug-resistant mutation, patients must comply with their treatment regimens; however, it has been estimated that at any given time approximately 70% of patients strictly adhere to their therapy. Each of the FDA-approved HIV therapies is susceptible to a mutation that confers drug resistance. New drug-resistant forms of HIV continue to emerge, and as a result, new therapies to fight drug-resistant HIV will continue to be needed.

From their experience with HIV, clinicians have learned much about how to optimally treat infected patients and delay the emergence of drug-resistant virus. As previously described, HAART, the current standard of care for patients infected with HIV, is comprised of three or more drugs that are ideally directed against different targets. This approach is based on two principles. First, the onset of viral resistance can be delayed by using multiple drugs that maximally suppress viral replication, thereby making it more difficult for a virus to generate the mutations that allow for the emergence of dominant drug-resistant virus. Second, based on scientific studies, it is much more difficult for drug-resistant virus to arise in the presence of drugs that inhibit different viral targets (such as reverse transcriptase and protease).

Racivir

Racivir is an oral, once-daily cytidine nucleoside analog that we are developing as an HIV therapy for use in combination with other approved HIV drugs. Racivir contains a racemic mixture, half of which is ( ) FTC and half of which is (+) FTC. A racemic mixture is comprised of two forms of the same chemical structure that are mirror images of each other. ( ) FTC is a chemical name abbreviation for emtricitabine, an FDA-approved HIV therapy marketed as Emtriva by Gilead, and one of the components of Truvada and Atripla, which are fixed-dose combination HIV therapies. Racivir has been generally well-tolerated in three clinical trials. In a completed Phase 2 clinical trial, for those treatment-experienced patients carrying the M184V mutation and less than three TAMs, replacing lamivudine (a component of the first treatment regimen for HIV patients, with annual sales of approximately $1 billion) with Racivir in their existing therapies caused a mean decrease in viral load of 0.7 log (80% reduction) in the second week of treatment, with 28% of these patients achieving an undetectable level of virus (less than 400 copies per milliliter) and 64% of these patients achieving at least a 0.5 log decrease (68% reduction) in viral load.

We are developing Racivir to be used with other HIV drugs for possible use in a combination therapy for patients failing their first treatment regimen. Our goal is to conduct future clinical trials with a collaborator that will study combination therapies that include Racivir for HIV patients receiving second-line therapy. Based on the results of our preclinical studies demonstrating activity against the HBV polymerase, we may also develop Racivir for the treatment of HBV or HIV/HBV co-infected individuals.

Clinical Development. We have completed a Phase 2 clinical trial, Study 201, to assess the safety, tolerability and antiviral effect of a 600 mg dose of Racivir head-to-head against lamivudine in HIV-infected, treatment-experienced patients with the M184V mutation who have been on lamivudine therapy. The study was a randomized, double-blind, placebo-controlled, multicenter study of 54 patients in the United States, Argentina, Mexico and Panama. Patients were randomized into two groups: one substituting Racivir in place of lamivudine in their existing therapies, and one continuing on their current lamivudine-containing therapy without any change. The study entry criteria included patients who were failing a HAART regimen. Specifically, participants were required to have received lamivudine as part of their antiviral therapy for the previous 60 days, to carry the M184V HIV mutation, and to have an HIV RNA viral load of greater than or equal to 2,000 viral copies per milliliter of blood plasma. The study had a blinded treatment period of up to 28 days, followed by an open label treatment period of up to 20 weeks. Patients were subsequently followed for an additional four weeks after the conclusion of the study treatment periods. The goal of this study was to evaluate the benefit of Racivir in patients carrying the M184V mutation by replacing lamivudine with Racivir in existing therapies.

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In this study, 42 subjects were randomized to receive either Racivir (n=26) in place of lamivudine or to continue with lamivudine (n=16) in a double-blind manner for 28 days. HIV viral loads and genotypes were determined at baseline (mean viral load = 4.1 log) and throughout the study. After the blinded treatment period, subjects were allowed to continue Racivir in an open label manner with or without optimized background therapy for an additional 20 weeks, based on their primary care physicians advice. After 28 days of blinded treatment, the mean viral load rose by 0.13 log (a 34.9% increase) in the lamivudine group and dropped by 0.4 log (60.2% reduction) in the Racivir group (p=0.02). A subset analysis of the Racivir-treated group revealed that the change in viral load was largely due to a positive antiviral response in subjects who had an HIV mutation pattern that included M184V and less than 3 TAMs with or without NNRTI or PI mutations. In this subset of patients (n=14), replacing lamivudine with Racivir in their existing therapies caused a mean drop in viral load of 0.7 log (80% reduction, p=0.004) in the second week of treatment, with 28% of these patients achieving an undetectable level of virus (less than 400 copies per milliliter) and 64% of these patients achieving at least a 0.5 log (68%) drop in viral load. No serious adverse events attributed to therapy were noted in either group over the 28 days. Clonal genotypic analysis of virus from responders indicated that the M184V mutation was found in all clones in addition to multi-drug resistance-associated mutations observed with first line therapy failure.

In summary, Racivir demonstrated antiviral activity in patients harboring HIV with the M184V mutation and less than three TAMs. These patients have genotypes consistent with first-line therapy failure and may be candidates for second line treatment regimens that contain Racivir. Future studies will be designed to explore this potential use of Racivir in a combination therapy for second-line therapy.

We conducted a Phase 1 clinical trial with Racivir as a single agent and a Phase 1 clinical trial, Study 101, with Racivir in combination with two FDA-approved therapies for the treatment of HIV infection. Racivir was shown to be generally well-tolerated in both studies. In Study 101, Racivir was tested at 200, 400 and 600 mg doses against lamivudine once daily for 14 days in combination with stavudine and efavirenz in 32 HIV-infected, treatment-naïve individuals. In this study, mean viral loads of 4.7 log to 4.85 log were reduced by approximately 99% on average by day 14 at all dose levels and in the lamivudine control arm. In this study, replacing lamivudine with Racivir did not affect the efficacy of stavudine and efavirenz. The purpose of the Phase 1 study was to assess the safety of Racivir and was not designed to provide statistical evidence of efficacy. Therefore, a p value measuring the statistical significance of this viral load reduction was not calculated.

Mechanism of Action. Racivir s primary resistance mutation in vitro is M184V. In our head-to-head preclinical studies, the M184V viral mutation took longer to emerge when using Racivir than lamivudine or emtricitabine. In collaboration with the National Institutes of Health, or the NIH, we compared the activity of Racivir to emtricitabine against common HIV mutations in a head-to-head laboratory study and observed that both Racivir and emtricitabine were similarly active in inhibiting naturally occurring HIV, as well as viruses containing the T215Y (which is one of the TAMs), K65R, and other drug-resistant mutations. In this laboratory

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study, Racivir lost activity against viruses containing the M184V mutation, but to a lesser degree than emtricitabine. In other head-to-head preclinical studies, we evaluated Racivir s time to selection of resistant mutants. We observed *in vitro* that -FTC selected for the M184V mutation in 9 weeks, +FTC selected for the T215Y mutation in 17 weeks and Racivir selected for the M184V mutation in 14 weeks. We believe that the +FTC component of Racivir is delaying the selection of M184V by Racivir.

In head-to-head preclinical studies, we evaluated Racivir s potency and cytotoxicity. We observed that +FTC has potent antiviral activity, although it is approximately 10-fold less potent than -FTC. Neither -FTC or +FTC demonstrated cytotoxicity.

DFC

Dexelvucitabine (DFC) is an oral, once-daily cytidine nucleoside analog. We had been developing DFC in collaboration with Incyte Corporation (Incyte) until April 3, 2006, when Incyte announced its decision to discontinue its development of DFC. Incyte has now terminated our license agreement and returned its rights related to DFC to us. As a result of this termination, we will no longer be eligible to receive milestone payments or royalties from Incyte with respect to DFC, and we will be solely responsible for any additional expenses that we may incur in connection with the development of DFC. We have analyzed the preclinical and clinical data on DFC generated by Incyte. A path for further development of DFC has not yet been identified.

Our Research Programs

We have a library of cataloged nucleoside analogs, as well as several other chemically diverse antiviral, anticancer and antibacterial compounds. This library is the result of substantial collective effort, and we continue to enhance the compound library s value through the addition of new compounds. We screen potential new targets against this library as a means of identifying promising chemical compounds to pursue for further development. We use preclinical discovery and development technologies and viral and cellular assays that we believe form a reasonable basis for anticipating clinical results. Developing additional compounds to treat HCV, HBV and HIV is the primary focus of our nucleoside research and development activities.

Collaborations and Licensing Agreements

Boehringer Ingelheim Chemicals, Inc.

On August 8, 2008, we entered into a manufacturing services agreement with Boehringer Ingelheim Chemicals, Inc. (BICI) for the manufacture of clinical supplies of the active pharmaceutical ingredient (API) of clevudine. In addition to covering the clinical supply of the API, the Manufacturing Services Agreement also contains terms related to any eventual commercial manufacture and supply of the API by BICI. The Manufacturing Services Agreement has an initial term of five years and at our option may be extended for an additional three years, and under certain circumstances, may be terminated by either us or BICI in advance of the expiration of its term. We also entered into a license agreement with BICI pursuant to which BICI granted us a non-exclusive, worldwide, perpetual, royalty-free license, with the right to sublicense to contract manufacturing organizations solely for the purpose of manufacturing the API on behalf of us, to use and practice certain BICI technology related to the manufacture of the API (the License). We agreed that in exchange for the License, and in addition to certain cash payments we will pay to BICI, we may, if certain product development milestones are reached for products incorporating the API, source a certain minimum amount of its commercial requirements for the API exclusively from BICI.

University of Cincinnati

In October 2007, we entered in a three year research collaboration and license agreement with the University of Cincinnati (UC) on behalf of its Genome Research Institute (GRI) to identify active and selective compounds against antiviral targets for HBV, HCV and HIV. As part of the agreement, UC granted us

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access to the GRI Lead Generation Library, which includes over 250,000 compounds. We will also gain access to GRI s drug discovery capabilities, including high-throughput screening, computational chemistry and in silico docking expertise. UC granted us commercial rights for any lead compounds that are identified for HBV, HIV and HCV. We will make an annual payment to UC in support of the research collaboration and shall be responsible for all development expenses of products that may result from the collaboration. If a lead compound progresses through clinical development activities and achieves regulatory approval, we will make certain milestone payments to UC and pay to UC a royalty on any net sales of the product.

Bukwang Pharm. Co., Ltd.

Bukwang Pharm. Co., Ltd. is a pharmaceutical, oral hygiene, and cosmetics company based in Seoul, Korea. On December 28, 1995, Bukwang entered into an exclusive, worldwide license agreement with the University of Georgia Research Foundation, or UGARF, and Yale University to develop and commercialize clevudine. On June 23, 2005, Bukwang granted us exclusive rights to develop, manufacture, and market clevudine in North America, Europe, Central and South America, the Caribbean, and Israel. Bukwang retained rights to the rest of the world, excluding those Asian territories that were licensed to Eisai in November 2004. The agreement permits us to sublicense these rights, without Bukwang s consent, to any of the top one hundred pharmaceutical companies based on sales ranked by IMS Health Incorporated.

We paid Bukwang an up-front payment of $6.0 million and may pay up to an aggregate of $24.0 million in milestone payments related to development, regulatory and commercialization events, as well as future royalties on net sales, including a minimum royalty obligation in certain years. We incurred our first milestone payment to Bukwang in the amount of $1.0 million upon initiation of our Phase 3 registration study during the quarter ended September 30, 2007. Other than the up-front payment and this $1.0 milestone payment, we have made no additional milestone payments through September 30, 2008 to Bukwang under this agreement. We have the right to use the clinical data generated by Bukwang or Eisai, as well as all historical data collected by the prior licensee, Triangle Pharmaceuticals (acquired by Gilead Sciences in 2003) or Gilead Sciences. We will be responsible for conducting any future clinical trials, regulatory filings, and the commercialization of clevudine in our territories. Bukwang and Eisai are responsible for all ongoing clinical trials, regulatory filings, and the commercialization of clevudine in their respective territories. Subject to the rights of any third party, including Gilead, we granted Bukwang a right of first refusal for Racivir for the treatment of HBV in Korea, the royalties for which would be based on net sales, and without any license fee or milestone obligations.

With respect to patents owned by Bukwang, we are primarily responsible for the patent prosecution and maintenance activities with respect to the licensed patent applications and patents in our licensed territories, at our expense. With respect to the licensed patent applications and patents owned by the primary licensors, UGARF and Yale University, the primary licensors are primarily responsible for the patent prosecution and maintenance activities with respect to the licensed patents, while we are afforded reasonable opportunities to advise the primary licensors on, and cooperate with the primary licensors in, such activities. Under the primary license agreement, Bukwang and the primary licensors agreed that in the event of any suspected infringement, (i) Bukwang and the primary licensors may first agree to institute suit jointly, (ii) in the absence of such agreement, the primary licensors may institute suit, and (iii) in the absence of agreement and if the primary licensors do not institute suit, then Bukwang may institute suit. Bukwang granted us the sole right to exercise its enforcement rights with respect to our territories.

Our collaboration and license agreement with Bukwang will terminate on a country-by-country basis upon the expiration of the last to expire of the licensed patents, including any renewals or extensions, or the invalidation of such patents. The last expiration of these patents is scheduled to occur in March 2022. In the event that there are no valid patent claims in a country, the agreement will terminate with respect to that country in 2015. We may terminate the agreement by providing written notice to Bukwang six months prior to termination. In addition, either party may terminate the agreement if the other party commits a material breach of the agreement that is not timely cured. In the event of termination at will by us or for our breach, we must license

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or transfer to Bukwang all regulatory filings, trademarks, patents, preclinical and clinical data related to this agreement. In the event of termination for Bukwang s breach, Bukwang must license or transfer to us all patents, know-how, and manufacturing processes related to this agreement.

University of Georgia Research Foundation, Inc. and Yale University

As part of the collaboration and license agreement with Bukwang, we sublicensed certain patents and technology related to clevudine. On June 23, 2005, we, along with UGARF and Yale University, signed a memorandum of understanding with regard to the patents and technology related to clevudine that had been exclusively licensed to Bukwang, and which we currently sublicense from Bukwang. The memorandum of understanding provides that UGARF and Yale will grant us a license to these patents and technology in the event that the primary license with Bukwang is terminated, under substantially the same terms as the primary license with Bukwang, including term, termination and financial provisions, provided that the reason for such termination does not relate to any breach of our sublicense by us or on our behalf. We made no up-front payments to UGARF or Yale University in connection with this agreement. The memorandum of understanding contains no stated termination date.

Incyte Corporation

On September 3, 2003, we entered into a collaboration and license agreement with Incyte to develop and commercialize DFC. On April 3, 2006, Incyte announced its decision to discontinue its development of DFC. Incyte has subsequently terminated our license agreement and returned its rights related to DFC to us. We have analyzed the clinical data on DFC generated by Incyte. A path for further development of DFC has not yet been identified.

Hoffmann-La Roche Inc.

Hoffmann-La Roche Inc. is the U.S. affiliate of F. Hoffmann-La Roche Ltd, a Swiss company (collectively Roche). In October 2004, we entered into a collaboration and license agreement with Roche to develop PSI-6130, its pro-drugs and chemically related nucleoside polymerase inhibitors for all indications, including the treatment of chronic HCV infections. Roche paid us an up-front payment of $8.0 million. Roche has also agreed to make milestone payments to us for PSI-6130 or a pro-drug of PSI-6130, including R7128, of up to an aggregate of approximately $105 million, assuming successful development and regulatory approval in Roche s territories. In addition, we will receive royalties paid as a percentage of total annual net product sales, if any, and we will be entitled to receive up to $30 million of one-time performance payments should net sales from the product exceed specified thresholds. Under this collaboration, Roche will reimburse us for all of the currently expected external expenses (up to $4.5 million) associated with, and we will be responsible for, certain preclinical work, the IND filing, and the initial clinical trial. Roche will fund all of the expenses of, and be responsible for, other preclinical studies, future clinical development and commercialization of R7128. In addition to the $8.0 million up-front payment, we have received milestone payments of $25.0 million and research reimbursement payments of $5.0 million from Roche under this agreement as of September 30, 2008.

We granted Roche worldwide rights, excluding Latin America and Korea, to which we refer as our retained territory, to PSI-6130 and its pro-drugs and derivatives. With respect to our retained territory, we may grant rights to a third party to distribute, promote, market or sell a product covered by this collaboration agreement, so long as we first offer these rights to Roche, subject to certain exceptions. We retained certain co-promotion rights in the United States, including the right to market and promote products comprising these compounds to physicians who treat HIV patients. We will be required to pay to Roche royalties on our net product sales, if any, in the territories we have retained.

We also granted Roche an option to license from us additional nucleoside polymerase inhibitors related to PSI-6130 and its pro-drugs and other product candidates developed through our research collaboration. We will continue to discover, develop and retain worldwide rights to ongoing and future HCV programs unrelated to the Roche collaboration.

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With respect to patents owned by us that are the subject of this collaboration, we have the right to prosecute, maintain, enforce and defend these patents, while Roche has the same right with respect to certain designated territories if we choose not to exercise our rights. With respect to Roche s patents that are the subject of this collaboration, Roche has the right to prosecute, maintain, enforce and defend these patents, while we have the same right with respect to certain designated territories if Roche chooses not to exercise its rights. With respect to joint patents that are the subject of this collaboration, Roche and we are each responsible for prosecuting, maintaining, enforcing and defending those joint patents in our respective territories. Subject to certain exceptions, we have agreed to share with Roche any damages, monetary awards and other amounts recovered, after costs and expenses, in connection with patent litigation related to this collaboration.

This agreement will terminate once there are no longer any royalty or payment obligations. Additionally, Roche may terminate the agreement in whole or in part by providing six months written notice to us. Provided that Roche has not terminated the agreement, our royalty obligations under this agreement terminate on a product-by-product and country-by-country basis upon either the expiration of the last to expire patent that covers a licensed compound in each country, or 10 years from the launch of such licensed compound in such country, whichever occurs later. Otherwise, either party may terminate the agreement in whole or in part in connection with a material breach of the agreement by the other party that is not timely cured. In the event of termination, Roche must assign or transfer to us all regulatory filings, trademarks, patents, preclinical and clinical data related to this collaboration.

In conjunction with the agreement, Roche purchased 400,000 shares of our Series R redeemable convertible preferred stock and received warrants to purchase up to an additional 470,588 shares of our Series R-1 redeemable convertible preferred stock for $4.0 million. These shares and warrants were initially recorded at fair value for financial reporting purposes. The 400,000 shares of Series R redeemable convertible preferred stock were converted into 266,666 shares of our common stock on May 2, 2007 when we completed our initial public offering, or IPO, and the related warrants expired without exercise on October 26, 2006.

Emory University

Emory University is a non-profit Georgia corporation located in Atlanta, Georgia. In December of 1998, we entered into two licensing arrangements with Emory University related to the active pharmaceutical ingredients in DFC and Racivir.

DFC. On December 30, 1998, Emory University granted us an exclusive license to make, have made, use, import, offer for sale and sell medical products based on a compound now known as DFC, including certain of its

analogs and derivatives. As part of the consideration for this agreement, we issued to Emory University 66,667 shares of our redeemable common stock valued at $1.50 per share and agreed to pay Emory University royalties as a percentage of net product sales and up to an aggregate of $1.0 million in future marketing milestone payments. The 66,667 shares of our redeemable common stock were converted into 66,667 shares of our common stock on May 2, 2007 when we completed our IPO. Beginning in the second year after NDA registration, these royalties are subject to specified minimums. The agreement permits us to sublicense these rights, subject to Emory University s prior written consent, provided that we pay a percentage of milestone and royalty payments that we receive from a sublicensee. In September 2003, we sublicensed the rights to DFC in certain territories to Incyte, under a collaboration and license agreement, which was terminated as described above.

Emory University is primarily responsible for the patent prosecution and maintenance activities pertaining to the licensed patents, while we are afforded reasonable opportunities to advise Emory University on, and cooperate with Emory University in, such activities. In the event of any suspected infringement, (i) we and Emory University may first agree to institute suit jointly, (ii) in the absence of such agreement, Emory University may institute suit, and (iii) in the absence of agreement and if Emory University does not institute suit, then we may institute suit.

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Our agreement with Emory University will expire upon the expiration of all licensed patents. The last expiration of these patents is scheduled to occur in April 2020. Emory University has the right to terminate the agreement if we fail to make required payments or reports when due, if we become insolvent or bankrupt, or if we materially breach the agreement. To exercise this right, Emory University must give us 60 days written notice, after which time the agreement automatically terminates unless we have cured the breach. We have the right to terminate the agreement at our sole discretion on three months written notice.

Racivir. On December 8, 1998, Emory University granted us an exclusive, worldwide license, which we refer to as the Racivir License Agreement, to make, have made, use, import, offer for sale and sell drug products based on a specified range of mixtures of ( ) FTC and (+) FTC, or enriched FTC, which includes the mixture that we are developing as Racivir. As part of the consideration for this agreement, we issued to Emory University 66,667 shares of our redeemable common stock valued at $1.50 per share, and agreed to pay Emory University royalties as a percentage of net product sales. We subsequently issued to Emory University an additional 13,307 shares of our redeemable common stock valued at $4.95 per share pursuant to an anti-dilution provision in our agreement. The 79,974 aggregate shares of our redeemable common stock were converted into 79,974 shares of our common stock on May 2, 2007 when we completed our IPO. We may also pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments. Beginning in the second year after NDA registration, these royalties are subject to specified minimums. The agreement permits us to sublicense these rights under certain circumstances, provided that we pay a percentage of milestone and royalty payments that we receive from a sublicensee.

Emory University is primarily responsible for the patent prosecution and maintenance activities pertaining to the licensed patent applications and patents, while we are afforded, pursuant to a license agreement relating to emtricitabine that Emory University entered into with Triangle Pharmaceuticals, now Gilead Sciences, Inc., in 1996, which we refer to as the Emory/Gilead License Agreement, reasonable opportunities to advise Emory University on, and cooperate with Emory University in, such activities. Pursuant to the Emory/Gilead License Agreement, in the event of any suspected infringement, (i) we and Emory University may first agree to institute suit jointly, (ii) in the absence of such agreement, Emory University may institute suit, and (iii) in the absence of agreement and if Emory University does not institute suit, then we may institute suit.

The Racivir License Agreement will expire upon the expiration of all licensed patents. The last expiration of these patents is scheduled to occur in November 2020. Emory University has the right to terminate the agreement if we fail to make required payments or reports when due, if we become insolvent or bankrupt, or if we materially breach the agreement. To exercise this right, Emory University must give us 60 days written notice, after which time the agreement automatically terminates unless we have cured the breach. We have the right to terminate the Racivir License Agreement at our sole discretion on three months written notice.

In the Emory/Gilead License Agreement, Emory University previously had granted a right of first refusal to Gilead that is applicable to any license or assignment relating to enriched FTC (which includes Racivir). The terms of this right of first refusal contains an exception permitting Emory University to license or assign its rights in respect of enriched FTC to a permitted transferee, which includes any of the inventors (which included two of our founders) or to any corporate entity formed by or on behalf of the inventors for purposes of clinically developing enriched FTC so long as the licensee agrees in writing to be bound by the terms of Gilead s right of first refusal to the same extent as Emory University. Our license to Racivir was granted to us by Emory University pursuant to this exception and therefore we are bound by the terms of Gilead s right of first refusal to the same extent as Emory University. The terms of this right of first refusal as set forth in the Emory/Gilead License Agreement require that, prior to the entry into any license or assignment agreement with a third party relating to any of Emory University s rights in respect of enriched FTC, Emory University shall notify Gilead of the terms of the proposed agreement and provide a copy of the proposed agreement to Gilead together with all data and information in Emory University s possession relating to enriched FTC and its use as a therapeutic agent. Gilead has 30 days to accept or decline the offer. Although Emory University considers us to be a permitted transferee under the Emory/Gilead License Agreement, Emory University has subsequently taken the

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position that its grant of commercialization rights (i.e., the rights to offer for sale and sell Racivir) to us exceeded the rights that were permitted to be granted to a permitted transferee under its agreement with Gilead. While we believe that Gilead is aware of the Racivir License Agreement through both our and Emory University s communications with Gilead, Gilead has not contacted us regarding its interpretation of the terms of the Racivir License Agreement.

In March 2004, we entered into a supplemental agreement with Emory University in which we and Emory University agreed that, prior to any commercialization of enriched FTC by us, or by any licensee or assignee of our rights under the Racivir License Agreement, we and Emory University would adhere strictly to the terms of the right of first refusal granted to Gilead in the Emory/Gilead License Agreement and offer to Gilead the same terms and conditions under which we, our licensee or our assignee, propose to commercialize enriched FTC. The supplemental agreement also outlines a procedure by which Emory University and we would jointly offer the terms of a proposed license and commercialization agreement between us and a third party to Gilead after Emory University has the opportunity to approve them. Therefore, before we could enter into a commercialization agreement for Racivir with a third party or commercialize Racivir on our own, we would be required to offer Gilead the opportunity to be our commercialization partner on the same terms on which we intend, or our prospective partner intends, to commercialize Racivir. It is uncertain whether a third party would be willing to negotiate the terms of a commercialization agreement with us knowing that Gilead can take their place as licensee by accepting the negotiated terms and exercising its right of first refusal.

These uncertainties related to our commercialization rights may result in our being prevented from obtaining the expected economic benefits from developing Racivir. In addition, we could become involved in litigation or arbitration related to our commercialization rights to Racivir in the future.

Apath, LLC

Apath, LLC is a Missouri company that is engaged in the commercial application of molecular virology and viral genetics. On October 18, 2000, as amended on January 30, 2004, Apath granted us a non-exclusive right to use its HCV Replicon technology for the design, discovery, development and commercialization of compounds inhibiting HCV in humans. The agreement required us to pay Apath royalties on sales of compounds discovered using this technology, and on any consideration received by us from a licensee of such compounds. Although this agreement is not related to the development of a specific product candidate, we used this technology in our development of PSI-6130.

We do not have the right to advise or to consult with Apath regarding the prosecution or maintenance of the licensed patent rights. We are one of several sublicensees of the licensed patents and have no rights to enforce such patents.

This agreement was terminated on August 26, 2005, on which date we entered into a new agreement with Apath. Under the terms of the new agreement, we paid Apath a one-time sublicense fee of $550,000, and an annual maintenance fee of $75,000, subject to annual renewals, retroactive to October 18, 2000. Going forward, we will only pay the annual maintenance fee for any year for which we choose to renew this agreement, and we will have no other financial obligations to Apath in connection with the design, discovery, development and commercialization of compounds inhibiting HCV in humans.

This agreement expires on the date of expiration of the last-to-expire U.S. patent in the licensed patent rights. The last expiration of these patents is scheduled to occur in March 2018. Apath retains no rights to the compounds we discover, and they will receive no payments for any of the compounds we discover. We are entitled to sublicense these compounds to a third party without Apath s permission or consent. We may terminate the agreement for any reason or no reason by giving Apath 30 days prior written notice without any penalties. Apath is entitled to terminate the contract, but only should we breach the agreement, on 30 days notice in the event of any uncured breach.

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RFS Pharma LLC

As of February 10, 2006, we entered into a license agreement with RFS Pharma LLC (RFS Pharma) to pursue the research, development and commercialization of an antiviral nucleoside analog product candidate called dioxolane thymine (DOT). Dr. Schinazi, one of our significant stockholders, is the founder and majority stockholder of RFS Pharma and is a named inventor of DOT. Under this agreement, we paid to RFS Pharma an upfront payment of $400,000 and we may also pay up to an aggregate of $3.9 million in future milestone payments, royalties on future sales, and expense reimbursements for reasonable out-of-pocket costs incurred by RFS Pharma in assisting us in complying with all regulatory obligations, for certain orders of DOT by RFS Pharma and, upon obtaining regulatory approval for the sale of a product containing DOT in one of the countries listed below, for certain administrative costs and expenses associated with RFS Pharma s performance of its obligations under the license agreement. For the first five years after we initially sell a product containing DOT in any of the U.S., Japan, China, Germany, France, Great Britain, Italy or Spain, we have agreed to pay minimum royalty payments. To date, other than the initial upfront payment we have paid a total of $119,120 to RFS Pharma under these provisions. Additionally, this license agreement provided for the purchase of specified amounts of DOT by us from RFS Pharma for $82,000. With respect to licensed patent applications and patents owned by the primary licensors which claim DOT, the primary licensors, UGARF and Emory University, are primarily responsible for the prosecution and maintenance activities. With respect to licensed patent applications and patents owned by RFS Pharma which claim DOT, RFS Pharma is primarily responsible for the prosecution and maintenance activities through patent counsel reasonably acceptable to us. Under the primary license agreement, RFS Pharma and the primary licensors agreed that, in the event of any suspected patent infringement, (i) RFS Pharma and the primary licensors may first agree to institute suit jointly, (ii) in the absence of such agreement, RFS Pharma may institute suit, and (iii) in the absence of agreement and if RFS Pharma does not institute suit, then the primary licensors may institute suit. RFS Pharma granted us all its enforcement rights under the primary license agreement. We may terminate the license agreement on a country-by-country basis and/or product-by-product basis or in its entirety at any time upon 30 days advance written notice to RFS Pharma prior to the launch of any licensed product, or upon 180 days advance written notice to RFS Pharma following the launch of any licensed product. Additionally, upon a material breach of this agreement by either party, if the breaching party fails to cure the material breach during a 90 day period after notice of the breach has been provided, then the non-breaching party may terminate the agreement on a country-by-country or product-by-product basis with respect to the country(ies) and licensed product(s) to which the breach relates. The license agreement may also terminate on a country-by-country and licensed product-by-licensed product basis upon the expiration of the obligation to pay royalties on the sale of each licensed product in such country. Such royalties shall be payable for so long as there exists in such country a valid claim of an issued patent covering a licensed product, or, if longer, the term of the license agreement among UGARF, Emory University and RFS Pharma with respect to such licensed product in such country.

Manufacturing and Supply

We do not have our own manufacturing capabilities and we rely on third-party manufacturers for supply of the APIs, we use in our preclinical studies and clinical trials. We do not expect to establish our own manufacturing facilities and we will continue to rely on third-party manufacturers to produce commercial quantities of any drugs that we market.

We are party to a manufacturing services agreement with BICI for the manufacture of clinical supplies of the API of clevudine. In addition to covering the clinical supply of the API, the Manufacturing Services Agreement also contains terms related to any eventual commercial manufacture and supply of the API by BICI. We are also party to a license agreement with BICI pursuant to which BICI granted us a non-exclusive, worldwide, perpetual, royalty-free license, with the right to sublicense to contract manufacturing organizations solely for the purpose of manufacturing the API on behalf of us, to use and practice certain BICI technology related to the manufacture of the API. In exchange for the License, and in addition to certain cash payments it will pay to BICI, we may, if certain product development milestones are reached for products incorporating the API, source a certain minimum amount of its commercial requirements for the API exclusively from BICI.

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We have a sufficient quantity of clevudine for our future preclinical studies and Phase 3 clinical trials, but if we obtain marketing approval for clevudine, we will need to procure additional supplies of clevudine from BICI or other qualified third-party manufacturers.

Roche has responsibility for establishing a single source of API for R7128 for both the Roche territory and our territory. We also have the right to establish ourselves as the secondary source of API supply for R7128, provided, however, that we may not supply in excess of 20% of the requirements for the global supply.

We may need to procure additional supplies of Racivir to complete our future preclinical studies and clinical trials. Our goal is to conduct future clinical trials with a collaborator that will study combination therapies that include Racivir for HIV patients receiving second-line therapy. If necessary, we plan to enter into a supply agreement after an evaluation of potential suppliers that could manufacture Racivir, including the company that manufactures our current supply of Racivir.

Incyte was responsible for the clinical trials of DFC and for obtaining a sufficient supply of DFC for its trials. If we conduct our own clinical trials of DFC, we will need to establish our own source of supply of DFC.

We have relied on contract manufacturers specializing in nucleoside chemistry to provide us with drug product. The company that manufactured our current supply of Racivir and PSI-6130 made a $1.5 million equity investment in us in 1999. All of the materials required for the manufacture of our product candidates are currently available from more than one qualified source.

Government Regulation

Regulation by governmental authorities in the United States and other countries is a significant factor in the development, manufacture and marketing of pharmaceutical products and in ongoing research and development activities. Government authorities in the United States at the federal, state, and local levels and in foreign countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution, sampling, marketing, and import and export of pharmaceutical products, biologics, and medical devices. All of our products will require regulatory approval by governmental agencies prior to commercialization. Various federal, state, local and foreign statutes and regulations also govern, among other things, testing, manufacturing, safety, labeling, marketing, storage and record-keeping related to such products. The process of obtaining these approvals and subsequent process of maintaining substantial compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of extensive time and financial resources. In addition, these statutes, rules, regulations and policies may change and our products may be subject to new legislation or regulations.

Pharmaceutical Regulation in the United States

In the United States, drugs are subject to rigorous regulation by the FDA. The Federal Food, Drug and Cosmetic Act (FDCA), and other federal and state statutes and regulations govern, among other things, the research, development, testing, safety, effectiveness, manufacture, quality control, storage, record keeping, labeling, promotion, marketing, and distribution of pharmaceutical products. The failure to comply with the applicable regulatory requirements may subject a company to a variety of sanctions, including, among other things, administrative, or judicially imposed sanctions. These sanctions could include, among other things, the FDA s refusal to approve pending applications, withdrawals of approvals, clinical holds, warning letters, product recalls, product seizures, total or partial suspension of operations, injunctions, fines, civil penalties or criminal prosecution. The FDA also administers certain controls over the export of drugs and biologics from the United States.

The steps ordinarily required before a new drug product may be marketed in the United States include preclinical laboratory tests, animal tests and formulation studies, the submission to the FDA of a notice of claimed exemption for an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication for which FDA approval is sought. The following paragraphs provide a general overview of the development and approval process for a new drug.

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Preclinical Phase. Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA.

If a company wants to test a new drug in human patients/subjects, an IND must be prepared and filed with the FDA to request FDA authorization to begin human testing of the drug. The IND application automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions such as those relating to the adequacy of the preclinical studies, the preclinical product characterization and/or the proposed conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The submission of an IND may not result in FDA authorization to commence a clinical trial. A separate supplemental submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must review each supplemental IND before each clinical trial can begin. Furthermore, an independent institutional review board (IRB) for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center, and the IRB must monitor the study until completed.

Certain preclinical tests must be conducted in compliance with the FDA s good laboratory practice regulations and the United States Department of Agriculture s Animal Welfare Act. Violations of these regulations can, in some cases, lead to invalidation of the studies, requiring such studies to be reconducted.

Clinical Phase. The clinical phase of development follows successful IND submission and involves the activities necessary to demonstrate safety, tolerability, efficacy and dosage of the substance in humans, as well as the ability to produce the substance and finished drug product in accordance with the FDA s current Good Manufacturing Practice, or cGMP, requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study and the parameters to be used in assessing the safety and the efficacy of the drug. Each protocol must be submitted to the FDA as part of the IND prior to beginning the trial. Each trial must be reviewed, approved and conducted under the auspices of an IRB, and each trial (with very limited exceptions), must include the patient s/subject s informed consent. Sponsors, investigators, other clinical study staff, and IRBs also must satisfy extensive Good Clinical Practice, or GCP, including regulations and guidelines for obtaining informed consent from the study subjects, complying with the protocol and investigational plan, adequately monitoring the clinical trial, and reporting adverse events adequately and timely. The FDA, the IRB, independent data or safety reviewers or the sponsor may suspend a clinical trial at any time for any reason, including a finding that the subjects/patients are being exposed to an unacceptable health risk.

Foreign studies performed under an IND must meet the same requirements that apply to U.S. studies. The FDA will accept a foreign clinical study not conducted under an IND only if the study is well-designed, well-conducted, performed by qualified investigators, and conforms to the ethical principles contained in the Declaration of Helsinki, or with the laws and regulations of the country in which the research was conducted, whichever provides greater protection of the human subjects.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, Phases 1, 2 and 3, with Phase 4 clinical trials conducted after marketing approval. Phase 4 clinical trials are generally required for products that receive accelerated approval. The FDA also may require sponsors to conduct Phase 4 clinical trials to study certain safety issues. Data from these studies are compiled in an NDA for submission to the FDA requesting approval to market the drug. These phases might be compressed, might overlap, or might be omitted in some circumstances.

Phase 1 Clinical Trials: After an IND becomes effective, Phase 1 human clinical trials can begin. These studies are initially conducted in a limited population to evaluate, among other things, a drug candidate s safety and tolerability. Phase 1 clinical trials also determine, among other things, how a drug candidate is absorbed, distributed, metabolized and excreted by the body, and its duration of

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action. In some cases, a sponsor may decide to run what is referred to as a Phase 1b evaluation, which is a second, safety-focused Phase 1 clinical trial typically designed to evaluate the drug candidate in combination with currently approved drugs.

Phase 2 Clinical Trials: Phase 2 studies are generally conducted in a limited patient population to identify possible adverse events and safety risks, to determine, among other things, the efficacy of the drug candidate for specific targeted indications and to determine, among other things, dose tolerance and optimal dosage. These trials are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects. Phase 2 clinical trials of antiviral drugs typically are designed to evaluate the potential efficacy of the drug on patients and to further ascertain the safety of the drug, at the dosage given, in a larger patient population. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. In some cases, a sponsor may decide to run what is referred to as a Phase 2b evaluation, which is a second, confirmatory Phase 2 clinical trial that could, in certain circumstances and if accepted by the FDA, serve as a registrational clinical trial in the approval of a drug candidate.

Phase 3 Clinical Trials: These are commonly referred to as registrational (or pivotal) studies, and are undertaken when Phase 2 clinical trials suggest that a dose range of the drug candidate is effective and has an acceptable safety profile. In Phase 3 clinical trials, the drug is usually tested in a controlled randomized trial comparing the investigational new drug to an approved form of therapy in an expanded and well-defined patient population and at multiple clinical sites. The goal of these studies is to obtain, among other things, definitive statistical evidence of safety and efficacy of the investigational new drug regimen as compared to an approved standard treatment in defined patient populations with a given disease and stage of illness. Phase 3 trials usually include from several hundred to several thousand subjects.

In the case of products for life-threatening diseases, the initial human testing is often conducted in patients/subjects with the target disease rather than in healthy volunteers. These studies may provide initial evidence of efficacy traditionally obtained in Phase 2 clinical trials, and so these trials are frequently referred to as Phase 1/2 clinical trials.

In addition, a company may hold an End-of-Phase 2 Meeting with the FDA to assess, among other things, the safety of the drug regimen to be tested in the Phase 3 clinical trial, to evaluate the Phase 3 plan, and to identify any additional information that will be needed to support an NDA. If the Phase 3 clinical trials had been the subject of discussion at an End-of-Phase 2 Meeting, the company is eligible for a Special Protocol Assessment (SPA) by the FDA, a process by which the FDA, at the request of the sponsor, will evaluate protocols and issues relating to the protocols within 45 days to assess whether they are adequate to meet scientific and regulatory requirements identified by the sponsor. If the FDA and the sponsor reach agreement on the design and size of clinical trials intended to form the primary basis of an efficacy claim in an NDA, the FDA will reduce the agreement to writing. The SPA agreement, however, is not a guarantee of product approval by FDA or approval of any permissible claims about the product.

Success in early-stage clinical trials does not necessarily assure success in later-stage clinical trials. Data obtained from clinical activities is not always conclusive and may be subject to alternative interpretations that could delay, limit or even prevent regulatory approval.

Throughout the clinical phase, samples of the product made in different batches are tested for stability to establish shelf life constraints. In addition, large-scale production protocols and written standard operating procedures for each aspect of commercial manufacture and testing must be developed.

Phase 1, 2, and 3 testing may not be completed successfully within any specified time period, if at all. The FDA closely monitors the progress of each of the phases of clinical trials that are conducted under an IND and

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may, at its discretion, reevaluate, alter, suspend, or terminate the testing based upon the data accumulated to that point and the FDA s assessment of the risk/benefit ratio to the patient. The FDA, IRB, independent data or safety reviewers or the sponsor may suspend or terminate clinical trials at any time for any reason, including a finding that the subjects/patients are being exposed to an unacceptable health risk. The FDA can also request additional clinical trials be conducted as a condition to product approval. Additionally, new government requirements may be established that could delay or prevent regulatory approval of our products under development. Furthermore, IRBs and independent data or safety reviewers, which are independent entities constituted to protect human subjects in the clinical trials that are being conducted at the IRBs institutions, have the authority to suspend clinical trials in their respective institutions at any time for a variety of reasons, including safety issues.

Certain information about clinical trials, including a description of the study, participation criteria, location of study sites, and contact information, shall be submitted for listing on the National Institutes of Health (NIH) publicly-accessible clinical trial registry. Section 113 of the FDA Modernization Act mandates registration of IND efficacy trials for serious diseases or conditions. In addition, the Food and Drug Administration Amendments Act of 2007 directs the FDA to issue regulations that will require sponsors to submit to the NIH the results of all controlled clinical studies, other than Phase I studies. Sponsors also are subject to certain state laws imposing requirements to make publicly available certain information on clinical trial results.

New Drug Application. After successful completion of the required clinical testing of a drug candidate, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. An NDA is a comprehensive, multi-volume application that includes, among other things, the results of all preclinical and clinical studies, information about the drug s composition, and the sponsor s plans for producing, packaging, and labeling the drug. If the FDA determines that a risk evaluation and mitigation strategy (REMS) is necessary to ensure that the benefits of the drug outweigh the risks, a sponsor may be required to include as part of the application a proposed REMS, including a package insert directed to patients, a plan for communication with healthcare providers, restrictions on a drug s distribution, or a medication guide to provide better information to consumers about the drug s risks and benefits. Under the Pediatric Research Equity Act of 2003, an application is also required to include an assessment, generally based on clinical study data, on the safety and efficacy of drugs for all relevant pediatric populations before the NDA is submitted. The statute provides for waivers or deferrals in certain situations. The cost of preparing and submitting an NDA is substantial. Under federal law, in most cases, the submission of an NDA is also subject to substantial application user fees. The manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. These fees are typically increased annually.

The submission of the application is no guarantee that the FDA will find it complete and accept it for filing. The FDA reviews all NDAs submitted before it accepts them for filing. It may refuse to file the application and request additional information rather than accept the application for filing, in which case, the application must be resubmitted with the supplemental information. After the application is deemed filed by the FDA, agency staff of the FDA reviews an NDA to determine, among other things, whether a product is safe and efficacious for its intended use. The FDA has substantial discretion in the approval process and may disagree with an applicant s interpretation of the data submitted in its NDA. As part of this review, the FDA may refer the application to an appropriate advisory committee, typically a panel of physicians, for review, evaluation, and an approval recommendation. For any drug containing an active ingredient not previously approved under the FDCA, the application automatically will be referred to an appropriate advisory committee for review prior to approval of the drug, unless the FDA decides otherwise and specifies such reasons to the sponsor. The FDA is not bound by the opinion of the advisory committee. Drugs that successfully complete NDA review, and for which an approval letter is received, may be marketed in the United States, subject to all conditions imposed by the FDA and all applicable laws and regulations.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the

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Prescription Drug User Fee Act (PDUFA), the FDA has agreed to specific performance goals in the review of NDAs, including a performance goal of 10-12 months for review of a standard NDA. The initial review cycle for applications submitted under FDCA § 505(b) or § 505(j) is 180 days. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission.

Prior to granting approval, the FDA generally conducts an inspection of the facilities, including outsourced facilities that will be involved in the manufacture, production, packaging, testing and control of the drug substance and finished drug product for cGMP compliance. The FDA will not approve the application unless cGMP compliance is satisfactory. If the FDA determines that the marketing application, manufacturing process, or manufacturing facilities are not acceptable, in a complete response letter it will outline the deficiencies in the submission and will often request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the marketing application does not satisfy the regulatory criteria for approval and refuse to approve the application.

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter. If the FDA determines the NDA cannot be approved in its current form, it may issue a complete response letter. A complete response letter generally identifies deficiencies, and where possible, recommends actions to be taken towards approval which must be met in order to secure approval of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug (typically authorized on the date of the approval letter, with certain exceptions) with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require post-approval testing and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling and distribution restrictions that can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn for many reasons, including where compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The length of the FDA s NDA review can range from a few months, particularly for drugs related to life-threatening conditions, to many years.

Fast-Track Review. The Food and Drug Administration Modernization Act of 1997 (Modernization Act), establishes a statutory program for the approval of Fast-Track products, which are defined under the Modernization Act as new drugs or biologics intended for the treatment of a serious or life-threatening condition that demonstrate the potential to address unmet medical needs for this condition. To determine whether a condition is serious for the purposes of Fast-Track designation, the FDA considers several factors, including, among other things, the condition s impact on survival, day-to-day functioning, and the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. If awarded, the Fast-Track designation applies to the product only for the indication for which the designation was received. Under the Fast-Track program, the sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a Fast-Track product in writing at any time during the clinical development of the product. The Modernization Act specifies that the FDA must determine if the product qualifies for Fast-Track designation within 60 days of receipt of the sponsor s request.

Fast-Track designation offers a product the benefit of approval based on surrogate endpoints that generally would not be acceptable for approval and possible early or rolling acceptance of the marketing application for review by the agency. Traditional approval requires data demonstrating that the product has an effect on clinically meaningful endpoints or well-established surrogate endpoints. The FDA may approve the application of a Fast-Track product on the basis of clinical trials using less than well-established surrogate endpoints where the agency determines that the effect on the surrogate endpoint is reasonably likely to predict clinical benefit. Confirmatory post-approval studies likely will still need to be conducted. If a preliminary review of the clinical data suggests that a Fast-Track product may be effective, the FDA may also initiate review of sections of a

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marketing application for a Fast-Track product before the sponsor completes the application. This rolling review is available if the applicant provides a schedule for submission of remaining information and pays applicable user fees. However, the time periods to which the FDA has committed in reviewing an application do not begin until the sponsor actually submits the application.

The FDA may subject approval of an application for a Fast-Track product to post-approval studies to validate the surrogate endpoint or confirm the effect on the clinical endpoint, and the FDA will also subject such approval to prior review of all promotional materials. In addition, the FDA may withdraw its approval of a Fast-Track product on a number of grounds, including, among other things, the sponsor s failure to conduct any required post-approval study with due diligence and failure to continue to meet the criteria for designation.

Fast-Track designation should be distinguished from the FDA s other programs for expedited development and review although products awarded Fast-Track status may also be eligible for these other benefits. Accelerated approval refers to the use of less than well-established surrogate endpoints discussed above. Priority review is a designation of an application after it has been submitted to the FDA for approval for drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. The agency sets the target date for agency actions on the applications of products that receive priority designation for six months where products under standard review receive a 10-month target.

Post-Approval Phase. As a condition of NDA approval, the FDA may require post-marketing Phase 4 clinical trials to confirm that the drug is safe and efficacious for its intended uses. After NDA approval, if the FDA becomes aware of new safety information, the agency may require post-approval studies, including clinical trials to investigate known serious risks or signals of serious risks, or identifying unexpected serious risks. If required to conduct a post-approval study, periodic status reports must be submitted to the FDA. Failure to conduct such post-approval studies in a timely manner may result in withdrawal of approval, substantial civil fines, among other things.

Where drugs are approved under accelerated approval regulations or the FDA otherwise requests, additional studies will likely be required to document a clinical benefit and to monitor the long-term effects of the therapy. We expect that for any product for which a single pivotal clinical trial is authorized for approval, we will be required to conduct extended Phase 4 clinical trials to monitor the long-term effects of the therapy. Recent developments have prompted heightened government focus on safety reporting and pharmacovigilance. The FDA may require applicants to implement a REMS or risk minimization action plan (RiskMAP) to minimize known and preventable safety risks or otherwise impose burdens, such as limits on prescribing and/or distribution and on direct-to-consumer advertising, on an applicant s ability to commercialize its drug products.

In addition, following FDA approval of a product, discovery of problems with a product or the failure to comply with requirements may result in, among other things, restrictions on a product, manufacturer or holder of an approved marketing application, including withdrawal or recall of the product from the market or other voluntary or FDA-initiated action that could delay or prevent further marketing. Newly discovered or developed safety or efficacy data may require changes to an approved product s distribution or labeling including the addition of new warnings and contraindications.

Any products manufactured or distributed under FDA approvals are subject to pervasive and continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the products. Drug manufacturers and their subcontractors are required to register with the FDA and, where appropriate, state agencies, and are subject to periodic unannounced inspections by the FDA and state agencies to ensure compliance with applicable regulations, including cGMP, which impose manufacturing procedural, documentation and quality control requirements. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties.

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FDA Regulation of Post-Approval Marketing and Promotion. The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, dissemination of off-label information for uses of the product not approved by the FDA, industry-sponsored scientific and educational activities, and promotional activities involving the internet. A company can make only those claims relating to safety and efficacy of a product for the indications that are approved by the FDA. Failure to comply with these requirements can result in, among other things, adverse publicity, enforcement letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses for which the drugs are not indicated, that are not described in the drug s labeling, and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers communications regarding off-label uses.

Drug Price Competition and Patent Term Restoration Act of 1984. Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, Congress created an abbreviated FDA review process for generic versions of pioneer (brand name) drug products. In order to preserve the incentives of pioneer drug manufacturers to innovate, the Hatch-Waxman Act also provides for patent term restoration and the award, in certain circumstances, of non-patent marketing exclusivities.

Abbreviated New Drug Application (ANDA). An ANDA is a type of application in which approval is based on a showing of pharmaceutical equivalence and bioequavalence to an already approved drug product. ANDAs do not contain full reports of safety and efficacy, as do NDAs, but rather demonstrate that their proposed products are the same as reference products with regard to their conditions of use, active ingredient(s), route of administration, dosage form, strength, and labeling. ANDA applicants are also required to demonstrate the bioequivalence of their products to the reference product. Bioequivalence generally means that there is no significant difference in the rate and extent to which the active ingredient(s) in the products becomes available at the site of drug action.

An applicant may obtain permission from the FDA to submit an ANDA for a product that differs from the reference product in active ingredient (in combination products), route of administration, dosage form, or strength by submitting a suitability petition to the FDA. The FDA will approve a suitability petition unless investigations must be conducted to show the safety and efficacy of the altered product, or unless significant labeling changes would be required. If the FDA approves the suitability petition, the applicant may submit an ANDA for its proposed product. When approving a suitability petition, the FDA may also inform the applicant of any additional information that the FDA may require to support the ANDA. The FDA has the authority during its review of the ANDA to request additional information regarding the change in the product that was the subject of the suitability petition, and may also withdraw its approval of the suitability petition.

All ANDAs must contain data relating to product formulation, raw material suppliers, stability, manufacturing, packaging, labeling, and quality control, among other information. Approval limits manufacturing to a specifically identified site(s). Supplemental filings, which generally require FDA review and approval, may allow the manufacture of such products at new sites also generally require review and approval. In addition, certain changes to manufacturing processes, ingredients, and labeling can require FDA review and approval.

The timing of final FDA approval of an ANDA depends on a variety of factors, including, among other things, whether the applicant has challenged any patents listed in the FDA s Orange Book for the reference product and whether the pioneer manufacturer is entitled to one or more periods of non-patent marketing exclusivity. In certain circumstances, these marketing exclusivities can extend beyond the life of a patent, and block the approval of ANDAs after the date on which the patent expires. Once the FDA concludes that all substantive ANDA requirements have been satisfied, but final approval is blocked because of a patent or marketing exclusivity, the FDA may issue the ANDA applicant a tentative approval letter.

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505(b)(2) Applications. If a proposed drug product represents a change from an already approved product, but does not qualify for submission under an ANDA or pursuant to an approved suitability petition, the applicant may be able to submit a type of an NDA application referred to as a 505(b)(2) application. A 505(b)(2) application is an NDA for which one or more of the investigations relied upon by the applicant for approval was not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the entity by or for which the investigation was conducted. The FDA has determined that 505(b)(2) applications may be submitted for products that represent changes from approved products in conditions of use, active ingredient(s), route of administration, dosage form, strength, or bioavailability. A 505(b)(2) applicant also has the flexibility to reference more than one approved product.

A 505(b)(2) applicant must provide the FDA with any additional clinical data necessary to demonstrate the safety and effectiveness of the product with the proposed change(s). Consequently, although duplication of preclinical and certain clinical studies is avoided through the use a 505(b)(2) application, specific clinical studies may be required.

Patent Term Restoration. The Hatch-Waxman Act also provides for the restoration of a portion of the patent term lost during product development and FDA review of an application for approval. However, the maximum period of restoration cannot exceed 5 years or restore the total remaining term of the patent to greater than 14 years from the date of FDA approval of the product. The patent term restoration period is generally one-half the time between the effective date of the IND and the date of submission of the NDA, plus the time between the date of submission of the NDA and the date of FDA approval of the product. The term restoration only applies to the claim or claims directed toward the approved drug product. Only one term extension can be granted per patent, and only one patent may be extended per approved product. The patent holder must apply for restoration within 60 days of approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for patent term restoration. In the future, we may consider applying for patent term restoration for some of our currently owned or licensed patents, depending on the expected length of clinical trials and other factors involved in the filing of an NDA.

ANDA and 505(b)(2) Applicant Challenges to Patents and Generic Exclusivity. NDA and 505(b)(2) applicants are required to list with the FDA each patent that claims their approved products and for which claims of patent infringement could reasonably be asserted against unauthorized manufacturers. ANDA and 505(b)(2) applicants must then certify regarding each of the patents listed with the FDA for the product(s) it references. ANDA and 505(b)(2) applicants can certify that there is no listed patent, that the listed patent has expired, that the application may be approved upon the date of expiration of the listed patent, or that the patent is invalid or will not be infringed by the marketing of the applicant s product. This last certification is referred to as a Paragraph IV certification.

If a Paragraph IV certification is filed, the applicant must also provide notice to the NDA holder and patent owner stating that the application has been submitted and provide the factual and legal basis that the patent is invalid or not infringed. The NDA holder or patent owner may sue the ANDA or 505(b)(2) applicant for patent infringement. If the NDA holder or patent owner files suit within 45 days of receiving notice of the application, a one-time 30-month stay of the FDA s ability to approve the ANDA or 505(b)(2) application is triggered. The FDA may approve the proposed product before the expiration of the 30-month stay if a court finds the patent invalid or not infringed or shortens the period because parties have failed to cooperate in expediting the litigation.

As an incentive to encourage generic drug manufacturers to undertake the expenses associated with Paragraph IV patent litigation, the first ANDA applicant to submit a substantially complete ANDA with a Paragraph IV certification to any patent listed with the FDA may be eligible for a 180-day period of marketing exclusivity. The exclusivity period runs from the date when the generic drug is first commercially marketed, and blocks final approval of any later-filed ANDA referencing the same product.

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The 180-day exclusivity period is triggered by the first commercial marketing of the generic drug (whether marketed by the ANDA filer or by an authorized generic) or by a final decision by the District Court that the patent is invalid or not infringed if there is no appeal, or by the Court of Appeals for the Federal Circuit if the District Court decision is appealed.

If multiple generic drug manufacturers submit substantially complete ANDAs with Paragraph IV certifications on the same day, all of these manufacturers will share in a single 180-day exclusivity period. Note also that the 180-day exclusivity may be subject to forfeiture provisions, requiring relinquishment of the exclusivity in some situations, including cases where commercial marketing of the generic drug does not occur within a certain time period.

Non-Patent Marketing Exclusivities. Under the Hatch-Waxman Act, newly approved drug products and changes to the conditions of use of approved products may benefit from periods of non-patent marketing exclusivity. The Hatch-Waxman Act provides five years of new chemical entity marketing exclusivity to the first applicant to gain approval of an NDA for a product that does not contain an active ingredient found in any other approved product. Where this exclusivity is awarded, the FDA is prohibited from accepting any ANDAs or 505(b)(2) applications during the five-year period (this period is shortened to four years for ANDAs containing Paragraph IV certifications). This exclusivity protects the entire new chemical entity franchise, including all products containing the active ingredient for any approved use and in any strength or dosage form. This exclusivity will not prevent the submission or approval of stand-alone NDAs, but such applicants would be required to conduct their own adequate and well-controlled clinical studies to demonstrate the safety and effectiveness of their products.

The Hatch-Waxman Act also provides three years of new use marketing exclusivity for the approval of NDAs, 505(b)(2) applications, and supplements, where those applications contain the results of new clinical investigations (other than bioavailability studies) essential to the FDA s approval of the applications. Such applications may be submitted for new indications, dosage forms, strengths, or new conditions of use of already approved products. So long as the new clinical investigations are essential to the FDA s approval of the change, this three-year exclusivity prohibits the final approval of ANDAs or 505(b)(2) applications for products with the specific changes associated with those clinical investigations. It does not prohibit the FDA from approving ANDAs or 505(b)(2) applications for other products containing the same active ingredient.

Pediatric Exclusivity. The Modernization Act included a pediatric exclusivity provision that was reauthorized by the Food and Drug Administration Amendments Act of 2007 through fiscal year 2012. Pediatric exclusivity provides an incentive to pioneer drug manufacturers for conducting research into the safety and efficacy of their products in children. Manufacturers are eligible for pediatric exclusivity when they conduct and submit the results of pediatric studies requested by the FDA. When granted, pediatric exclusivity provides an additional six months of market exclusivity and patent protection in the United States.

Orphan Drug Designation and Exclusivity. Some jurisdictions, including the United States and the European Union, designate drugs intended for relatively small patient populations as orphan drugs. The FDA, for example, grants orphan drug designation to drugs intended to treat rare diseases or conditions that affect fewer than 200,000 individuals in the United States or drugs for which there is no reasonable expectation that the cost of developing and making the drugs available in the United States will be recovered. In the United States, orphan drug designation must be requested before submitting an application for approval of the product.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to seven-year market exclusivity. For seven years, the FDA may not approve any other application, including NDAs, ANDAs, or 505(b)(2) applications, to market the same drug for the same indication. The only exception is where the second product is shown to be clinically superior to the product with orphan drug exclusivity, as that phrase is defined by the FDA, and if there is an inadequate supply.

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Foreign Regulatory Requirements

Outside the United States, our ability to market our products will also be contingent upon receiving marketing authorizations from the appropriate regulatory authorities and compliance with applicable post-approval regulatory requirements. Although the specific requirements and restrictions vary from country to country, as a general matter, foreign regulatory systems include risks similar to those associated with FDA regulation, as described above. Under EU regulatory systems, marketing authorizations may be submitted either under the centralized or decentralized procedure. Under the centralized procedure, a single application to the European Medicines Evaluation Agency (EMEA), may lead to an approval granted by the European Commission that permits the marketing of the product in the member states of the European Union. The centralized procedure is mandatory for certain classes of medicinal products, but is optional for others. We assume that the centralized procedure will apply to our products.

The decentralized procedure may lead to mutual recognition of nationally approved decisions and is used for products that are not required to be authorized by the centralized procedure, and for those products for which the centralized procedure is optional but which shall be marketed in select EU member countries only.

Under the decentralized procedure, an applicant applies for national marketing authorization in one state, and then may submit further applications to the competent authorities of other member states, which will then be requested to recognize the original authorization based upon an assessment report prepared by the original authorizing competent authority. If any member state makes an objection, we have the option to withdraw the application from that country or take the application to arbitration by the Committee for Proprietary Medicinal Products (CPMP) of the EMEA. If a referral for arbitration is made, the procedure is suspended, and in the intervening time, the only EU country in which the product can be marketed will be the country where the original authorization has been granted, even if all the other designated countries are ready to recognize the product. The opinion of the CPMP, which is binding, could support or reject the objections or alternatively could reach a compromise position acceptable to all EU countries concerned. Arbitration can be avoided if the application is withdrawn in the objecting country, but once the application has been referred to arbitration, it cannot be withdrawn.

As with FDA approval, we may not be able to secure regulatory approvals in Europe in a timely manner, if at all. Additionally, as in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution, would apply to any product that is approved in Europe, and failure to comply with such obligations could have a material adverse effect on our ability to successfully commercialize any product.

Hazardous Materials

Our research and development processes involve the controlled use of numerous hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations, and may be subject to foreign laws and regulations, governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products, including certain regulations promulgated by the U.S. Environmental Protection Agency, or EPA. The EPA regulations to which we are subject require that we register with the EPA as a generator of hazardous waste. Although we have safety procedures for handling and disposing of these materials, we cannot assure investors that accidental contamination or injury from these materials will not occur. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposures to blood-borne pathogens and the handling, transporting and disposing of biohazardous or radioactive materials. We do not expect the cost of complying with these laws and regulations to be material.

Competition

We face a broad range of current and potential competitors, from established global pharmaceutical companies with significant resources to development-stage companies. In addition, we face competition from

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academic and research institutions and government agencies for the discovery, development and commercialization of novel therapeutics to treat HBV, HCV and HIV. Many of our competitors, either alone or with their collaborative partners, have significantly greater financial, product development, technical, manufacturing, sales and marketing resources than we do. In addition, many of our direct competitors are large pharmaceutical companies with internal research and development departments that have significantly greater experience in testing pharmaceutical products, obtaining FDA and other regulatory approvals of products and achieving widespread market acceptance for those products.

We believe that a significant number of drugs are currently under development and will become available in the future for the treatment of HBV, HCV and HIV. We anticipate that we will face intense and increasing competition as new products enter the marketplace and advanced technologies become available. Our competitors products may be safer, more effective, or more effectively marketed and sold, than any product we may commercialize. Competitive products may render one or more of our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. It is also possible that the development of a cure, effective vaccine, or new treatment methods for HBV, HCV and HIV could render one or more of our product candidates non-competitive or obsolete or reduce the demand for our product candidates.

We believe that our ability to compete depends, in part, upon our ability to develop products, complete the clinical trials and regulatory approval processes, and effectively market any products we develop. Further, we need to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary product candidates or processes and secure sufficient capital resources for the substantial time period between the discovery of lead compounds and their commercial sales, if any.

HBV Therapeutics Competition

In the United States, the current standard of care for the treatment of HBV infection is monotherapy with one of five nucleoside analog drugs, or one of two alpha interferon protein therapies, as listed in the following table.

FDA-Approved Therapies for the Treatment of HBV

Brand Name	Chemical Name	Chemical Name Abbreviation	Drug Class	Company
Epivir-HBV	lamivudine	3TC	nucleoside analog	GlaxoSmithKline
Hepsera	adefovir	ADV	nucleotide analog	Gilead Sciences
Baraclude	entecavir	ETV	nucleoside analog	Bristol-Myers Squibb
Tyzeka	telbivudine	LdT	nucleoside analog	Novartis
Intron-A	interferon alfa-2b	IFN	interferon	Schering Plough
Pegasys	peginterferon alfa-2a	PEG IFN	interferon	Roche
Viread	tenofovir	TDF	nucleotide analog	Gilead Sciences

As of August 2008, Hepsera represented approximately 43% of approved HBV nucleoside prescriptions in the US, while Baraclude, Epivir-HBV and Tyzeka represented approximately 36%, 16% and 5% of approved HBV nucleoside prescriptions, respectively. From March 2000 through August 2008, the total prescriptions for approved HBV nucleosides grew at a compound annual growth rate, or CAGR, of approximately 35%. Gilead Sciences has recently received EU and US approval for Viread® (tenofovir) for the treatment of HBV in April and August 2008, respectively.

Although a safe and effective vaccine against HBV has been available for decades, it only benefits those not yet infected with this virus. We believe that additional drugs will become available in the future for the treatment

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of HBV, considering the major unmet medical need for therapy. We also believe that the introduction of new HBV therapeutics will expand the current market and increase the likelihood of combination therapy for HBV. Our HBV product candidate may compete directly or be used in combination with the current standard of care, with the drug candidates that are currently in development and with those that may be developed in the future. As a result of its mechanism of action, we believe that clevudine may be complementary to some existing HBV treatments and could therefore be used as either a single agent or in combination with existing therapies. To further support this concept, in July 2008 the French National Agency for Research on AIDS and Viral Hepatitis (ANRS), with our support and Gilead Sciences, initiated the first head-to-head study of clevudine and Viread administered separately, versus their combination, for the treatment of chronic HBV infection in non-cirrhotic patients. The study treatments include clevudine 30mg/day, tenofovir 300mg/day or the combination of both drugs administered to 150 treatment-naïve hepatitis B e-antigen negative HBV-infected patients for 96 weeks. At that time, all therapy will be discontinued, and patients will be monitored for SVR after being off therapy for 24 weeks, the primary endpoint of the study.

In March 2007, we engaged MEDACorp to conduct a survey to assess the current market for HBV therapies and opportunities for new HBV therapies, including clevudine. In this market study, 99 U.S. physicians participated, representing the medical specialties of gastroenterology, hepatology, infectious disease and primary care. The physicians surveyed reported currently managing an average of approximately 80 HBV patients, an average increase of more than 30% in their HBV patient volume as compared to the previous year. These physicians reported prescribing, on average, oral nucleoside HBV therapies for 80% of all their HBV patients and 50% of their treatment-naïve HBV patients. Additionally, a majority of the physicians surveyed indicated that achieving sustained undetectable levels of HBV DNA off-treatment, or SVR, is the most important factor for them in making treatment decisions, while maintaining undetectable levels of HBV DNA on-treatment is the second most important factor for them in making treatment decisions.

The physicians surveyed were asked to consider hypothetical patient scenarios and describe their related prescribing patterns for HBV therapies. There were a number of important trends that emerged from this portion of the market survey. For example, 97% of physicians surveyed indicated that SVR is a meaningful measure of efficacy and will likely be an important criterion in the future development of novel HBV therapies and the survey results indicated that oral HBV therapies with higher SVR rates were selected more often for HBV therapeutic utilization. This marketing study was based on a small survey sample size and the results may have been different if a larger survey were conducted. Also, clevudine has not completed long-term clinical studies to quantify its SVR rate and we cannot assure you that clevudine will have the efficacy profile that doctors surveyed indicated was important.

HCV Therapeutics Competition

In the United States, the current standard of care for the treatment of HCV is a combination of alpha interferon and a nucleoside analog named ribavirin. Alpha interferon is approved in several chemically modified forms and is marketed by Roche, Schering-Plough, and Three Rivers Pharmaceuticals. Roche, Schering-Plough, and several generic manufacturers market ribavirin. We are aware that Roche and other companies are also developing new drugs for the treatment of HCV. For example, Novartis/Human Genome Sciences, Vertex and Schering-Plough have advanced their drug candidates into Phase 3 clinical trials. In October 2008, Roche announced that development of R1626, a polymerase inhibitor being investigated as a treatment for infection with HCV, was terminated due to safety findings from a Phase 2b study. The following table presents information about approved drugs and drug candidates for the treatment of HCV.

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FDA-Approved HCV Therapeutics or HCV Therapeutics in Development

Brand Name	Chemical Name or Abbreviation	Drug Class	Phase of Development	Company
Pegasys plus	peginterferon alfa-2a + ribavirin	Interferon	Approved	Roche
Peg-Intron plus	peginterferon alfa-2b + ribavirin	Interferon	Approved	Schering-Plough
Infergen	interferon alfacon-1	Interferon	Approved	Three Rivers Pharmaceuticals
Albuferon	albumin interferon alfa-2b	Interferon	Phase 3	Human Genome Sciences/ Novartis
	R7128	Nucleoside Polymerase Inhibitor	Phase 2	Pharmasset/Roche
	PSI-7851	Nucleotide Polymerase Inhibitor	Pre-Clin	Pharmasset
	PF-868554	Non-nucleoside Polymerase Inhibitor	Phase 2	Pfizer
	GS-9190	Non-nucleoside Polymerase Inhibitor	Phase 2	Gilead
	Telaprevir (VX-950)	Protease Inhibitor	Phase 3	Vertex/ Johnson & Johnson
	Boceprevir	Protease Inhibitor	Phase 3	Schering-Plough
	TMC435350	Protease Inhibitor	Phase 2	Medivir/Tibotec
	R7227	Protease Inhibitor	Phase 1	InterMune/Roche
	BMS-790052 (ITMN-191)	NS5A Inhibitor	Phase 1	Bristol-Myers Squibb
	BI201335	Protease Inhibitor	Phase 2	Boeringer Ingelheim
	IDX184	Nucleotide Polymerase Inhibitor	Phase 1	Idenix

HIV Therapeutics Competition

HAART, the standard of care for the treatment of HIV infection, generally includes two NRTIs combined with a third drug from another class (either an NNRTI or a protease inhibitor). Racivir and DFC are NRTIs and, therefore, our primary competitors are those companies that develop and market other NRTIs.

To provide additional convenience to HIV patients, companies have developed combination therapies that combine two or more NRTIs into a single tablet or capsule. These fixed-dose combination therapies have become leaders in the HIV marketplace.

Several of the FDA-approved individual NRTIs and combination products face patent expiration in the next several years. As a result, generic versions of these drugs may become available. We expect to face competition from these generic drugs, including price-based competition.

Other classes of HIV therapeutics include NNRTIs, PIs, integrase inhibitors, and entry or fusion inhibitors. Although NNRTIs and PIs are often complementary to NRTIs, there are certain protease-based regimes that are competitors to NRTIs. Entry inhibitors have a unique mechanism of action, but are often used only to treat individuals who have failed other treatment options because they are administered by injection. There is one fusion inhibitor, one entry inhibitor and one integrase inhibitor approved by the FDA.

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The following table presents information about the various classes of HIV therapeutics.

Multi-class Combination Products

Brand Name	Generic Names	Company	Chemical Name Abbreviation	Component Analog Type
Atripla	efavirenz	Bristol-Myers Squibb, Gilead Sciences and Merck	EFV	cytidine
	emtricitabine		FTC	adenosine
	tenofovir disoproxil fumarate		TDF	

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Brand Name	Generic Name(s)	Company	Chemical Name Abbreviation	Component Analog Type
Combivir	lamivudine	GlaxoSmithKline	3TC	cytidine
	zidovudine		AZT	thymidine
Emtriva	emtricitabine	Gilead Sciences	FTC	cytidine
Epivir	lamivudine	GlaxoSmithKline	3TC	cytidine
Epzicom	abacavir	GlaxoSmithKline	3TC	guanosine
	lamivudine		ABC	cytidine
Hivid	zalcitabine	Hoffmann-La Roche	ddC	cytidine
Retrovir	zidovudine	GlaxoSmithKline	ZDV	thymidine
Trizivir	abacavir,	GlaxoSmithKline	ABC	guanosine
	zidovudine		AZT	thymidine
	lamivudine		3TC	cytidine
Truvada	tenofovir disoproxil fumarate	Gilead Sciences, Inc.	TDF	adenosine
	emtricitabine		FTC	cytidine
Videx EC	enteric coated didanosine	Bristol Myers-Squibb	ddI EC	adenosine
Videx	didanosine	Bristol Myers-Squibb	ddI	adenosine
Viread	tenofovir disoproxil fumarate	Gilead	TDF	adenosine
Zerit	stavudine	Bristol Myers-Squibb	d4T	thymidine
Ziagen	abacavir sulfate	GlaxoSmithKline	ABC	guanosine

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Brand Name	Generic Name	Company	Chemical Abbreviation
Intelence	etravirine	Tibotec Therapeutics	ETR
Rescriptor	delavirdine	Pfizer	DLV
Sustiva	efavirenz	Bristol Myers-Squibb	EFV
Viramune	nevirapine	Boehringer Ingelheim	NVP

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Protease Inhibitors (PIs)

Brand Name	Generic Name(s)	Manufacturer Name	Chemical Abbreviation
Agenerase	amprenavir	GlaxoSmithKline	APV
Aptivus	tipranavir	Boehringer Ingelheim	TPV
Crixivan	indinavir	Merck	IDV
Invirase	saquinavir mesylate	Hoffmann-La Roche	SQV
Kaletra	lopinavir and ritonavir	Abbott Laboratories	LPV/RTV
Lexiva	fosamprenavir calcium	GlaxoSmithKline	FOS/APV
Norvir	ritonavir	Abbott Laboratories	RTV
Prezista	darunavir	Tibotec, Inc.	TMC114
Reyataz	atazanavir sulfate	Bristol-Myers Squibb	ATV
Viracept	nelfinavir mesylate	Agouron Pharmaceuticals	NFV

Fusion Inhibitors

Brand Name	Generic Name	Manufacturer Name	Approval Date
Fuzeon	enfuvirtide,	Hoffmann-La Roche & Trimeris	T-20

Entry Inhibitors CCR5 co-receptor antagonist

Brand Name	Generic Names	Manufacturer Name	Approval Date
Selzentry	maraviroc	Pfizer	UK-427857

HIV integrase strand transfer inhibitors

Brand Name	Generic Names	Manufacturer Name	Approval Date
Isentress	raltegravir	Merck & Co., Inc.	MK-0518

We are aware that many other companies are developing compounds targeting HIV, including pharmaceutical companies such as Pfizer Inc., Merck & Co., Inc., GlaxoSmithKline plc, Bristol-Myers Squibb Co., Schering-Plough Corp., Johnson & Johnson and biotechnology companies such as Gilead Sciences, Inc., Panacos Pharmaceuticals, Inc., Tibotec Pharmaceuticals Limited, Incyte Corporation, Avexa Limited and Achillion Pharmaceuticals, Inc. We believe that a significant number of drugs are currently under development and will become available in the future for the treatment of HIV. These drug candidates include NRTIs as well as drugs that block HIV protein functions and interactions, including integrase and maturation inhibitors. We are aware that Merck and other companies are pursuing the development of a prophylactic vaccine, which is a vaccine that prevents infections. If a prophylactic vaccine is successful, it could reduce the size of the market for our products.

Intellectual Property

Our policy is to pursue patents and to otherwise endeavor to defend our technologies, inventions, and improvements to inventions that are commercially important to the development of our business. We seek U.S. and international patent protection on the novel compounds, product candidates, and therapeutic processes we discover or improve, as well as the chemical synthesis and manufacturing of such compounds and product candidates. As of September 30, 2008, we hold or have licensed 729 issued patents and pending patent applications directed to our technologies, including recently discovered product candidates. As of September 30, 2008, our owned patent portfolio includes 10 issued U.S. patents, 29 issued foreign patents, 24 U.S. applications and 259 foreign applications, while our in-licensed patent portfolio includes 40 issued U.S. patents, 283 issued foreign patents, 5 U.S. applications and 79 foreign applications.

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We have an exclusive sublicense in North, Central and South America, Europe, the Caribbean and Israel from Bukwang to issued U.S. and corresponding foreign patents covering the composition of matter, methods of using clevudine to treat HBV and synthetic processes for clevudine, which expire between 2014 and 2022. Bukwang is the primary licensee from Yale University and the University of Georgia Research Foundation, Inc., who are the primary licensors that jointly own the intellectual property for this technology. Our sublicense with Bukwang also encompasses nonexclusive rights in the aforementioned territories to pending patents in the U.S. and certain foreign countries covering the use of clevudine in combination with other therapeutics for the treatment of HBV. Any patent issuing from these patent applications would expire no earlier than 2023.

On December 8, 1998, Emory University granted us an exclusive, worldwide license pursuant to the Racivir License Agreement to issued U.S. patents covering the composition of matter, methods of synthesizing Racivir and methods of using Racivir to treat HIV and HBV, which expire between 2010 and 2020. This license also encompasses rights to corresponding patents and pending patent applications in Europe, Japan, South Africa and other foreign countries.

In the Emory/Gilead License Agreement, Emory University previously had granted a right of first refusal to Gilead that is applicable to any license or assignment relating to enriched FTC (which includes Racivir). The terms of this right of first refusal contains an exception permitting Emory University to license or assign its rights in respect of enriched FTC to a permitted transferee, which includes any of the inventors (which included two of our founders) or to any corporate entity formed by or on behalf of the inventors for purposes of clinically developing enriched FTC so long as the licensee agrees in writing to be bound by the terms of Gilead s right of first refusal to the same extent as Emory University. Our license to Racivir was granted to us by Emory University pursuant to this exception and therefore we are bound by the terms of Gilead s right of first refusal to the same extent as Emory University. The terms of this right of first refusal as set forth in the Emory/Gilead License Agreement require that, prior to the entry into any license or assignment agreement with a third party relating to any of Emory University s rights in respect of enriched FTC, Emory University shall notify Gilead of the terms of the proposed agreement and provide a copy of the proposed agreement to Gilead together with all data and information in Emory University s possession relating to enriched FTC and its use as a therapeutic agent. Gilead has 30 days to accept or decline the offer. Although Emory University considers us to be a permitted transferee under the Emory/Gilead License Agreement, Emory University has subsequently taken the position that its grant of commercialization rights (i.e., the rights to offer for sale and sell Racivir) to us exceeded the rights that were permitted to be granted to a permitted transferee under its agreement with Gilead. While we believe that Gilead is aware of the Racivir license agreement through both our and Emory University s communications with Gilead, Gilead has not contacted us regarding its interpretation of the terms of the Racivir License Agreement.

In March 2004, we entered into a supplemental agreement with Emory University in which we and Emory University agreed that, prior to any commercialization of enriched FTC by us, or by any licensee or assignee of our rights under the Racivir License Agreement, we and Emory University would adhere strictly to the terms of the right of first refusal granted to Gilead in the Emory/Gilead License Agreement and offer to Gilead the same terms and conditions under which we, our licensee or our assignee, propose to commercialize enriched FTC. The supplemental agreement also outlines a procedure by which Emory University and we would jointly offer the terms of a proposed license and commercialization agreement between us and a third party to Gilead after Emory University has the opportunity to approve them. Therefore, before we could enter into a commercialization agreement for Racivir with a third party or commercialize Racivir on our own, we would be required to offer Gilead the opportunity to be our commercialization partner on the same terms on which we intend, or our prospective partner intends, to commercialize Racivir. It is uncertain whether a third party would be willing to negotiate the terms of a commercialization agreement with us knowing that Gilead can take their place as licensee by accepting the negotiated terms and exercising its right of first refusal.

These uncertainties related to our commercialization rights may result in us being prevented from obtaining the expected economic benefits from developing Racivir. In addition, we could become involved in litigation or arbitration related to our commercialization rights to Racivir in the future.

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We own pending U.S. and foreign patent applications directed to the PSI-6130 chemical compound, pro-drugs (including R7128), pharmaceutical formulations, therapeutic combinations and use to treat HCV infections. Any patent issuing from these patent applications would expire no earlier than 2024. We own pending U.S. and foreign patent applications directed to the synthesis of PSI-6130 chemical compound, including synthetic intermediates thereof. To date, no patents have issued from these applications. Any patent issuing from these patent applications would expire no later than 2025. To date, no patents have issued from these applications.

We have an exclusive, worldwide license from Emory University to issued U.S. patents covering a formulation of DFC in combination with other antiviral nucleoside analogs and methods of using DFC to treat HIV infection, which expire in 2015. This license also encompasses rights to corresponding patents and pending patent applications in Europe, Japan, South Africa and other foreign countries, which will expire in 2016. In addition, we own pending U.S. patent applications and corresponding foreign patent applications that cover methods of synthesizing DFC and its related compounds and pharmaceutical formulations of DFC. Any patent issuing from these patent applications would expire no earlier than 2022 and 2024, respectively.

The patent expiration dates stated above do not take into account any patent term adjustments that may accrue due to procedural delays by the United States Patent and Trademark Office or patent term extensions that may accrue due to regulatory delays.

Attempts to obtain patent protection both in the United States and abroad can be expensive, take years to complete, and may not be successful. In addition, issued patents are subject to attack, may not be enforceable, and may otherwise fail to protect our business. Moreover, the trade secret laws and other sources of intellectual property protection may also be insufficient to protect our product candidates. For more information on these and other risks related to intellectual property rights, see Risk Factors Risks Related to Our Intellectual Property.

Employees

As of September 30, 2008, we had 67 employees, 46 of whom performed research and development functions. We plan to add additional employees as we expand our business.

Available Information

All periodic and current reports, registration statements, and other filings that we are required to file with the SEC, including 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) of the Securities Exchange Act of 1934 (Exchange Act), are available free of charge from the SEC s website (www.sec.gov) or public reference room at 100 F Street N.E., Washington, DC 20549 (1-800-SEC-0330) or through our website at www.pharmasset.com. Such documents are available as soon as reasonably practicable after electronic filing of the material with the SEC. Copies of these reports (excluding exhibits) may also be obtained free of charge, upon written request to: Investor Relations, Pharmasset, Inc., 303-A College Road East, Princeton, NJ 08540. The website addresses included in this report are for identification purposes. The information contained therein or connected thereto are not intended to be incorporated into this report.

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ITEM 1A. RISK FACTORS
Risks Related to Our Business

Risks Related to Drug Discovery, Development and Commercialization

We are subject to significant regulatory requirements, which could delay, prevent or limit our ability to market our product candidates, including clevudine, Racivir, R7128, PSI-7851 and DFC.

Our research and development activities, preclinical studies, clinical trials, manufacturing and the anticipated marketing of our product candidates are subject to extensive regulation by a wide range of governmental authorities in the United States, including the FDA and by comparable authorities in European and other countries. To date, none of our product candidates have been approved for sale by the FDA or any foreign regulatory authority except clevudine, for which Bukwang has received marketing approval in Korea. Neither we nor our collaborators, independently or collectively, will be able to commercialize any of our product candidates until we or they obtain FDA approval in the United States or approval by comparable regulatory agencies in Europe or other countries. To satisfy FDA or foreign regulatory approval standards for the commercial sale of our product candidates, we must, among other requirements, demonstrate in adequate and well-controlled clinical trials that our product candidates are safe and effective. We, IRBs, the FDA or applicable foreign regulatory authorities could suspend the clinical trials of a drug candidate at any time if there is a concern that the patients/subjects participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. Adverse side effects of a product candidate on patients/subjects in a clinical trial could result in the FDA or foreign regulatory authorities refusing to approve a particular drug candidate for any and all indications of use.

We have conducted initial preclinical studies and early-stage clinical trials of Racivir, PSI-6130, R7128 and DFC, and initial preclinical studies of PSI-7851. These trials were not primarily designed to demonstrate the efficacy of Racivir, PSI-6130, R7128 or DFC as therapeutic agents, but rather to collect data on safety and assist in determining the appropriate dose. Even if our product candidates achieve positive results in preclinical and early clinical trials, similar results may not be observed in subsequent trials and results may not prove to be statistically significant or demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory agencies.

The FDA also regulates the manufacturing facilities of our third-party manufacturers. Prior to approval, the FDA inspects manufacturing facilities to ensure compliance with cGMP, including quality control and record-keeping measures. Post-approval, the FDA and certain state agencies subject these facilities to unannounced inspections to ensure continued compliance with cGMP. Failure to satisfy the pre-approval inspection or subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in an inability to receive approval, recall of products, delay in approval or restrictions on the product or on the manufacturing post-approval, including a withdrawal of the drug from the market or suspension of manufacturing.

We also will be required to obtain foreign regulatory approval for the sale of our products outside of the United States. Foreign regulatory approval processes include all of the risks associated with the FDA approval processes described above, as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not assure approval by foreign regulatory authorities, and the fact that clevudine has been approved by Korean regulatory authorities does not mean that the FDA or other foreign regulatory authorities will approve clevudine. Many foreign regulatory authorities have different approval standards from each other and from those required by the FDA and may impose additional testing requirements for our product candidates. Furthermore, international ethical review boards may cause our clinical trials to be delayed pending their review of safety data, clinical procedures, and comments provided by foreign regulatory authorities. We have had limited interaction with foreign regulatory authorities. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for foreign regulatory approvals and may not receive necessary approvals to commercialize our existing and future product candidates in any market.

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The regulatory approval process is expensive, and the time required to complete clinical trials and for FDA and foreign regulatory approval processes is uncertain and typically takes many years. Our analysis of data

obtained from our preclinical and clinical trials is subject to confirmation and interpretation by different regulatory authorities who may have different views on the design, scope or results of our clinical trials, which could delay, limit or prevent regulatory approval. Changes in the regulatory approval policy during the development period of any of our product candidates, changes in, or the enactment of, additional regulations or statutes, or changes in regulatory review practices for a submitted product application may cause a delay in obtaining approval or result in the rejection of an application for regulatory approval. We could also encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in FDA or foreign regulatory policies during the period of product development, clinical trials or regulatory review.

As a result of the foregoing factors, our product candidates could require a significantly longer time to gain regulatory approval than expected, or may never gain approval. We cannot assure you that, even after expending substantial time and resources, we will obtain regulatory approval for any of our product candidates. A delay or denial of regulatory approval could delay or prevent our ability to generate product revenues and to achieve profitability. If regulatory approval is obtained, our marketing of any product will be limited to its indicated uses, which will limit the size of the market for a product and affect our potential product revenues.

Our product candidates must undergo rigorous clinical trials, the results of which are uncertain and could substantially delay or prevent us from bringing drugs to market.

Before we can obtain regulatory approval for a product candidate, we must undertake extensive clinical trials in humans to demonstrate safety and efficacy to the satisfaction of the FDA or other regulatory agencies. Clinical trials of new product candidates sufficient to obtain regulatory marketing approval are complex and expensive and take years to complete. In addition, the results obtained in earlier-stage testing may not be indicative of results in future trials. For example, estimates of viral load reduction and activity against HBV, HCV and HIV obtained from preclinical studies and small-scale clinical trials are not necessarily indicative of results that could be achieved in larger clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier preclinical studies and clinical trials. We cannot assure you that we or our collaborators will successfully complete the planned clinical trials. Our collaborators or we may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent us from receiving regulatory approval or commercializing our product candidates, including the following events:

- our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical and/or preclinical studies or to abandon development programs;
- trial results may not meet the level of statistical significance required by the FDA or other regulatory agencies;
- we, IRBs, independent safety monitors or regulators, may suspend or terminate clinical trials if the participating patients/subjects are being exposed to unacceptable health risks; and
- the effects of our product candidates on patients/subjects may not be the desired effects or may include undesirable side effects or other characteristics that may delay or preclude regulatory approval or limit their commercial use.

We have limited experience in conducting clinical trials which could impair our timing or ability to obtain regulatory approval for our product candidates.

We have limited experience in conducting and managing the clinical trials necessary to obtain FDA approval or approval by other regulatory authorities. Our past clinical experience has been limited to a small

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number of drug candidates relating to a limited number of therapeutic areas. By contrast, large and established pharmaceutical companies often have staffs conducting clinical trials with multiple drug candidates across multiple indications. As a result, we may experience delays in obtaining regulatory approvals, if at all, for our product candidates for which we conduct or manage the clinical trial process.

Delays in clinical trials could result in increased costs to us and delay our ability to obtain regulatory approval and commercialize our product candidates.

Significant delays in clinical trials could materially affect our product development costs and delay regulatory approval of our product candidates. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including:

- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in trials;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an IRB to conduct a clinical trial at a prospective study site;
- delays in recruiting patients/subjects to participate in a clinical trial;
- failure of our clinical trials and/or clinical investigators to be in compliance with Good Clinical Practices;
- unforeseen safety issues;
- inability to monitor patients/subjects adequately during or after treatment;
- difficulty monitoring multiple study sites;
- failure of our third-party clinical trial managers to satisfy their contractual duties, comply with regulations or meet expected deadlines; and
- determination by regulators that the clinical design of the trials is not adequate.

Failure to recruit and enroll patients/subjects for clinical trials may cause the development of our product candidates to be delayed.

We have experienced, and expect to experience in the future, delays in patient/subject enrollment in our clinical trials for a variety of reasons. The completion of clinical trials depends, among other things, on our ability to enroll a sufficient number of patients/subjects who remain in the study until its conclusion. The enrollment of patients/subjects depends on many factors, including:

the patient/subject eligibility criteria defined in the protocol;

the size of the patient/subject population required for analysis of the trial s therapeutic endpoints;

the proximity of patients/subjects to study sites;

the design of the trial;

our ability to recruit clinical trial investigators with the appropriate competencies and experience;

our ability to obtain and maintain patient/subject consents;

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- the risk that patients/subjects enrolled in clinical trials will drop out of the trials before completion; and

- competition for patients/subjects by clinical trial programs for other treatments.

Our clinical trials compete with other clinical trials for drug candidates that are in the same therapeutic areas as our drug candidates, and this competition reduces the number and types of patients/subjects available to us, because some patients/subjects who might have opted to enroll in our trials opt to enroll in a trial being conducted by one of our competitors. We conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which reduces the number of patients/subjects who are available for our clinical trials in such clinical trial site. Delays in patient enrollment in the future as a result of these and other factors may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent us from completing these trials and adversely affect our ability to advance the development of our product candidates.

For example, in our Phase 2 study of Racivir, we anticipated that enrollment would take less than one year to complete, but it actually took 20 months. The primary reasons for this unexpected delay in enrollment included competition for patients/subjects with other longer-term clinical studies, larger investigator budgets and greater payments to study subjects for other clinical trials, very specific patient/subject enrollment criteria for our clinical study, and protocol modifications that were required to increase the duration of treatment. As a result of these delays, it took us longer to complete this study than we had initially planned, and we had to commit staffing and resources to this project for an extended period that could have otherwise been allocated to other research programs.

Our product candidates may have undesirable side effects when used alone or in combination with other products that prevent their regulatory approval or limit their use if approved.

We must demonstrate the safety of our product candidates to obtain regulatory approval. Although in clinical trials to date, clevudine, Racivir, PSI-6130 and R7128 were generally well tolerated, these trials involved a small number of patients/subjects and we may observe significant adverse events for these product candidates in the future. With respect to DFC, on April 3, 2006, Incyte announced its decision to discontinue its development of DFC after observing an increased incidence of grade 4 hyperlipasemia in the rollover portion of a Phase 2b clinical trial. It is possible that any side effects associated with our product candidates may outweigh the benefits of our product candidates and prevent regulatory approval or limit their market acceptance if they are approved. Recent developments in the pharmaceutical industry have prompted heightened government focus on safety reporting and pharmacovigilance. Global health authorities may impose regulatory requirements to monitor safety that may burden our ability to commercialize our drug products.

Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates, which would negatively affect our ability to achieve profitability.

If approved for marketing, the commercial success of our product candidates will depend upon their acceptance by physicians and the medical community, patients, and private, government and third-party payors as clinically useful, safe and cost-effective therapeutics. The degree of market acceptance of any of our approved products will depend upon a number of factors, including:

- the indication for which the product is approved and its approved labeling;

- the establishment and demonstration in the medical community of the safety and efficacy of the product;

- the prevalence and severity of adverse side effects;

- the presence of other competing approved therapies;

- the potential advantages of the product over existing and future treatment methods;

the relative convenience and ease of administration of the product;

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the strength of our sales, marketing and distribution support;

the price and cost-effectiveness of the product; and

sufficient third-party reimbursement.

We are aware that a significant number of drug candidates are currently under development and may become available in the future for the treatment of HIV, HBV and HCV, and may be approved prior to any of our drugs coming to market. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new therapeutics are introduced that are more favorably received than our products or that render our products obsolete, or if unacceptable levels of drug resistance or significant adverse events occur. If our products do not achieve and maintain market acceptance, we will not be able to generate sufficient revenue from product sales to attain profitability.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. and foreign regulations, we could lose our marketing approvals and our business would be seriously harmed.

Following initial regulatory approval of any drugs we or our collaborators may develop, we and our collaborators will be subject to continuing regulatory review by the FDA or other regulatory authorities, including the review of adverse drug events and clinical results that are reported after product candidates become commercially available. This would include results from any post-marketing follow-up studies or other reporting required as a condition to approval. The manufacturing, distribution, labeling, packaging, storage, advertising, promotion, reporting and record-keeping related to the product will also be subject to extensive ongoing regulatory requirements. In addition, incidents of adverse drug reactions, unintended side effects or misuse relating to our products could result in additional regulatory controls or restrictions, or even lead to withdrawal of a product from the market.

Furthermore, our third-party manufacturers and the manufacturing facilities that they use to make our product candidates are regulated by the FDA. Quality control and manufacturing procedures must continue to conform to cGMP after approval. Drug and biologics manufacturers and their subcontractors are required to register their facilities and products manufactured annually with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA, state and/or other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product, or on the manufacturing or laboratory facility, including a withdrawal of the drug from the market or suspension of manufacturing. In addition, any changes to an approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our third-party manufacturers will also be subject to ongoing FDA requirements for submission of safety and other post-market information. If we, our collaborators or our third-party manufacturers fail to comply with applicable continuing regulatory requirements, our business could be seriously harmed because a regulatory agency may:

issue warning letters;

suspend or withdraw our regulatory approval for approved products;

seize or detain products or recommend a product recall;

refuse to approve pending applications or supplements to approved applications filed by us;

suspend any of our ongoing clinical trials;

impose restrictions on our operations, including costly new manufacturing requirements;

close the facilities of our contract manufacturers; or

impose civil or criminal penalties.

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The FDA s policies may change and additional federal, state, local or foreign governmental regulations may be enacted that could affect our ability to maintain compliance. We cannot predict the likelihood, nature, or extent of adverse governmental regulation that may arise from future legislation or administrative action, either in the United States or abroad.

Our research and development efforts may not result in additional product candidates being discovered, which could limit our ability to generate revenues in the future.

Our research and development efforts may not lead to the discovery of any additional product candidates that would be suitable for further preclinical or clinical development. The discovery of additional product candidates requires significant research and preclinical studies, as well as a substantial commitment of resources. Many lead compounds that appear promising in preclinical studies fail to progress to become product candidates in clinical trials. There is a great deal of uncertainty inherent in our research and development efforts and, as a consequence, in our ability to fill our drug development pipeline with promising additional product candidates.

We have no sales, marketing or distribution experience. We expect to develop these capabilities, and expect to invest significant amounts of financial and management resources.

If clevudine receives marketing approval in the United States, we intend to commercialize clevudine ourselves with a sales force of approximately 40 to 45 employees. To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources. As a result, we could face a number of risks, including:

- we may not be able to attract and build a significant marketing or sales force;
- the cost of establishing, training and providing regulatory oversight for a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and
- our direct sales and marketing efforts may not be successful.

We and our collaborators will be subject to stringent federal, state and foreign regulation of sales and marketing of any approved drug candidate and a failure to comply with these regulations could result in substantial penalties.

The marketing and advertising of our drug products by our collaborators or us will be regulated by the FDA, certain state agencies or foreign regulatory authorities. Violations of these laws and regulations, including promotion of our products for unapproved uses or failing to disclose risk information, are punishable by criminal and civil sanctions and may result in the issuance of enforcement letters or other enforcement action by the FDA, Department of Justice, state agencies, or foreign regulatory authorities that could jeopardize our ability to market the product.

In addition to FDA, state or foreign regulations, the marketing of our drug products by us or our collaborators will be regulated by federal, state or foreign laws pertaining to health care fraud and abuse, such as the federal anti-kickback law prohibiting bribes, kickbacks or other remuneration for the order or recommendation of items or services reimbursed by federal health care programs. Many states have similar laws applicable to items or services reimbursed by commercial insurers. Violations of these laws are punishable by criminal and civil sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state health care programs, including the Medicare, Medicaid and Veterans Affairs healthcare programs. Because of the far-reaching nature of these laws, we will need to regularly evaluate, and as appropriate, potentially revise our practices to ensure compliance with these laws. Health care fraud and abuse regulations are complex, and even minor irregularities can potentially give rise to claims that a statute or prohibition has been violated. Any violations of these laws, or any action against us for violations of these laws, even if we successfully defend against it, could have a material adverse effect on our business, financial condition and results of operations.

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We could also become subject to false claims litigation under federal statutes, which can lead to civil money penalties, restitution, criminal fines and imprisonment, and exclusion from participation in Medicare, Medicaid and other federal and state health care programs. These false claims statutes include the False Claims Act, which allows any person to bring a suit on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, under federal programs or contracts claims or other violations of the statute and to share in any amounts paid by the entity to the government in fines or settlement. These suits against pharmaceutical companies have increased significantly in volume and breadth in recent years. Some of these suits against pharmaceutical companies have been brought on allegations that certain sales practices amount to the promotion of drug products for unapproved uses. This new growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay fines or restitution, or be excluded from the Medicare, Medicaid, Veterans Affairs and other federal and state healthcare programs as a result of an investigation arising out of such action. We may become subject to such litigation and, if we are not successful in defending against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Financial Performance and Business Operations

We have incurred net losses since our inception and our future profitability is uncertain and we anticipate that we will incur significant continued net losses for the next several years.

We are a clinical-stage pharmaceutical company with a limited operating history upon which an investor can evaluate our operations and future prospects. We have incurred net losses in each year since our inception in 1998. For the years ended September 30, 2008, 2007 and 2006, we had net losses of $54.7 million, $5.1 million and $11.3 million, respectively. As of September 30, 2008, we had an accumulated deficit of $111.8 million. We do not expect to generate significant revenue from our product candidates for the next several years and we expect to continue to incur significant operating losses in future periods. We expect to incur substantial costs to further our drug discovery and development programs and that our rate of spending will accelerate as a result of the increased costs and expenses associated with preclinical and clinical development of clevudine, Racivir, R7128, and PSI-7851, particularly our Phase 3 clinical trials for clevudine. In addition, as we expand our operations, we will need to continue to improve our facilities and hire additional personnel. As a result, we expect that our annual operating losses will increase significantly over the next several years.

Our revenue and profit potential is unproven, and our limited operating history makes our future operating results difficult to predict. To attain profitability, we and our collaborators will need to successfully develop products and effectively market and sell them. We have never generated revenue from the sale of products, and there is no guarantee that we will be able to do so in the future. If any of our drug candidates fail to show positive results in ongoing clinical trials, and we or our collaborators do not receive regulatory approval, or if our product candidates do not achieve market acceptance even if approved, we may never become profitable. If we fail to become profitable, or if we are unable to continue to fund our continuing losses, we may be unable to continue our clinical development programs, and you could lose your entire investment.

We will require substantial funds in the future and we may be unable to raise capital when needed, which could force us to delay, reduce or eliminate some of our drug discovery, product development and commercialization activities.

Developing drugs, conducting clinical trials and commercializing products is expensive and we will need to raise substantial additional funds to achieve our strategic objectives. Although we believe our existing cash resources as of September 30, 2008, together with anticipated payments under our existing collaboration agreement, will be sufficient to fund our projected cash requirements for the next 12 months, we will require significant additional financing in the future to fund our operations. Such financing may not be available on acceptable terms, if at all. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;

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the costs and timing of obtaining regulatory approval of our product candidates;

the scope, prioritization and number of our clinical trials and other research and development programs;

the costs of the development and expansion of our operational infrastructure;

the ability of our collaborators to achieve development milestones, marketing approval and other events or developments under our collaboration agreements;

the amount of revenues we receive under our collaboration agreements;

the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;

the costs and timing of securing manufacturing arrangements for clinical or commercial production;

the costs of establishing sales and marketing capabilities or contracting with third parties to provide these capabilities for us;

the costs of acquiring or undertaking development and commercialization efforts for any future product candidates;

the magnitude of our general and administrative expenses; and

any costs that we may incur under current and future licensing arrangements relating to our product candidates.

Our ability to raise additional funds will depend on financial, economic and market conditions and other factors, many of which are beyond our control. Additional financing may not be available when we need it or, if available, may not be on terms that are favorable to us. If we are unable to obtain adequate funding on a timely basis, we may be required to delay, reduce the scope of, or eliminate one or more of our drug discovery or development programs.

Raising additional capital may dilute our stockholders equity, limit our flexibility, or require us to relinquish rights.

We may need to raise additional capital to fund our operations through public or private equity offerings or debt financings. To the extent that we raise additional capital by issuing equity or equity-linked securities, our stockholders ownership will be diluted. Any debt financing we enter into may include covenants that limit our flexibility in conducting our business. We also could be required to seek funds through arrangements with collaborators or others, which might require us to relinquish valuable rights to our intellectual property or product candidates that we would have otherwise retained.

Our success depends in part on our ability to retain and recruit key personnel, and if we fail to do so, it may be more difficult for us to successfully develop our products or achieve our business objectives.

Our success depends in part on our ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent on our senior management and scientific staff, particularly P. Schaefer Price, our Chief Executive Officer, Kurt Leutzinger, our Chief Financial Officer, and M. Michelle Berry, M.D., M.P.H., our Chief Medical Officer . We do not maintain key man insurance for our senior management or scientific staff. The loss of the services of any of our senior management or key members of our scientific staff may significantly delay or prevent the successful completion of our clinical trials or the commercialization of our product candidates. To date, we are not aware

that any member of our senior management or scientific staff plans to leave the company.

The employment of each of our employees with us is at will, and each employee can terminate his or her employment with us at any time. We currently have an employment agreement in place with P. Schaefer Price.

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Our success will also depend on our ability to hire and retain additional qualified scientific and management personnel. Competition for qualified individuals in the pharmaceutical field is intense, and we face competition

from numerous pharmaceutical and biotechnology companies, universities and other research institutions. We may be unable to attract and retain qualified individuals on acceptable terms given the competition for such personnel. For example, in fiscal 2007 we encountered delays in hiring a Chief Medical Officer, since there were only a small number of qualified candidates and many of our competitors had the same or similar needs as we. Furthermore, there is a possibility that a qualified candidate we are recruiting might opt to accept a position with one of our competitors instead of with us because our competitor may have products that are already on the market and generating revenue. If we are unsuccessful in our recruiting efforts, we may be unable to execute our strategy.

The requirements of being a public company may strain our administrative and operational infrastructure and will increase our operating costs.

The obligations of being a public company require significant additional expenditures and place additional demands on our management, administrative, operational, internal audit and accounting resources as we comply with the reporting requirements of a public company. If we are unable to continue to update our procedures and adapt our management, administrative, operational and accounting functions in such a manner so as to meet such obligations in a timely and effective manner, our ability to comply with the rules that apply to public companies could be impaired. In meeting our obligations, we may need to upgrade our systems, implement additional financial and management controls, reporting systems and procedures, implement an internal audit function, and hire additional accounting, audit and financial staff with appropriate public company experience and technical accounting knowledge, which will increase our general and administrative expenses and capital expenditures. The rules and any related regulations that may be proposed in the future that are applicable to public companies may make it more difficult and more costly for us to obtain certain types of insurance, including directors and officers liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher premiums to obtain the same or similar coverage. We cannot predict or estimate the amount or timing of the additional costs we may incur as a result of the reporting requirements applicable to public companies, but we expect our operating results will be adversely affected by the costs of operating as a public company.

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

As of September 30, 2008, we had 67 employees, 46 of whom perform research and development functions. We plan to hire a significant number of additional employees in the future. For example, we expect to hire approximately 20 employees in the next year and plan to hire several additional employees as required in the future to add depth and specialized expertise to our scientific and management team. We expect that this substantial growth will place a strain on our administrative and operational infrastructure. If the product candidates that we are developing continue to advance in clinical trials, we will need to expand our development, regulatory, manufacturing, quality, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to develop additional relationships with various collaborators, contract research organizations, suppliers, manufacturers and other organizations. We may not be able to establish such relationships or may incur significant costs to do so. Our ability to manage our growth will also require us to continue to improve our operational, financial and management controls, reporting systems and procedures, which will further increase our operating costs. If we are unable to successfully manage the expansion of our operations or operate on a larger scale, we will not achieve our strategic objectives.

Our debt obligations include covenants which may adversely affect us.

On September 30, 2007, we entered into a Venture Loan and Security Agreement (Loan Agreement) with a lender. As of September 30, 2008, we had a $20.0 million outstanding principal balance under the Loan Agreement and we are currently negotiating to borrow an additional $3.3 million. Under the Loan Agreement we agreed that in the event our market capitalization is below $90.0 million for 15 consecutive days in which the

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principal market for our common stock is open for trading to the public, we will repay 50% of the then outstanding principal balance of the loans. We further agreed under the Loan Agreement that in the event our market capitalization is below $40.0 million for 15 consecutive days in which the principal market for our common stock is open for trading to the public, we will be required to repay all of the then outstanding principal balance of the loans. In addition, all of our assets other than our intellectual property secure the loans. There is a risk that the lender could obtain rights to the secured assets in the event we default on our obligations under the Loan Agreement.

The Loan Agreement also contains covenants that, among other things, require us to obtain consent from the lender prior to paying dividends, making certain investments, changing the nature of our business, assuming or guaranteeing the indebtedness of another entity or individual, selling or otherwise disposing of a substantial portion of our assets, or merging or consolidating with another entity.

A breach of any of the covenants in the Loan Agreement could result in a default under that agreement. Upon the occurrence of an event of default, the lender could elect to declare all amounts outstanding under the Loan Agreement to be immediately due and payable.

Changes in foreign currency exchange rates could result in increased costs.

We have entered into some agreements denominated, wholly or partly, in foreign currencies, and, in the future, we may enter into additional agreements denominated in foreign currencies. If the values of these currencies increase against the United States dollar, our costs would increase. To date, we have not entered into any contracts to reduce the risk of fluctuations in currency exchange rates. In the future, depending upon the amounts payable under any such agreements, we may enter into forward foreign exchange contracts to reduce the risk of unpredictable changes in these costs. However, due to the variability of timing and amount of payments under any such agreements, foreign exchange contracts may not mitigate the potential adverse impact on our financial results.

Risks Related to Our Dependence on Third Parties

We have licensed PSI-6130 and its pro-drugs, including R7128, to Roche, and we will depend on Roche to continue its development and commercialization.

We are developing R7128 under a collaborative licensing agreement that we entered into with Roche in October 2004. We are dependent on Roche to continue the development of R7128 and successfully commercialize it. Roche may terminate its agreement with us without cause on six months notice. If Roche fails to aggressively pursue the development and marketing approval of R7128, if a dispute arises with Roche over the terms or the interpretation of the collaboration agreement or an alleged breach of any provision of the agreement, or if Roche terminates its agreement, then the development and commercialization of R7128, or our ability to receive the expected payments under this agreement, could be delayed or adversely affected.

Roche is subject to many of the same development and commercialization risks to which we are subject. If Roche decides to devote resources to alternative products, either on its own or in collaboration with other pharmaceutical companies, Roche may not devote sufficient resources to the development of R7128. Further, if Roche decides to pursue additional therapies for HCV, future sales of R7128 could be adversely affected. Any adverse development in Roche s operations or financial condition could adversely affect the development and commercialization of R7128 or other pro-drugs of PSI-6130, and our receipt of future milestone payments and royalties on its sales.

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We and our collaborators depend on third parties to conduct our clinical trials, which may result in costs and delays that prevent us from obtaining regulatory approval or successfully commercializing our product candidates.

We and our collaborators engage clinical investigators and medical institutions to enroll patients/subjects in our clinical trials and contract research organizations to perform data collection and analysis and other aspects of our preclinical studies and clinical trials. As a result, we depend on these third parties to perform these activities on a timely basis in accordance with the clinical protocols, good laboratory practices, good clinical trial practices, and other regulatory requirements. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, if these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or for other reasons, our clinical trials may be

extended, delayed, terminated or our data may be rejected by the FDA. If it became necessary to replace a third party that was conducting one of our clinical trials, we believe that there are a number of other third-party contractors whom we could engage to continue these activities, although it may result in a delay of the applicable clinical trial. If there are delays in testing or obtaining regulatory approvals as a result of a third party s failure to perform, our drug discovery and development costs will increase, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

If parties on whom we rely to manufacture our product candidates do not manufacture the active pharmaceutical ingredients or finished products of satisfactory quality, in a timely manner, in sufficient quantities or at an acceptable cost, clinical development and commercialization of our product candidates could be delayed.

We do not currently own or operate manufacturing facilities. Consequently, we rely on third parties as sole suppliers of clinical investigational quantities of our product candidates. We do not expect to establish our own manufacturing facilities and we will continue to rely on third-party manufacturers to produce commercial quantities of any drugs that we market. Our current and anticipated future dependence on third parties for the manufacture of our product candidates may adversely affect our ability to develop and commercialize any product candidates on a timely and competitive basis.

To date, our product candidates have only been manufactured in quantities sufficient for preclinical studies or initial clinical trials. Other than our agreement with BICI for the manufacture of clinical supplies of the API of clevudine, as well as the eventual commercial manufacture and supply of the API of clevudine, we do not currently have any long-term supply agreements in place for our product candidates and will need to enter into supply agreements for additional supplies of each of our product candidates to complete clinical development and/or commercialize them. Additionally, in connection with our application for commercial approvals and if any product candidate is approved by the FDA or other regulatory agencies for commercial sale, we will need to procure commercial quantities from qualified third-party manufacturers. Other than our agreement with BICI for clevudine, we may not be able to contract for increased manufacturing capacity for any of our product candidates in a timely or economic manner or at all. A significant scale-up in manufacturing may require additional validation studies. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed, or there may be a shortage of supply, which could limit our sales.

Other risks associated with our reliance on contract manufacturers include the following:

- Contract manufacturers may encounter difficulties in achieving volume production, quality control, and quality assurance and also may experience shortages in qualified personnel and obtaining active ingredients for our products.

- If we need to change manufacturers, the FDA and corresponding foreign regulatory agencies must approve these manufacturers in advance. This would involve pre-approval inspections to ensure compliance with FDA and foreign regulations and standards.

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Contract manufacturers are subject to ongoing periodic, unannounced inspection by the FDA and corresponding state and foreign agencies or their designees to ensure strict compliance with cGMP and other governmental regulations and corresponding foreign standards. We do not have control over compliance by our contract manufacturers with these regulations and standards. Our present or future contract manufacturers may not be able to comply with cGMP and other FDA requirements or other regulatory requirements outside the United States. Failure of contract manufacturers to comply with applicable regulations could result in delays, suspensions or withdrawal of approvals, seizures or recalls of product candidates and operating restrictions, any of which could significantly and adversely affect our business.

Contract manufacturers may breach the manufacturing agreements that we or our development partners have with them because of factors beyond our control or may terminate or fail to renew a manufacturing agreement based on their own business priorities at a time that is costly or inconvenient to us.

Changes to the manufacturing process during or following the completion of clinical trials also require sponsors to demonstrate to the FDA that the product manufactured under the new conditions complies with cGMP requirements. This requirement applies to moving manufacturing functions to another facility. In each phase of investigation, sufficient information about changes in the manufacturing process must be submitted to the FDA.

We may experience difficulties in entering into contracts on favorable terms for supplies of our products for future preclinical studies and clinical trials, which could prevent us from completing these studies and delay the commercialization of our products.

Except for our agreement with BICI for the manufacture of clinical supplies of the API of clevudine, as well as the eventual commercial manufacture and supply of the API of clevudine, we will need to enter into supply agreements for additional supplies of each of our product candidates to complete clinical development and/or commercialize them. We cannot assure you that we will be able to do so on favorable terms, if at all.

We will need to procure additional supplies of R7128 to complete our future preclinical studies and clinical trials. Roche is supplying R7128 for our current preclinical studies and clinical trials. We are currently considering additional supply options of R7128. However, we have not yet entered into a definitive supply agreement with any company.

We will need to procure additional supplies of Racivir to complete our future preclinical studies and clinical trials. We are currently in the process of identifying and evaluating the qualifications of potential suppliers that could manufacture Racivir, including the company that manufactured our current supply of Racivir; however, we have not yet entered into a definitive supply agreement with any company.

Incyte was responsible for the clinical trials of DFC and for obtaining sufficient supply of DFC for its trials. If we conduct our own clinical trials of DFC, we will need to establish our own source of supply of DFC.

If conflicts arise between our collaborators and us, our collaborators may act in their best interest and not in our best interest, which could adversely affect our business.

Conflicts may arise with our collaborators if they pursue alternative therapies for the diseases that we have targeted or develop alternative products either on their own or in collaboration with others. Competing products, either developed by our present collaborators or any future collaborators or to which our present collaborators or any future collaborators have rights, may result in development delays or the withdrawal of their support for one or more of our product candidates.

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Additionally, conflicts may arise if there is a dispute about the progress of, or other activities related to, the clinical development of a product candidate, the achievement and payment of a milestone amount or the ownership of intellectual property that is developed during the course of the collaborative arrangement. Similarly, the parties to a collaboration agreement may disagree as to which party owns newly developed products. Should an agreement be terminated as a result of a dispute and before we have realized the benefits of the collaboration, our reputation could be harmed and we might not obtain revenues that we anticipated receiving.

We may rely on other collaborators in the future and if future collaborations are not successful, we may not be able to effectively develop and commercialize our product candidates.

We may decide to enter into future collaborations for the development and commercialization of clevudine, Racivir, DFC, PSI-7851 or other product candidates that we may identify in the future. We may not be successful in entering into any additional collaborations.

Relying on collaborative relationships poses a number of risks to us, including the following:

- we may be required to relinquish important rights, including intellectual property, marketing and distribution rights;
- we will not be able to control whether our collaborators will devote sufficient resources to the development or commercialization of the product candidates we license;
- we will not have access to all information regarding the products being developed and commercialized by our collaborators, including information about clinical trial design and execution, regulatory affairs, process development, manufacturing, marketing and other areas known by our collaborators. Thus, our ability to keep our stockholders informed about the status of our collaborated products will be limited by the degree to which our collaborators keep us informed;
- business combinations or significant changes in a collaborator s business strategy may also adversely affect a collaborator s willingness to actively pursue the development and commercialization of any products resulting from a collaboration;
- a collaborator may separately move forward with a competing product candidate either developed independently or in collaboration with others, including our competitors;
- collaborators with marketing rights may choose to devote fewer resources to the marketing of our products than they do to other products they are selling;
- our collaborators may experience financial difficulties and may be unable to fund the clinical trials, fulfill their obligations under collaboration agreements with us or delay paying us agreed-upon milestone payments, reimbursements, royalties or other committed amounts; and
- disputes may arise between us and our collaborators delaying or terminating the research, development or commercialization of our product candidates, resulting in litigation or arbitration that could be time-consuming and expensive.

A collaborator may terminate its agreement with us or simultaneously pursue alternative products, therapeutic approaches or technologies as a means of developing treatments for the diseases targeted by us or our collaborative effort. If a collaborator terminates its agreement with us, the development or commercialization of our product candidates could be delayed or terminated, or we could be required to undertake unforeseen additional responsibilities or devote unbudgeted additional resources to such development or commercialization.

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If we fail to enter into additional in-licensing agreements or if these arrangements are unsuccessful, our ability to fill our clinical pipeline may be adversely affected.

In addition to entering into collaboration agreements with third parties for the development and commercialization of our product candidates, we intend to continue to explore opportunities to further enhance our discovery and development capabilities and develop our clinical pipeline by in-licensing product candidates that fit within our expertise and research and development capabilities. We will face substantial competition for in-licensing opportunities from companies focused on antiviral therapies, many of which may have greater resources than we do. Additional in-licensing agreements for product candidates may not be available to us, or if available, the terms may not be favorable. We may also need to license additional technologies in order to continue to develop our clinical pipeline. If we are unable to enter into additional agreements to license product candidates or technologies, or if these arrangements are unsuccessful, our clinical pipeline may not contain a sufficient number of promising future product candidates and our research and development efforts could be delayed.

Risks Related to Our Intellectual Property

We licensed Racivir, one of our lead product candidates, from Emory University, and our rights to commercialize Racivir are subject to a right of first refusal held by Gilead, and uncertainties related to these rights may result in us being prevented from obtaining the expected economic benefits from developing Racivir.

We licensed Racivir from Emory University pursuant to an exclusive, worldwide license agreement to make, have made, use, import, offer for sale and sell Racivir, which we entered into in 1998, referred to as the Racivir License Agreement. In a license agreement relating to emtricitabine that Emory University entered into with Triangle Pharmaceuticals, now Gilead Sciences, Inc., or Gilead, in 1996, which we refer to as the Emory/Gilead License Agreement, Emory University previously had granted a right of first refusal to Gilead that is applicable to any license or assignment relating to a specified range of mixtures of ( ) FTC and (+) FTC, referred to as enriched FTC (which includes Racivir). The terms of this right of first refusal contains an exception permitting Emory University to license or assign its rights in respect of enriched FTC to a permitted transferee, which includes any of the inventors (which included two of our founders) or to any corporate entity formed by or on behalf of the inventors for purposes of clinically developing enriched FTC so long as the licensee agrees in writing to be bound by the terms of Gilead s right of first refusal to the same extent as Emory University. Our license to Racivir was granted to us by Emory University pursuant to this exception and therefore we are bound by the terms of Gilead s right of first refusal to the same extent as Emory University. The terms of this right of first refusal as set forth in the Emory/Gilead License Agreement require that, prior to the entry into any license or assignment agreement with a third party relating to any of Emory University s rights in respect of enriched FTC, Emory University shall notify Gilead of the terms of the proposed agreement and provide a copy of the proposed agreement to Gilead together with all data and information in Emory University s possession relating to enriched FTC and its use as a therapeutic agent. Gilead has 30 days to accept or decline the offer. Although Emory University considers us to be a permitted transferee under the Emory/Gilead License Agreement, Emory University has subsequently taken the position that its grant of commercialization rights (i.e., the rights to offer for sale and sell Racivir) to us exceeded the rights that were permitted to be granted to a permitted transferee under its agreement with Gilead. While we believe that Gilead is aware of the Racivir license agreement through both our and Emory University s communications with Gilead, Gilead has not contacted us regarding its interpretation of the terms of the Racivir License Agreement.

In March 2004, we entered into a supplemental agreement with Emory University in which we and Emory University agreed that, prior to any commercialization of enriched FTC by us, or by any licensee or assignee of our rights under the Racivir License Agreement, we and Emory University would adhere strictly to the terms of the right of first refusal granted to Gilead in the Emory/Gilead License Agreement and offer to Gilead the same terms and conditions under which we, our licensee or our assignee, propose to commercialize enriched FTC. The supplemental agreement also outlines a procedure by which Emory University and we would jointly offer the

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terms of a proposed license and commercialization agreement between us and a third party to Gilead after Emory University has the opportunity to approve them. Therefore, before we could enter into a commercialization agreement for Racivir with a third party or commercialize Racivir on our own, we would be required to offer Gilead the opportunity to be our commercialization partner on the same terms on which we intend, or our prospective partner intends, to commercialize Racivir. It is uncertain whether a third party would be willing to negotiate the terms of a commercialization agreement with us knowing that Gilead can take their place as licensee by accepting the negotiated terms and exercising its right of first refusal.

These uncertainties related to our commercialization rights may result in us being prevented from obtaining the expected economic benefits from developing Racivir. In addition, we could become involved in litigation or arbitration related to our commercialization rights to Racivir in the future.

If we are unable to obtain and maintain adequate patent protection for our product candidates, we may be unable to commercialize our product candidates or to prevent other companies from using our intellectual property in competitive products in certain countries.

Our commercial success will depend, in large part, on our ability and the ability of our licensors to obtain and maintain patents and proprietary intellectual property rights sufficient to prevent others from marketing our product candidates, as well as to successfully defend and enforce those patents against infringement and to avoid infringing the proprietary rights of others, both in the United States and in foreign countries. Roche and we have filed patent applications for R7128, and we have filed and may in the future file our own patent applications for our other technology. We have also licensed certain patents, patent applications and other proprietary rights from third parties. We have licensed patents for clevudine, Racivir and DFC. The patent covering the composition of matter for clevudine that we have licensed from Bukwang is scheduled to expire in January 2014. The patent covering the composition of matter for Racivir that we have licensed from Emory University is scheduled to

expire in September 2015. The patent covering methods of using DFC to treat HIV that we have licensed from Emory University is scheduled to expire in January 2015. The patent expiration dates stated above do not take into account any patent term adjustments that may accrue due to procedural delays by the United States Patent and Trademark Office or patent term extensions that may accrue due to regulatory delays.

Our patent position, like that of many pharmaceutical and biotechnology companies, is uncertain and involves complex legal and factual questions for which important legal principles are unresolved. We may not develop or obtain rights to products or processes that are patentable. Even if we or our licensors do obtain patents, such patents may not adequately protect the products or technologies we own or have licensed. In addition, we generally do not control the patent prosecution of subject matter that we license from others. Generally, the patent holders are primarily responsible for the patent prosecution and maintenance activities pertaining to the licensed patent applications and patents, while we are afforded opportunities to advise the primary licensors on such activities with respect to our licensed territories. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we would over our own. Others may challenge, seek to invalidate, infringe or circumvent any patents we own or license, and rights we receive under those patents may not provide competitive advantages to us. We cannot assure you as to the degree of protection that we will be afforded by any patents issued to, or licensed by, us. The laws of many countries may not protect intellectual property rights to the same extent as U.S. laws, and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, we may not be able to prevent a third party from infringing our patents in a country that does not recognize or enforce patent rights, or that imposes compulsory licenses on or restricts the prices of life-saving drugs. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property.

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The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our or our licensors pending patent applications and issued patents, and we may have to participate in expensive and protracted interference proceedings to determine priority of invention;
- we or our licensors might not have been the first to file patent applications for these inventions;
- our or our licensors pending patent applications may not result in issued patents;
- our or our licensors issued patents may not provide a basis for commercially viable products or may not provide us with any competitive advantages or may be challenged by third parties;
- others may design around our or our licensors patent claims to produce competitive products which fall outside the scope of our or our licensors patents; or
- the patents of others may prevent us from marketing one or more of our product candidates for one or more indications that may be valuable to our business strategy.

An issued patent does not guarantee us the right to practice the patented technology or commercialize the patented product. Third parties may have or obtain rights to blocking patents that could be used to prevent us from commercializing our patented products and practicing our patented technology. Our issued patents and those that may be issued in the future may be challenged, invalidated or circumvented, which could limit our ability to prevent competitors from marketing related product candidates or could limit the length of the term of patent protection of our product candidates. In addition, the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against competitors with similar technology and our competitors may independently develop similar technologies. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our product candidates can be commercialized, any related patent or potential patent extension may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent.

We may incur substantial costs or lose important rights as a result of litigation or other proceedings relating to patent and other intellectual property rights.

The defense and prosecution of intellectual property rights, U.S. Patent and Trademark Office interference proceedings and related legal and administrative proceedings in the United States and elsewhere are costly and time-consuming and their outcome is uncertain. In general, there is a substantial amount of litigation involving patent and other intellectual property rights in the biopharmaceutical industry. Litigation may be necessary to:

- assert or defend claims of infringement;
- enforce patents we own or license;
- protect trade secrets; or

determine the enforceability, scope and validity of the proprietary rights of others.

If we become involved in any litigation, interference or other administrative proceeding, we will incur substantial expense and it will divert the efforts of our scientific and management personnel. Uncertainties resulting from the initiation and continuation of litigation, interference or other administrative proceedings could have a material adverse effect on our ability to compete in the marketplace pending resolution of the disputed matters. An adverse determination may subject us to significant liabilities or require us to seek licenses that may not be available from third parties on commercially reasonable terms, if at all. We or our collaborators may be restricted or prevented from developing and commercializing our products in the event of an adverse

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determination in a judicial or administrative proceeding or if we fail to obtain necessary licenses. In such event, we may attempt to redesign our processes or technologies so that they do not infringe, which may not be commercially reasonable or technically possible.

While our product candidates are in clinical trials, we believe that the use of our product candidates in these clinical trials falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. As our product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We attempt to ensure that our product candidates and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

If we find during clinical evaluation that our product candidates for the treatment of HIV, HBV or HCV should be used in combination with a product that is covered by a patent held by another company or institution, and that a labeling instruction is required in product packaging recommending that combination, we could be accused of, or held liable for, infringement of the third-party patents covering the product recommended for co-administration with our product. In such a case, we could be required to obtain a license from the other company or institution to use the required or desired package labeling, which may not be available on commercially reasonable terms, or at all.

We may be subject to claims that our board members, employees or consultants or we have used or disclosed alleged trade secrets or other proprietary information belonging to third parties and any such individuals that are currently affiliated with one of our competitors may disclose our proprietary technology or information.

As is commonplace in the biotechnology and pharmaceutical industries, some of our board members, employees and consultants are or have been employed at, or associated with, other biotechnology or pharmaceutical companies that compete with us. While employed at or associated with these companies, these individuals may become exposed to or involved in research and technology similar to the areas of research and technology in which we are engaged. We may be subject to claims that we, or our employees, board members or

consultants, have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information of those companies. Litigation may be necessary to defend against such claims.

We have entered into confidentiality agreements with all of our employees. However, we do not have, and are not planning to enter into, any confidentiality agreements with our directors because they have a fiduciary duty of confidentiality as directors. There is the possibility that any of our former board members, employees or consultants who are currently employed at, or associated with, one of our competitors may unintentionally or willfully disclose our proprietary technology or information.

The rights we rely upon to protect our unpatented trade secrets may be inadequate.

We rely on unpatented trade secrets, know-how and technology, which are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval process. We seek to protect trade secrets, in part, by entering into confidentiality agreements with employees, consultants and others. These parties may breach or terminate these agreements, and we may not have adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection for our trade secrets or other proprietary information or result in the effective assignment to us of intellectual property, and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential information or other breaches of the agreements. Despite our efforts to protect our trade secrets, we or our collaboration partners, board members, employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors.

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There is a risk that our trade secrets could have been, or could, in the future, be shared by any of our former employees with and be used to the benefit of any company that competes with us. For example, a former director and founder of Pharmasset has, along with several of our former scientists, started a new pharmaceutical company to develop drugs to treat viral infections (including human retroviral and hepatitis infections), cancer and dermatological conditions, which may compete with us in the future. These individuals left Pharmasset in 2005. We have a confidentiality agreement in place with our former director, and have both confidentiality agreements and covenant not to compete agreements in place with the former scientists. The term of the confidentiality agreements is indefinite with regard to any confidential information that is not subsequently made public. The covenant not to compete agreements expired on February 28, 2007.

If we fail to maintain trade secret protection, our competitive position may be adversely affected. Competitors may also independently discover our trade secrets. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secrets against them and our business could be harmed.

Risks Related to Our Industry

Our industry is extremely competitive. If our competitors are able to develop and market products that are more effective, safer or more affordable than ours, or obtain marketing approval before we do, our commercial opportunities may be limited.

Competition in the biotechnology and pharmaceutical industries is intense and continues to increase, particularly in the area of antiviral drugs. Many companies are pursuing the development of novel drugs that target the same diseases we are targeting. There are a significant number of drugs that are approved or currently under development that will become available in the future for the treatment of HBV, HCV and HIV and other viral infections. If any of the product candidates that our competitors are developing are successful, we will have difficulty gaining market share.

We face a broad range of current and potential competitors, from established global pharmaceutical companies with significant resources to development-stage companies. Listed below are some of the pharmaceutical and biotechnology companies developing compounds targeting HBV, HCV and HIV and other viral infections.

HBV: Gilead Sciences has recently received EU and US approval for Viread® (tenofovir) for the treatment of HBV in April and August 2008, respectively. Our HBV product candidate may compete directly or be used in combination with the current standard of care, with the drug candidates that are currently in development and with those that may be developed in the future.

HCV: Alpha interferon, a component of the current standard of care, is approved in several chemically modified forms and is marketed by Roche, Schering-Plough and Three Rivers Pharmaceuticals. Roche, Schering-Plough and several generic manufacturers market ribavirin, which is the other component of the current standard of care for HCV. Roche and other companies, such as Valeant Pharmaceuticals International, Vertex Pharmaceuticals Incorporated, ViroPharma Incorporated, Gilead Sciences, Inc, Intermune, Schering-Plough, Novartis/Human Genome Sciences, and Idenix, are also developing new drugs for the treatment of HCV.

HIV: Pharmaceutical companies such as Pfizer Inc. and Merck & Co., Inc. and biotechnology companies such as Gilead Sciences, Inc., Incyte Corporation, Avexa Limited, Achillion Pharmaceuticals, Inc., Panacos Pharmaceuticals, Inc. and Human Genome Sciences, Inc. are developing compounds targeting HIV. We also believe that a significant number of drugs are currently under development and will become available in the future for the treatment of HIV. In addition, we are aware that Merck and other companies are pursuing the development of a prophylactic vaccine, which would prevent infections. If a prophylactic vaccine is successful, it could reduce the size of the market for our products.

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In addition, we face competition from academic and research institutions and government agencies for the discovery, development and commercialization of novel therapeutics to treat HIV, HBV and HCV. Some early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies.

Many of our competitors have:

- significantly greater financial, technical and human resources than we have and may be better equipped to develop, manufacture and market products;
- more extensive experience in preclinical studies and clinical trials, obtaining regulatory approvals and manufacturing and marketing products; and
- products that have already been approved or are in the late stage of development and operate large, well-funded research and development programs.

Our competitors may succeed in developing or commercializing more effective, safer or more affordable products, which would render our product candidates less competitive or noncompetitive. Our competitors may discover technologies and techniques, or enter into partnerships with collaborators, in order to develop competing products that are more effective or less costly than the products we develop. This may render our technology or products obsolete and noncompetitive. These competitors also compete with us to recruit and retain qualified scientific and management personnel, establish clinical trials sites and patient registration for clinical trials, as well as to acquire technologies and technology licenses complementary to our programs or advantageous to our business. Moreover, competitors that are able to achieve patent protection, obtain regulatory approvals and commence commercial sales of their products before we do, and competitors who have already done so, will enjoy a significant competitive advantage. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

If we successfully develop and obtain approval for our product candidates, we will face competition for market share based on the safety and efficacy of our products, the timing and scope of regulatory approvals, the availability of supply, marketing and sales capability, reimbursement coverage, price, patent position and other factors.

If third-party payors do not adequately reimburse patients for any of our product candidates, that are approved for marketing, we may not be successful in selling them.

Our ability to commercialize any products successfully will depend in part on the extent to which reimbursement will be available from governmental and other third-party payors, both in the United States and in foreign markets. Even if we succeed in bringing one or more products to the market, the amount reimbursed for our products may be insufficient to allow our products to compete effectively with products that are reimbursed at a higher level. If the price we are able to charge for any products we develop is inadequate in light of our development costs, our profitability could be adversely affected.

Reimbursement by governmental and other third-party payors may depend upon a number of factors, including the governmental and other third-party payors determination that the use of a product is:

- a covered benefit under their health plan or part of their formulary;
- safe, effective and medically necessary;
- appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

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Obtaining reimbursement approval for a product from each third-party and government payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor. We may not be able to provide data sufficient to obtain reimbursement.

Eligibility for coverage does not imply that any drug product will be reimbursed in all cases or at a rate that allows us to make a profit. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not become permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or Medicare or Medicaid data used to calculate these rates. Net prices for products also may be reduced by mandatory discounts or rebates required by government health care programs or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the United States.

The health care industry is experiencing a trend toward containing or reducing costs through various means, including lowering reimbursement rates, limiting therapeutic class coverage and negotiating reduced payment schedules with service providers for drug products. The Medicare Prescription Drug, Improvement and Modernization Act of 2003, or the MMA, created a broader prescription drug benefit for Medicare beneficiaries. The MMA also contains provisions intended to reduce or eliminate delays in the introduction of generic drug competition at the end of patent or nonpatent market exclusivity. The impact of the MMA on drug prices and new drug utilization over the next several years is unknown. The MMA also made adjustments to the physician fee schedule and the measure by which prescription drugs are presently paid. The effects of these changes are unknown but may include decreased utilization of new medicines in physician prescribing patterns, and further pressure on drug company sponsors to provide discount programs and reimbursement support programs. There have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect reimbursement levels for our future products. In addition, the Centers for Medicare and Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates and may have sufficient market power to demand significant price reductions. Future legislation may also limit the prices that can be charged for drugs we develop.

Foreign governments tend to impose strict price controls, which may adversely affect our future profitability.

In most foreign countries, particularly in the European Union, prescription drug pricing and/or reimbursement is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our profitability will be negatively affected.

Even if we achieve market acceptance for our products, we may experience downward pricing pressure on the price of our drugs because of generic competition and social pressure to lower the cost of drugs to treat HIV, HBV and HCV.

Several of the FDA-approved individual and combination products face patent expiration in the next several years. The following table lists expected patent expiration dates of FDA-approved individual and combination products the patents for which are expected to expire in the next several years and that we expect may compete

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with our product candidates, according to the FDA s compilation of patents covering approved drug products in a collection entitled Approved Drug Products with Therapeutic Equivalence Evaluations (known universally as the Orange Book).

Drug Brand Name	Patent Expiry Date or Range of Patent Expiry Dates*
Epivir-HBV	November 17, 2009 to May 18, 2016
Hepsera	April 21, 2006 to July 23, 2018
Baraclude	March 29, 2010
Epivir	November 17, 2009 to May 18, 2016
Emtriva	May 11, 2010 to March 9, 2021
Videx	August 29, 2006 to July 22, 2011
Ziagen	December 18, 2011 to May 14, 2018
Hivid	November 7, 2006 to July 2, 2008
Combivir	September 17, 2005 to May 18, 2016
Truvada	May 11, 2010 to March 9, 2021
Atripla	May 11, 2010 to March 9, 2021
Epzicom	December 18, 2011 to May 14, 2018
Trizivir	September 17, 2005 to May 14, 2018
Tyzeka	August 10, 2019

* These dates do not take into account any patent term adjustments that may accrue due to procedural delays by the United States Patent and Trademark Office or patent term extensions that may accrue due to regulatory delays nor any exclusivity periods granted by the FDA.

As a result, generic versions of these drugs may become available. We expect to face competition from these generic drugs, including price-based competition.

Pressure from AIDS awareness and other social activist groups to reduce HIV drug prices may also put downward pressure on the prices of HIV drugs, including Racivir and DFC if they are commercialized. Similar trends of generic competition or social pressure may occur for HBV or HCV, which would result in downward pressure on the price for clevudine, R7128 or PSI-7851, if they are commercialized.

We face a risk of product liability claims and if we are not able to obtain adequate liability insurance, a product liability claim could result in substantial liabilities.

Our business exposes us to the risk of significant potential product liability claims that are inherent in the manufacturing, testing and marketing of human therapeutic products, and we will face an even greater risk if our

collaborators or we sell any products commercially. Regardless of their merit or eventual outcome, product liability claims may result in:

- delay or failure to complete our clinical trials;
- withdrawal of clinical trial participants and difficulty in recruiting participants;
- inability to commercialize our product candidates;
- decreased demand for our product candidates;
- injury to our reputation;

inability to establish new collaborations;

litigation costs;

substantial monetary awards against us; and

diversion of management or other resources from key aspects of our operations.

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Product liability claims could result in an FDA investigation of the safety or efficacy of our products, our manufacturing processes and facilities or our marketing programs. An FDA investigation could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the indications for which they may be used, or suspension or withdrawal of approval.

We currently have product liability insurance that covers our clinical trials for up to $15.0 million for each occurrence and up to a $15.0 million annual aggregate limit, subject to deductibles of $50,000 per occurrence and $250,000 annual aggregate limit and coverage limitations. We intend to increase our insurance coverage and include the sale of commercial products if marketing approval is obtained. Because insurance coverage is becoming increasingly expensive, we may not be able to obtain or maintain adequate protection against potential product liabilities at a reasonable cost or at all, and the insurance coverage that we obtain may not be adequate to cover potential claims or losses.

We may incur significant costs to comply with laws regulating the protection of health and human safety and the environment, and failure to comply with these laws and regulations could expose us to significant liabilities.

Our research and development activities involve the controlled use of numerous hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations, and may be subject to foreign laws and regulations, governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products, including certain regulations promulgated by the U.S. Environmental Protection Agency, or EPA. The EPA regulations to which we are subject require that we register with the EPA as a generator of hazardous waste. The risk of accidental contamination or injury from the handling, transporting and disposing of hazardous materials and waste products cannot be entirely eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposures to blood-borne pathogens and the handling, transporting and disposing of biohazardous or radioactive materials. Although we maintain workers compensation insurance to cover us for the costs and expenses we may incur if our employees are injured as a result of using these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain, nor do we plan to obtain, additional insurance coverage relating to damage claims arising from our use of hazardous materials. Further, we may be required to indemnify our collaborators or licensees against damages and other liabilities arising out of our development activities or products. Compliance with the applicable environmental and workplace laws and regulations is expensive. Future changes to environmental, health, workplace and safety laws could cause us to incur additional expenses or may restrict our operations or impair our research, development and production efforts.

Risks Related to our Common Stock

Our stock price is volatile.

The stock market in general, and the market for clinical-stage pharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has often been unrelated or disproportionate to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price for our common stock.

In this market environment, the sale of a substantial number of shares of our common stock in the public market or the perception that such a sale might occur would likely have an adverse effect on the market price of our common stock. We have a number of investors who hold relatively large positions in our securities. A decision by any of these investors to sell all or a block of their holdings of our common stock could cause our stock price to drop significantly.

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The market also continues to experience significant price and volume fluctuations, some of which are unrelated to the operating performance of particular companies. Since our IPO, the price of our common stock has fluctuated significantly and may continue to do so in the future. Many factors could have a significant effect on the market price for our common stock, including:

- adverse results or delays in our clinical trials or the clinical trials of our collaborators;
- announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;
- adverse actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities;
- introductions or announcements of new products or technological innovations or pricing by our competitors;
- the loss of a significant collaborator;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to patent our product candidates and technologies;
- changes in estimates of our financial performance by securities analysts or failure to meet or exceed securities analysts or investors expectations of our annual or quarterly financial results, clinical results or our achievement of any milestones or changes in securities analysts recommendations regarding our common stock, other comparable companies or our industry generally;
- fluctuations in stock market prices and trading volumes of similar companies or of the markets generally;
- changes in accounting principles;
- sales of large blocks of our common stock, or the expectation that such sales may occur, including sales by our executive officers, directors and significant stockholders;
- issuance of new shares of common stock in future offerings, or upon the exercise of existing warrants;
- issuance of convertible debt;
- discussion of our business, products, financial performance, prospects or our stock price by the financial and scientific press and online investor communities, such as chat rooms;

regulatory developments in the United States and abroad;

third-party healthcare reimbursement policies;

conditions or trends in the pharmaceutical and biotechnology industries;

departures of key personnel;

announcements by us or our competitors of significant acquisitions, strategic partnerships, clinical trial results, joint ventures or capital commitments; and

actual or anticipated variations in our annual or quarterly operating results.

Any litigation brought against us as a result of this volatility could result in substantial costs and a diversion of our management s attention and resources, which could negatively impact our financial condition, results of operations, and the price of our common stock.

If we raise additional capital by issuing equity securities in a fluctuating market, many or all of our existing stockholders may experience substantial dilution, and if we need to raise capital by issuing equity securities at a time when our stock price is lower, we may have difficulty raising sufficient capital to meet our requirements. If any of the risks described in these RISK FACTORS occurred, or if any unforeseen risk affected our performance, it could have a dramatic and adverse impact on the market price of our common stock.

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Provisions of our amended and restated certificate of incorporation, bylaws and Delaware law could delay or discourage another company from acquiring us and may prevent attempts by our stockholders to replace or remove our current management.

Provisions of our amended and restated certificate of incorporation, bylaws and Delaware law may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable. In addition, these provisions could make it more difficult for our stockholders to replace or remove our board of directors.

These provisions include:

- the application of a Delaware law prohibiting us from entering into a business combination with the beneficial owner of 15% or more of our outstanding voting stock for a period of three years after such 15% or greater owner first reached that level of stock ownership, unless we meet specified criteria;
- authorizing the issuance of preferred stock with rights that may be senior to those of our common stock without any further vote or action by the holders of our common stock;
- providing for a classified board of directors with staggered terms;
- requiring that our stockholders provide advance notice when nominating our directors or proposing matters that can be acted on by stockholders at stockholders meetings;
- eliminating the ability of our stockholders to convene a stockholders meeting; and
- prohibiting our stockholders from acting by written consent.

Our executive officers, directors and current principal stockholders own a large percentage of our voting common stock and could limit new stockholders influence on corporate decisions.

As of September 30, 2008, our executive officers, directors, current holders of more than 5% of our outstanding common stock and their respective affiliates beneficially own, in the aggregate, approximately 47.7% of our outstanding common stock. These stockholders, acting together, would be able to exert significant influence over all matters requiring approval by our stockholders, including mergers, sales of assets, the election of directors, the approval of mergers or other significant corporate transactions. The interests of these stockholders may not always coincide with our corporate interests or the interests of other stockholders, and they may act in a manner with which you may not agree or that may not be in the best interests of our other stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

In July 2005, we relocated our operations to Princeton, New Jersey from Atlanta, Georgia. On May 23, 2005, we entered into a lease for a 30,800 square foot building that has 12,000 square feet of laboratory space and approximately 18,000 square feet of administrative offices in Princeton, New Jersey. The annual occupancy expense under this lease is approximately $834,423. This lease expires on May 22, 2010 and may be extended for a total of an additional 10 years. These facilities are equipped to perform drug research activities. In April 2007, we also entered into a lease for office space in Durham, North Carolina. The annual occupancy expense under this lease is approximately $82,183. This lease

expires on April 30, 2009 and may be extended for a total of an additional three years.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings.

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 began trading on the Global Market of The NASDAQ Stock Market LLC (NASDAQ) on April 27, 2007 under the symbol VRUS. Prior to that time, there was no established public trading market for our common stock. The following table sets forth for the periods indicated the high and low closing sale prices per share of our common stock as reported by NASDAQ:

Fiscal Year Ended September 30, 2008:	High	Low
Fourth fiscal quarter 2008	$ 24.68	$ 17.62
Third fiscal quarter 2008	$ 20.47	$ 13.43
Second fiscal quarter 2008	$ 36.44	$ 13.50
First fiscal quarter 2008	$ 14.73	$ 11.96
Fiscal Year Ended September 30, 2007:		
Fourth fiscal quarter 2007	$ 12.60	$ 8.06
Third fiscal quarter (beginning April 27, 2007)	$ 9.42	$ 7.54

Holders of Record

As of November 30, 2008, there were 28 holders of record of our common stock.

Comparative Stock Performance

The following graph and related information should not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

CUMULATIVE TOTAL RETURN

(Based on an initial investment of $100.00 on April 27, 2007 using

end of the quarter closing prices for each of the three investment options.)

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Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future. Moreover, under the terms of our Loan Agreement with our lender, we are not permitted to pay any dividends without its written consent.

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ITEM 6. SELECTED FINANCIAL DATA

The following table presents our selected financial information. In 2005, we changed our fiscal year end from December 31 to September 30 for financial reporting purposes. The change was effective for the nine-month period ended September 30, 2005. The statement of operations data for the years ended September 30, 2008, 2007 and 2006 and the balance sheet data as of September 30, 2008 and 2007 have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. In the opinion of management, the unaudited selected financial data presented below reflect all adjustments necessary for a fair presentation of this data. The statement of operations data for the nine months ended September 30, 2005 and the year ended December 31, 2004, and the balance sheet data as of September 30, 2005 and December 31, 2004 have been derived from our audited financial statements that are not included in this Annual Report on Form 10-K. The results from the nine-month period ended September 30, 2005 are not indicative of results that would have been achieved for the twelve-month period ended September 30, 2005.

The selected financial data set forth below should be read together with our financial statements and the related notes to those financial statements, as well as Management s Discussion and Analysis of Financial Condition and Results of Operations, appearing elsewhere in this Annual Report on Form 10-K. The historical results are not necessarily indicative of results to be expected in any future period.

	Years Ended September 30,			Nine Months Ended	Year Ended
	2008	2007	2006	September 30, 2005	December 31, 2004
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Revenues:					
Contract revenues	$ 1,857	$ 22,010	$ 5,425	$ 3,719	$ 2,208
Government grant revenues					545
Total revenues	1,857	22,010	5,425	3,719	2,753
Cost and expenses:					
Research and development	42,996	20,319	10,498	10,468	5,317
General and administrative	13,289	9,211	7,912	8,096	2,898
Total costs and expenses	56,285	29,530	18,410	18,564	8,215
Operating loss	(54,428)	(7,520)	(12,985)	(14,845)	(5,462)
Investment income (1)	1,986	2,471	1,659	1,136	495
Interest expense	(2,216)	(15)			
Loss before income taxes	(54,658)	(5,064)	(11,326)	(13,709)	(4,967)
Provision for income taxes					17
Net loss	(54,658)	(5,064)	(11,326)	(13,709)	(4,984)
Redeemable preferred stock accetion (1)		1,776	1,111	2,287	1,317
Net loss attributable to common stockholders	$ (54,658)	$ (6,840)	$ (12,437)	$ (15,996)	$ (6,301)
Net loss per common share:					
Basic	$ (2.51)	$ (0.46)	$ (1.19)	$ (2.42)	$ (1.53)
Diluted	$ (2.51)	$ (0.46)	$ (1.19)	$ (2.42)	$ (1.53)
Weighted average number of shares used in per common share calculations:					
Basic (1)	21,808,283	14,990,472	10,462,369	6,630,463	4,110,997
Diluted (1)	21,808,283	14,990,472	10,462,369	6,630,463	4,110,997

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	As of September 30,			Nine Months Ended	
	2008	2007	2006	September 30, 2005	As of Dec. 31, 2004
		(in thousands)			
Balance Sheet Data:					
Cash and cash equivalents (1)	$ 63,073	$ 68,746	$ 26,182	$ 33,442	$ 307
Short-term investments	497	1,252	1,250	12,007	54,932
Working capital	52,425	60,764	25,004	38,822	51,687
Total assets (1)	68,982	75,844	32,998	47,441	57,417
Deferred revenue	5,726	7,583	9,168	12,044	12,136
Current portion of and long-term debt, net	19,174				
Redeemable convertible preferred stock (1)			19,641	18,530	50,178
Total stockholders equity (deficit) (1)	$ 35,187	$ 58,936	$ (220)	$ 11,668	$ (7,431)

(1) On May 2, 2007, we completed our IPO of 5,050,000 shares of our common stock at a public offering price of $9.00 per share. Net cash proceeds from the initial public offering were $40.7 million after deducting offering costs paid during fiscal 2007 and $39.1 million after deducting additional offering costs paid in fiscal 2006.

In connection with the IPO, the outstanding shares of our Series B, Series C, Series D and Series R redeemable convertible preferred stock, our Series A convertible preferred stock, and our redeemable common stock were converted into 4,405,683 shares of our common stock as of May 2, 2007. In addition, holders of our Series D redeemable convertible preferred stock were entitled to receive quarterly dividends at a rate equal to 7.5% per annum of the purchase price per share. Such dividends accrued from February 4, 2006 through May 2, 2007 and were paid out in the form of 131,864 shares of our common stock. Our Series D-1 warrants were also exercised in full in connection with our IPO on a net exercise basis, which resulted in us issuing 822,689 shares of our common stock to the warrant holders.

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

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our audited financial statements and related notes appearing elsewhere in this report. In addition to historical information, this discussion and analysis contains forward-looking statements based on current expectations that involve risks, uncertainties and assumptions, such as our plans, objectives, expectations and intentions set forth in the Cautionary Statement Regarding Forward-Looking Statements, which can be found at the beginning of this report, and in Item 1A, Risk Factors. Our actual results and the timing of events may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth in the Risk Factors section and elsewhere in this report.

Overview

We are a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Our primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus, or HBV, hepatitis C virus, or HCV, and human immunodeficiency virus, or HIV. Our research and development efforts focus on a class of compounds known as nucleoside analogs, which act to inhibit the natural enzymes required for viral replication. We currently have three clinical-stage product candidates, two of which we are developing ourselves and one of which we are developing with a strategic partner:

- Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central, and South America (the Americas) and Europe;
- R7128, a pro-drug of PSI-6130 for the treatment of HCV, has completed Phase 1 clinical trials in combination with Pegasys plus Copegus through a strategic collaboration with F. Hoffmann-LaRoche Ltd. and Hoffmann-La Roche Inc. (collectively, Roche); and
- Racivir, for the treatment of HIV, which has completed a Phase 2 clinical trial.

We have also identified proprietary, next generation HCV development candidates that are being evaluated for advancement into clinical development. One of these compounds, PSI-7851, was recently nominated as a lead candidate and is being advanced into Good Laboratory Practice (GLP) toxicity studies required for submission of an IND application with the FDA or an equivalent foreign regulatory filing.

Clevudine

Clevudine is an oral, once-daily pyrimidine nucleoside analog that we are developing for the treatment of HBV. We licensed clevudine from Bukwang, a Korean pharmaceutical company. Bukwang received final product approval from Korean regulators in December 2006 and commercially launched clevudine in the Korean market in February 2007 under the brand name Levovir. In two completed Korean Phase 3 clinical trials in 337 patients, Studies 301 and 302, clevudine demonstrated the ability to significantly reduce HBV viral load in patients to undetectable levels and normalized liver enzyme levels. Furthermore, in Study 302, 16% of the e-antigen negative patients who had received clevudine demonstrated a sustained virologic response (SVR) 24 weeks after stopping therapy, versus 0% of the patients who had received the placebo. In March 2006, Bukwang completed Study 303, a Korean open-label follow-on study of clevudine in 55 HBV patients, including 15 e-antigen negative patients and who were treatment-naïve patients. The results of Study 303 are consistent with the results of Studies 301 and 302 in terms of significantly reducing HBV viral load in patients to undetectable levels and normalizing liver enzyme levels. Additionally, in Study 303, 80% of e-antigen negative patients sustained a viral load that was undetectable 12 weeks after completing the 48-week course of therapy.

We initiated two Phase 3 clinical trials of clevudine for registration in the Americas and Europe during the third calendar quarter of 2007. The clevudine registration studies include two 48-week Phase 3 clinical trials

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designed to test the superiority of once-daily doses of clevudine 30mg over Hepsera 10mg (adefovir) on predetermined primary and secondary endpoints. Study 305 will be conducted in approximately 376 e-antigen positive patients, and Study 306 will be conducted in approximately 480 e-antigen negative patients. The primary endpoint of these registration studies is expected to be a composite endpoint measuring the percentage of patients with undetectable HBV DNA (less than 300 copies/ml) and the normalization of liver enzyme levels at 48 weeks on therapy. We plan to continue the clevudine Phase 3 studies from week 48 to week 96 to gather additional safety and efficacy data, as well as assess clevudine s SVR rate for HBV.

R7128

During September 2008, we completed the clinical activities in Part 3 of a Phase 1 clinical trial with R7128 that was initiated by Roche and us in October 2006 under an IND filing. This expanded Phase 1 trial was a multiple center, observer-blinded, randomized and placebo-controlled study designed to investigate the pharmacokinetics, pharmacodynamics, safety, tolerability and food effect of R7128 in healthy volunteers and in patients chronically infected with HCV genotype 1, 2 or 3. This Phase 1 trial also provided antiviral potency data over 14 and 28 days in patients chronically infected with HCV genotype 1 and following 28 days of treatment in patients chronically-infected with HCV genotypes 2 or 3. This adaptive Phase 1 study was comprised of three parts:

Part 1 was a single ascending dose study conducted in 46 healthy volunteers. The primary objective of Part 1 was to assess the safety, tolerability and pharmacokinetics of R7128 following single ascending doses under fasting conditions. The secondary objective of Part 1 was to explore the effect of food on the pharmacokinetics of R7128. Single oral doses of R7128 were administered to 46 healthy volunteers in five sequential dose groups (500 mg, 1500 mg, 4500 mg, 6000 mg and 9000 mg) and one food effect group (1500 mg). Results from the single ascending dose portion of the study indicated:

- All doses of R7128 studied (500 mg to 9000 mg) were generally safe and well-tolerated.
- All patients completed the study, and none experienced gastrointestinal adverse events or serious adverse events during the study.
- No hematologic or other safety laboratory abnormalities of clinical significance were noted.
- No maximum tolerated dose was identified.

Part 2 was a multiple ascending dose study conducted in 40 patients chronically infected with HCV genotype 1 who had previously failed interferon therapy. The primary objective of Part 2 was to assess the safety, tolerability and pharmacokinetics of R7128 after once-daily (QD) or twice-daily (BID) dosing for 14 days. The secondary objective was to assess antiviral efficacy by measuring the change in HCV RNA. Results from the multiple ascending dose portion of the study indicated:

- R7128 demonstrated potent, dose-dependent antiviral activity in four patient cohorts (8 active, 2 placebo per cohort) receiving 750 mg or 1500 mg administered either QD or BID for 14 days as monotherapy. The maximum decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg BID. R7128 demonstrated mean HCV RNA decreases from baseline of 0.9 log (87.4% reduction), 1.5 log (96.8% reduction), 2.1 log (99.2% reduction) and 2.7 log (99.8% reduction) in patients receiving 750 mg QD, 1500 mg QD, 750 mg BID and 1500 mg BID, respectively. Based on the mean data, all four dose groups reached nadir values at Day 15. A maximum 4.2 log (99.9% reduction) HCV RNA decrease was demonstrated in a patient following 14 days of monotherapy with 1500 mg BID of R7128, a value also below the level of detection, which was less than 15 International Units per milliliter (IU/ml).

There was no evidence of viral rebound in any dose cohort during the 14 days of dosing.

R7128 was generally safe and well tolerated over 14 days of treatment of patients chronically infected with HCV genotype 1 who had previously failed interferon therapy. There were no serious adverse events, no adverse events requiring dose modification, and no dose-related gastrointestinal adverse events.

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Part 3 was a 4-week study of R7128 in combination with the current standard of care for chronic HCV infection, Pegasys (pegylated interferon) plus Copegus (ribavirin) in 81 treatment-naïve patients chronically infected with HCV genotype 1, and additionally, in 25 prior treatment non-responders, or patients who did not achieve an SVR with previous interferon-based therapy, who were chronically infected with HCV genotypes 2 or 3. The primary objective of this study was to assess the safety, tolerability, and pharmacokinetics of R7128 in the clinically-relevant setting of combination therapy with the current standard of care for chronic HCV infection. The secondary objective of Part 3 was to evaluate the short-term change in HCV RNA. The study included three oral dose regimens of R7128 (500 mg, 1500 mg and 1000 mg cohorts 1,2 and 3, respectively) in patients chronically infected with HCV genotype 1 and one oral dose regimen of R7128 (1500 mg cohort 4) in patients chronically infected with HCV genotypes 2 or 3. All four dose regimens were administered twice-daily with Pegasys plus Copegus for 4 weeks. Dose cohorts 1, 2 and 4 enrolled 25 patients, with 20 patients randomized to receive R7128 and five patients randomized to receive placebo, and cohort 3 enrolled 31 patients, with 25 patients randomized to receive R7128 and six patients randomized to receive placebo, all administered in combination with standard of care. After completing four weeks of the triple combination regimen and a follow-up of four weeks of Pegasys plus Copegus, all patients are scheduled to receive up to 40 weeks of open-label standard of care dosing under a separate protocol.

Results from cohorts 1, 2 and 3 in 81 treatment-naïve patients chronically infected with HCV genotype 1 indicated:

Following 4 weeks of treatment with R7128 500mg BID with Pegasys plus Copegus (cohort 1), patients achieved a mean 3.8 log10 IU/mL decrease in HCV RNA and 30% (6 of 20) achieved undetectable levels of HCV RNA (<15 IU/ml), or rapid virologic response (RVR).

Following 4 weeks of treatment with R7128 1500mg BID with Pegasys plus Copegus (cohort 2), patients achieved a mean 5.1 log10 IU/mL decrease in HCV RNA and 85% (17 of 20) achieved RVR.

Following 4 weeks of treatment with R7128 1000mg BID with Pegasys plus Copegus (cohort 3), preliminary results indicated patients achieved a mean 5.1 log10 IU/mL decrease in HCV RNA and 88% (22 of 25) patients achieved RVR.

Following 4 weeks of treatment with placebo with Pegasys plus Copegus, patients achieved a mean 2.9 log10 IU/mL decrease in HCV RNA and 18.75% (3 of 16) achieved RVR.

For cohorts 1, 2 and 3 in treatment-naïve genotype 1 patients, safety and tolerability for the 4-week treatment period were similar for R7128 with Pegasys plus Copegus compared to placebo with Pegasys plus Copegus. There were no serious adverse events reported during the 4-week treatment periods of triple therapy, and most of the adverse events reported were of mild to moderate intensity. Headache and fatigue were the most frequently reported adverse events in patients who received active R7128 plus Pegasys plus Copegus, with an overall frequency of 66% and 42% reporting at least one of these events, respectively. These events were also the most frequently reported adverse events in patients who received placebo with Pegasys and Copegus. In general, the adverse events reported were consistent with the clinical safety profile for Pegasys and Copegus, including the frequency and severity of these adverse events, as well as any general body system observations. Grade 3/4 neutropenia was observed in 31% of the placebo patients and in 12% to 30% of the R7128 patients in each active dosing cohort. Grade 3 changes in hemoglobin were observed in 19% of the placebo patients and in 31% of the R7128 patients. There were no clinically significant changes in hepatic, renal, or other safety laboratory parameters, vital signs, or electrocardiograms. Overall, there was no clinical evidence of any major organ toxicities related to R7128. One patient in the active treatment group discontinued the study during the 4 week treatment period due to lower-gastrointestinal adverse events. At the time of study discontinuation, this patient had undetectable HCV RNA. R7128 was generally safe and well-tolerated when administered for 4 weeks in combinations with Pegasus plus Copegus in patients with HCV genotype 1.

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Results from the 1500 mg dose cohort (cohort 4) in 25 prior treatment non-responders, or patients who did not achieve an SVR with previous interferon-based therapy, and who were chronically infected with HCV genotypes 2 or 3 indicated:

Following 4 weeks of treatment with R7128 1500mg BID with Pegasys plus Copegus (cohort 4), preliminary results indicated patients achieved a mean 5.0 $\log_{10}$ IU/mL decrease in HCV RNA and 90% (18 of 20) patients achieved RVR.

Following 4 weeks of treatment with placebo with Pegasys plus Copegus, patients achieved a mean 3.7 $\log_{10}$ IU/mL decrease in HCV RNA and 60.0% (3 of 5) achieved RVR.

For cohort 4, safety and tolerability during the 4-week treatment period were similar for R7128 with Pegasys plus Copegus compared to placebo with Pegasys plus Copegus. There were no serious adverse events reported during the 4-week treatment period, and most of the adverse events reported were of mild to moderate intensity. One subject discontinued R7128, Pegasys and Copegus due to protocol specified stopping criteria (not treatment-emergent), and ECG changes. Adverse events reported in cohort 4 were similar to those reported in Cohorts 1-3. Grade 3/4 neutropenia was observed in 0% of the 5 placebo patients and in 20% of the 20 R7128 patients in the active dosing cohort. Grade 3 changes in hemoglobin were observed in 20% of the placebo patients and in 25% of the R7128 patients. There were no clinically significant changes in hepatic, renal, or other safety laboratory parameters, vital signs, or electrocardiograms. As seen in the patients infected with HCV genotype 1, there was no clinical evidence of any major organ toxicities related to R7128. R7128 was generally safe and well-tolerated when administered for 4 weeks in combination with Pegasus plus Copegus in patients with HCV genotypes 2 and 3.

We cannot guarantee that the final results of this study or any future study of R7128 will corroborate earlier results, and further testing will be required to provide sufficient evidence regarding safety and efficacy to support an NDA filing with the FDA in the future. We and Roche expect to meet with the FDA during January 2009 to discuss a Phase 2b study plan, as well as additional studies to support desired product label claims.

On October 12, 2007, we were informed by the FDA that R7128 received fast track designation.

Mechanism of Action. In a study evaluating the mechanism of action of PSI-6130, the compound was found to be active against the HCV RNA polymerase by terminating HCV RNA synthesis.

Preclinical Development. We and Roche have performed and will continue to perform in vitro and animal studies to determine the preclinical pharmacokinetics and safety of PSI-6130 administered as its pro-drug, R7128. PSI-6130 did not cause genetic mutations or cellular damage in preclinical models. The goal of longer-term animal studies is to identify the potential target organs and to determine the reversibility and monitorability of changes to their function and physical structure. In general, following single and repeated doses, R7128 was well tolerated in mice (up to 13 weeks), rats (up to 6 months), and dogs (up to 4 weeks) up to the highest doses tested (2000 mg/kg/day) for repeat dose studies. Manifestations of toxicity in monkeys, the most sensitive species tested, appeared to be time and dose dependent, causing significant changes in the kidney.

Oral administration of R7128 at doses of 200, 600 and 2000 mg/kg/day in monkeys, in a study designed to be six months but stopped at 13 weeks, did not establish a No Observed Adverse Effect Level (NOAEL) dose. A thorough examination of the monkeys tissues in every organ system determined that the only significant treatment-related pathology changes were confined to the glomeruli of the kidney. We believe these changes were dose-related, appearing in all animals in the high and middle dose groups and one animal in the low dose group, in which the glomerulopathy appeared in a much milder form. No scarring was observed, so changes were considered likely to be reversible.

A second long-term R7128 safety study in monkeys began in April 2008 at doses of 10, 40, 100, and 600 mg/kg/day, administered for 13 weeks in preparation for the start of a Phase 2b study in which humans are

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expected to receive R7128 for up to 12 weeks. Histopathology data confirmed the glomerulopathy findings in the previous study. In addition, in animals that had been followed for an additional 8 weeks after treatment was stopped, renal function had returned to normal as measured by standard tests of kidney function. Therefore, we believe the changes in kidney function observed in monkeys are both reversible and monitorable. In this study, we established a NOAEL dose in monkeys over 13 weeks.

In January 2008, Roche completed the dosing portion of a six month safety study of R7128 in rats. The results of this study revealed no toxicities at any dose level tested, which were 200, 600 and 2000 mg/kg/day.

In 2008, Roche completed a 13 week safety study of R7128 in mice. The results of this study showed that the drug was well tolerated with no observable toxicities at any dose level tested, which were 200, 600 and 2000 mg/kg/day.

Species-specific differences in drug metabolism and excretion that may render the monkey more susceptible to the pathology changes observed with R7128 than the rat or humans continue to be under review.

PSI-7851

We are developing PSI-7851 for the treatment of HCV. PSI-7851 was nominated as a lead candidate and has advanced into preclinical safety studies required for submission of an IND application with the FDA or an equivalent foreign regulatory filing. This pyrimidine nucleotide analog is being investigated as part of our research and development efforts to identify another compound that might be used in a proprietary combination treatment for HCV.

In vitro antiviral testing has shown that this compound is approximately 20 fold more potent than PSI-6130. In animal studies following oral dosing, PSI-7851 preferentially localizes in liver cells where it is efficiently converted to the active triphosphate form. The rapid and efficient delivery to liver cells and the improved in vitro potency observed in our early preclinical studies may allow for lower and less frequent dosing in the clinic. We anticipate filing an IND with the FDA during the first calendar quarter of 2009.

Purine Research

We are researching a third generation of nucleosides and nucleotides utilizing a purine base with the goal of generating a product candidate that has comparable activity to PSI-7851 and a resistance profile that is complementary to PSI-7851 to enable a proprietary fixed-dose combination that has the potential to eliminate or reduce the use of interferon for the treatment of HCV.

Racivir

Racivir is an oral, once-daily deoxycytidine nucleoside analog that we are developing as an HIV therapy for use in combination with other approved HIV drugs. In a recently completed Phase 2 clinical trial, for the subset of patients carrying the M184V mutation and less than three thymidine analog mutations, replacing lamivudine with Racivir in their existing combination therapies caused a mean decrease in plasma HIV RNA of 0.7 log (80% reduction) in the second week of treatment. Twenty-eight percent of these patients achieved an undetectable level of virus (less than 400 copies per milliliter) and 64% of these patients achieved at least a 0.5 log decrease (68% reduction) in plasma HIV RNA.

DFC

DFC is an oral, once-daily cytidine nucleoside analog. We had been developing DFC in collaboration with Incyte Corporation (Incyte) until April 2006 when Incyte terminated our collaborative and license agreements and returned its rights related to DFC to us. We have analyzed the preclinical and clinical data on DFC generated by Incyte. A path for further development of DFC has not yet been identified.

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Results of all prior clinical trials do not provide enough evidence to support an NDA filing with the FDA and additional trials will be needed. Results of all of our ongoing trials and any future trials we may conduct may not corroborate earlier results.

We have incurred substantial operating losses since our inception because we have devoted substantially all of our resources to our research and development activities and have not generated any revenue from the sale of approved drugs. As of September 30, 2008, we had an accumulated deficit of $111.8 million. We expect our operating losses to increase for at least the next several years as we continue to pursue the clinical development of clevudine, Racivir and our other product candidates, and as we expand our discovery and development pipeline. We expect our compensation expense to increase in the future as well, as we implement our planned increase in the number of our employees.

We have funded our operations primarily through the sale of equity securities, payments received under collaboration agreements, borrowings under our Loan Agreement, government grants and interest earned on investments. We expect to continue to fund our operations over the next several years through the net proceeds of our completed public offerings, our existing cash resources, borrowings under our Loan Agreement, potential future milestone payments that we expect to receive from Roche if certain conditions are satisfied, interest earned on our investments and additional capital to be raised through public or private equity offerings or debt financings. We will require significant additional financing in the future to fund our operations. Additional financing may not be available on acceptable terms, if at all. As of September 30, 2008, we had approximately $63.1 million of cash and cash equivalents and approximately $0.5 million of short-term investments.

Revenues

All of our product candidates are currently in development, and, therefore, we do not expect to generate any direct revenues from drug product sales for at least the next several years, if at all. Our revenues to date have been generated primarily from milestone payments under our collaboration agreements, license fees, research funding and grants. We currently have one collaboration agreement with Roche for the development of PSI-6130, its pro-drugs. We entered into our collaboration agreement with Roche in October 2004. Roche subsequently paid us an up-front payment of $8.0 million. Pursuant to the terms of our collaboration agreement with Roche, we did not receive any milestone payments during the year ended September 30, 2008. As of September 30, 2008, we had received an aggregate of $33.0 million in payments under the Roche collaboration agreement, including research funding and related fees as well as up-front and milestone payments.

Under the current terms of the Roche collaboration agreement, if we succeed in obtaining all of the regulatory approvals specified in the agreement for PSI-6130 or a pro-drug of PSI-6130, including R7128, as of September 30, 2008 the maximum future development and commercialization milestone payments payable to us are $115.0 million. Receipt of any additional milestone payments depends on many factors, some of which are beyond our control. We cannot assure you that we will receive any of these future payments. Additional milestone funding may be payable to us if molecules in addition to PSI-6130 or its pro-drugs are developed under the Roche agreement.

We expect our revenues for the next several years to be derived primarily from payments under our current collaboration agreement with Roche and any additional collaborations that we may enter into in the future. In addition to the payments described above, we may receive future royalties on product sales, if any, under our collaboration agreement with Roche.

Research and Development Expenses

Our research and development expenses consist primarily of salaries and related personnel expenses, fees paid to external service providers, up-front and milestone payments under our license agreements, patent-related legal fees, costs of preclinical studies and clinical trials, drug and laboratory supplies and costs for facilities and

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equipment. We use external service providers to manufacture our product candidates for clinical trials and for the majority of our preclinical and clinical development work. We charge all research and development expenses to operations as they are incurred. Our development activities are primarily focused on the development of clevudine, Racivir and R7128, and our research activities are primarily focused on discovering and developing novel drugs such as PSI-7851, to treat viral infections. We are responsible for all costs incurred in the future in the clinical development of clevudine for registration in the Americas, Europe and certain other territories, where we have the rights to develop and commercialize clevudine, which we in-licensed from Bukwang. We are responsible for all costs incurred in the clinical development of Racivir, as well as the research costs associated with our other internal research programs. Under our collaboration with Roche, Roche will fund the clinical development and commercialization of PSI-6130 and its pro-drugs, including R7128. Under this collaboration, Roche reimbursed us for all of the external expenses associated with, and we were responsible for, certain preclinical work, the IND filing, and the proof-of-concept clinical trial. Going forward, Roche will fund all of the expenses of, and be responsible for, other preclinical studies and future clinical development. We will continue to develop and retain worldwide rights to ongoing and future HCV programs unrelated to the PSI-6130 series of nucleoside polymerase inhibitors licensed to Roche. Incyte had been funding the clinical development and commercialization of DFC, but since its return to us by Incyte in April 2006, we are responsible for any additional expenses.

We are currently focused on advancing the clinical development of clevudine, Racivir and R7128 (in collaboration with Roche), as well as advancing the preclinical development of PSI-7851. We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis. These determinations will be made in response to the scientific and clinical success of each product candidate, as well as an ongoing assessment as to the product candidate s commercial potential. Clevudine is in Phase 3 registration clinical trials which commenced dosing during the third calendar quarter of 2007. We currently estimate it will cost approximately $54.0 million, excluding internal personnel costs associated with conducting these two registration trials, to progress clevudine s clinical program from September 30, 2008 to the point of enabling the filing of an NDA with the FDA. We do not believe, however, that it is possible at this time to accurately project total program-specific expenses through commercialization for clevudine or any of our other product candidates, as there are numerous factors associated with the successful commercialization of any of our drug candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Product candidates that may appear promising at early stages of development may not reach the market for a number of reasons. Product candidates may be found ineffective or may cause harmful side effects during clinical trials, may take longer to progress through clinical trials than anticipated, may fail to receive necessary regulatory approvals and may prove impracticable to manufacture in commercial quantities at reasonable cost and with acceptable quality. The lengthy process of seeking FDA approvals requires the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining regulatory approvals could materially adversely affect our product development efforts. Because of these risks and uncertainties, we cannot predict when or whether we will successfully complete the development of our product candidates, or the ultimate product development cost or whether we will obtain any approval required by the FDA on a timely basis, if at all.

As we obtain results from clinical trials, we may elect to discontinue or delay preliminary studies or clinical trials for a product candidate or development program in order to focus our resources on more promising product candidates or programs. We expect our research and development expenses to increase substantially as we continue the clinical development of clevudine and Racivir and as we continue our research and development activities. The maximum aggregate future milestone payments related to clevudine that we will have to pay to Bukwang if we succeed in obtaining all of the regulatory approvals and reach all marketing milestones specified in our agreement with Bukwang are $23.0 million. Additionally, we may pay up to an aggregate of $3.9 million in future milestone payments related to development and regulatory events under our license agreement for dioxolane thymine (DOT) with RFS Pharma LLC.

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General and Administrative Expenses

General and administrative expenses consist primarily of compensation for employees in executive and operational functions, including accounting, finance, legal, business development, investor relations, information technology and human resources. Other significant general and administration costs include facilities costs and professional fees for outside accounting and legal services, travel, insurance premiums and depreciation.

Results of Operations

Year Ended September 30, 2008 Compared with Year Ended September 30, 2007

Revenues. Revenues were $1.9 million and $22.0 million during 2008 and 2007, respectively. Revenues during 2008 and 2007 reflect amortization of upfront and subsequent collaborative and license payments received from Roche previously recorded as deferred revenue of $1.9 million and $2.0 million, respectively, and the revenues from the year ago period include milestone payments totaling $20.0 million received pursuant to our Roche collaboration.

The following is a reconciliation between cash payments received under contract revenue agreements and contract revenues reported:

	Years Ended September 30,	
	2008	2007
	(in thousands)	
Cash received/receivable	$	$ 20,425
Deferred		(375)
Amortization	1,857	1,959
Revenues	$ 1,857	$ 22,009

Research and Development Expenses. Research and development expenses increased to $43.0 million during 2008 from $20.3 million in 2007. This net increase of $22.7 million consists primarily of a $16.5 million increase in Phase 3 registration clinical trial expenses for clevudine, an increase in compensation expenses of $4.0 million ($1.1 million of which was non-cash stock compensation expense) resulting from an increase in headcount, and a $2.7 million increase in new drug discovery expenses, including PSI-7851. Partially offsetting this increase was a $0.5 million reduction in Phase 2 clinical trial expenses for Racivir during 2008, compared to the same period in 2007.

General and Administrative Expenses. General and administrative expenses were $13.3 million during 2008, an increase of $4.1 million from $9.2 million in 2007. The increase of $4.1 million was due primarily to increases in compensation expenses of $0.9 ($0.2 million of which was non-cash stock compensation expense), legal expenses of $0.7 million, insurance expenses of $0.6 million, audit and related fees of $0.6 million (including consulting fees in support of our compliance with Section 404 of the Sarbanes-Oxley Act of 2002), marketing expenses of $0.5 million, facility expenses of $0.2 million, and miscellaneous administrative expenses of $0.6 million.

Investment Income. Investment income decreased to $2.0 million in 2008 from $2.5 million in 2007. The decrease was primarily due to lower rates of return on the average invested cash balances.

Interest Expense. Interest expense increased to $2.2 million in 2008 from $0.0 million in 2007. The $2.2 million of interest expense in 2008 is from $20.0 million of long-term debt we incurred during 2008 ($10.0 million on October 5, 2007 and $10.0 million on March 28, 2008).

Income Taxes. As of September 30, 2008, we had United States federal net operating loss carryforwards of approximately $88.0 million available to offset future taxable income, if any. Of the federal net operating losses,

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$8.8 million was generated from windfall tax benefit stock option deductions. The tax benefit of this portion of the net operating loss will be accounted for directly to equity as additional paid in capital as the stock option related losses are utilized. As of September 30, 2008 we also had research and development tax credits of approximately $0.1 million available to offset future tax liabilities. As of September 30, 2008, we had a net deferred tax asset of $36.9 million, before consideration of a valuation allowance. We established a full valuation allowance on our net deferred tax asset as it is more likely than not that such tax benefits will not be realized. The loss carryovers and the research and development tax credits expire over a period of 2020 to 2029.

Preferred Stock Accretion. Preferred stock accretion was $1.8 million in 2007. There has been no redeemable preferred stock accretion subsequent to May 2, 2007 (when we completed our IPO) because all of the redeemable preferred stock outstanding was converted into common stock upon completion of our IPO.

Year Ended September 30, 2007 Compared with Year Ended September 30, 2006

Revenues. Revenues increased to $22.0 million in 2007 from $5.4 million in 2006. This $16.6 million increase in revenues was due primarily to our receipt of milestone payments from Roche totaling $20.0 million during 2007. In 2006, $3.2 million of the $5.4 million of revenues was related to our license agreement with Incyte ($2.8 million of which represented accelerated recognition of deferred revenue caused by Incyte s termination of this license agreement in April 2006).

The following is a reconciliation between cash payments received under contract revenue agreements and contract revenues reported:

	Years Ended September 30,	
	2007	2006
	(in thousands)	
Cash received/receivable	$ 20,425	$ 2,548
Deferred	(375)	(2,500)
Amortization	1,959	5,377
Revenues	$ 22,009	$ 5,425

Research and Development Expenses. Research and development expenses were $20.3 million in 2007 and $10.5 million in 2006. This net increase of $9.8 million consists primarily of a $6.8 million increase in Phase 3 registration clinical trial expenses for clevudine, a $1.7 million increase in new drug discovery expenses and related laboratory operating expenses, $0.5 million in depreciation expense, and $0.8 million of non-cash stock compensation expenses (primarily resulting from the adoption of Statement of Financial Accounting Standards (SFAS) No. 123R, Share-Based Payment (SFAS 123R) on October 1, 2006).

General and Administrative Expenses. General and administrative expenses were $9.2 million in 2007 and $7.9 million in 2006. The increase of $1.3 million was due to an increase in non-cash stock compensation expenses of $1.0 million (resulting from the adoption of SFAS 123R on October 1, 2006), increased compensation expenses of $0.2 million resulting from an increase in headcount, an increase in insurance expense of $0.4 million, and increases in travel and other general and administrative expenses of $0.5 million. These increases were partially offset by decreases in legal and audit fees of $0.6 million and relocation expenses of $0.2 million during 2007, compared to 2006.

Investment Income. Investment income was $2.5 million in 2007 and $1.7 million in 2006. The increase was due to higher average invested cash balances during 2007, compared to 2006, as a result of our investment of the net proceeds of our IPO, which closed on May 2, 2007.

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Income Taxes. As of September 30, 2007, we had United States federal net operating loss carryforwards of approximately $25.1 million available to offset future taxable income, if any. As of September 30, 2007 we also had research and development tax credits of approximately $0.1 million available to offset future tax liabilities. As of September 30, 2007, we had a net deferred tax asset of $17.0 million, before consideration of a valuation allowance. We established a full valuation allowance on our net deferred tax asset as it is more likely than not that such tax benefits will not be realized. The loss carryovers and the research and development tax credits expire over a period of 2020 to 2028.

Preferred Stock Accretion. Preferred stock accretion was $1.8 million during 2007 and $1.1 million in 2006. The accretion recorded during 2007 includes $1.0 million of accretion to bring the carrying amounts of the redeemable convertible preferred stock to their redemption values as of May 2, 2007, the date we completed our IPO and converted all of our then outstanding redeemable convertible preferred stock into our common stock.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily through public and private offerings of our equity securities, payments received under our collaboration agreements, borrowings under our Loan Agreement and government grants. Since our inception, we have raised approximately $129.6 million in net proceeds from sales of our equity securities, including $24.1 million from our follow-on common stock offering completed on July 21, 2008, and $40.7 million from our IPO, completed May 2, 2007, after deducting offering costs paid during fiscal 2007 ($39.1 million after deducting additional offering costs paid in fiscal 2006). During the fiscal year ended September 30, 2008, we also borrowed $20.0 million under our Loan Agreement entered into on September 30, 2007. At September 30, 2008, we held approximately $63.1 million in cash and cash equivalents and approximately $0.5 million of short-term investments, and have invested substantially all of our available cash funds in short-term U.S. Treasury securities through mutual and money market funds.

Net cash provided by (used in) operating activities was ($52.1) million, $0.9 million, and ($14.6) million during the years ended September 30, 2008, 2007 and 2006, respectively. The $53.0 million increase in net cash used in operating activities during 2008, as compared to 2007, was due to (1) a decrease in revenues of $20.2 million, as the revenues from the year ago period include milestone payments totaling $20.0 million from Roche, (2) an increase in cash outflows for operating expenses (including interest expense) of $27.6 million primarily resulting from our Phase 3 clinical trials for clevudine, and (3) an increase of $5.2 million of cash outflows associated with changes in operating assets and liabilities. The $15.5 million reduction in net cash used in operating activities during 2007, as compared to 2006, was due primarily to increased revenues of $16.6 million resulting from the receipt of $20.0 million of milestone payments from Roche during 2007.

Net cash (used in) provided by investing activities was ($0.2) million, ($0.4) million, and $8.5 million during the years ended September 30, 2008, 2007 and 2006, respectively. The cash used in investing activities during 2008 of $0.2 million consists of $0.9 million of purchases of equipment (and leasehold improvements) that were partially offset by cash proceeds received from the maturity of certain short-term investments of $0.7 million. The net cash used in investing activities in 2007 of $0.4 million was for the purchases of equipment (and leasehold improvements). The net cash provided by investing activities in 2006 included proceeds from the sale of investments of $10.8 million. Such investments were sold to fund our operations. No such investments were sold during 2007, as milestone payments received from Roche were used to fund operations. Partially offsetting this cash inflow in 2006 were purchases of equipment and leasehold improvements of $2.3 million for our lab and office space in Princeton, New Jersey.

Net cash provided by (used in) financing activities was $46.6 million, $42.1 million and ($1.1) million, during the years ended September 30, 2008, 2007 and 2006, respectively. The net cash provided by financing activities during the year ended September 30, 2008 includes $24.1 million of net proceeds, after deducting placement agent fees and offering expenses, from the registered direct public offering we completed in July

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2008, borrowings of long-term debt of $20.0 million under the Loan Agreement we entered into during September 2007, and proceeds from the exercise of stock options of $2.6 million. The net cash provided by financing activities during 2007 includes net proceeds from our IPO of $40.7 million after deducting offering costs paid during fiscal 2007, along with proceeds from the exercise of stock options of $1.6 million. Net cash used in financing activities in 2006 resulted from IPO offering costs paid of $1.5 million that were partially offset by proceeds from the exercise of stock options of $0.3 million.

On September 30, 2007, we entered into a Loan Agreement that allowed us to borrow up to $30.0 million in $10.0 million increments. We borrowed the first and second $10.0 million increments by signing two Secured Promissory Notes (Notes) on October 5, 2007 and March 28, 2008, respectively. The Notes bear interest at 12% and are to be repaid over a 45-month period with the first 15 monthly payments representing interest only followed by 30 equal monthly payments of principal and interest. The principal monthly repayments on the first $10.0 million begin on March 1, 2009 and end on August 1, 2011. The principal monthly repayments on the second $10.0 million begin on August 1, 2009 and end on January 1, 2012. Total principal repayments of the two Notes amount to $2.7 million in fiscal 2009, $7.6 million in fiscal 2010, $8.2 million in fiscal 2011, and $1.5 million in fiscal 2012. We are currently in the process of amending the Loan Agreement to extend the commitment beyond its original expiration date of November 30, 2008 and to draw down $3.3 million, and no more, of the remaining facility. Prepayment of the loans made pursuant to the Loan Agreement is subject to penalty and substantially all of our tangible and intangible assets (except for intellectual property) are collateral for the Loan Agreement.

Under the Loan Agreement, we agreed that in the event our market capitalization is below $90.0 million for 15 consecutive days in which the principal market for our common stock is open for trading to the public, we will repay 50% of the then outstanding principal balance of the loans. We further agreed that in the event our market capitalization is below $40.0 million for 15 consecutive days in which the principal market for our common stock is open for trading to the public, we will repay all of the then outstanding principal balance of the loans.

The Loan Agreement also contains covenants that, among other things, require us to obtain consent from the lender prior to paying dividends, making certain investments, changing the nature of our business, assuming or guaranteeing the indebtedness of another entity or individual, selling or otherwise disposing of a substantial portion of our assets, or merging or consolidating with another entity.

Developing drugs, conducting clinical trials and commercializing products is expensive and we will need to raise substantial additional funds to achieve our strategic objectives. Although we believe our existing cash resources, together with anticipated payments under our existing collaboration agreements, will be sufficient to fund our projected cash requirements for the next 12 months, we will require significant additional financing in the future to complete our clinical trials for clevudine and fund our other operations. Additional financing may not be available on acceptable terms, if at all. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- the amount of revenues we receive under our collaboration agreements;
- the costs of the development and expansion of our operational infrastructure;
- the costs and timing of obtaining regulatory approval of our product candidates;
- the ability of our collaborators to achieve development milestones, marketing approval and other events or developments under our collaboration agreements;
- the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;

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the costs and timing of securing manufacturing arrangements for clinical or commercial production;

the costs of establishing sales and marketing capabilities or contracting with third parties to provide these capabilities for us;

the costs of acquiring or undertaking development and commercialization efforts for any future product candidates;

the magnitude of our general and administrative expenses; and

any costs that we may incur under current and future licensing arrangements relating to our product candidates.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through payments received under our collaborations, debt or equity financings, or by out-licensing other product candidates. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts.

Contractual Obligations and Commitments

In May 2005, we entered into an operating lease for office and laboratory space through May 22, 2010, in Princeton, New Jersey. In April 2007, we entered into a lease for office space in Durham, North Carolina through April 30, 2009. In December 2006, we entered into a capital lease for lab equipment with monthly payments beginning in January 2007 through December 2008. In October 2007 and March 2008, we executed two secured promissory notes totaling $20.0 million. Pursuant to the terms of the secured promissory notes, we are required to make payments of interest only for the first 15 months followed by 30 equal monthly payments of principal and interest. As of September 30, 2008, future payments under the Loan Agreement, capital leases and minimum future payments under non-cancellable operating leases are as follows:

	Payments Due By Period				
	Total	Less than 1 year	1-3 Years	4-5 Years	After 5 Years
			(In thousands)		
Long term debt obligations					
Debt maturities	$ 20,000	$ 2,652	$ 15,836	$ 1,512	$
Contractual interest	4,749	2,336	2,375	38	
Capital lease obligations					
Debt maturities	42	42			
Contractual interest					
Operating leases	1,343	835	508		
Purchase obligations					
Total contractual obligations	$ 26,134	$ 5,865	$ 18,719	$ 1,550	$

The above contractual obligations table does not include amounts for milestone payments related to development, regulatory or commercialization events to licensors or collaboration partners, as the payments are contingent on the achievement of these milestones, which we have not achieved. DOT, which we licensed from RFS Pharma, is in the early stage of research and therefore it is not possible to predict when we would need to make a milestone payment. We may pay up to an aggregate of $4.5 million in milestone payments and certain cost reimbursements if we reach milestones related to development and regulatory events under our license agreement with RFS Pharma LLC. We also agreed to pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments under our license agreement for DFC. Under our collaboration and license agreement with Bukwang, in the future we may pay up to an aggregate of $23.0 million in milestone payments related to development, regulatory and commercialization events. Under our license agreement with Emory University for Racivir, we agreed to pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments.

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Off-Balance Sheet Transactions

To date, we have not had any relationships with unconsolidated entities or financial partnerships, such as entities referred to as structured finance or special purpose entities, which are established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and related disclosures. We review our estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Our actual results may differ substantially from these estimates under different assumptions or conditions. Our significant accounting policies are described in more detail in Note 2 of the Notes to Financial Statements included elsewhere in this Annual Report on Form 10-K; however, we believe that the following accounting policies are critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition We recognize revenues in accordance with the Securities and Exchange Commission (SEC) Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition* (*SAB No. 104*). SAB No. 104 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectibility is reasonably assured. For arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets, we follow the guidance of Emerging Issues Task Force (EITF) No. 00-21, *Revenue Arrangements with Multiple Deliverable*s. In accordance with SAB No. 104 and EITF No. 00-21, the elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the collaborator and whether there is objective and reliable evidence of the fair value of the undelivered obligation(s). The consideration received is allocated among the separate units either on the basis of each unit s fair value or using the residual method, and the applicable revenue recognition criteria are applied to each of the separate units.

Our revenues are primarily related to our collaboration agreements, and these agreements provide for various types of payments to us, including non-refundable upfront license fees, research and development payments, and milestone payments.

Where we have continuing performance obligations under the terms of a collaboration agreement, non-refundable upfront license payments received upon contract signing are recorded as deferred revenue and recognized as revenue as the related activities are performed. The period over which these activities are to be performed is based upon our estimate of the development period. Changes in our estimate could change the period over which revenue is recognized. Payments for research funding are recognized as revenues as the related research activities are performed.

We recognize revenue from milestone payments when earned, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) we do not have ongoing performance obligations. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment is non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved to achieve the milestone; and the amount of the milestone appears reasonable in relation to the effort expended, the other milestones in the arrangement and the related risk associated with the achievement of the milestone. Any amounts received under the agreements in advance of performance, if deemed substantive, are recorded as deferred revenue and recognized as revenue as we complete our performance obligations.

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Where we have no continuing involvement under a collaborative arrangement, we record nonrefundable license fee revenues when we have the contractual right to receive the payment, in accordance with the terms of the license agreement, and records milestones upon appropriate notification to us of achievement of the milestones by the collaborative partner.

Deferred revenues associated with a non-refundable payment received under a collaborative agreement that is terminated prior to its completion result in an immediate recognition of the deferred revenues.

Accrued Expenses

We are required to estimate accrued expenses as part of our process of preparing financial statements. This process involves estimating the level of service performed on our behalf and the associated cost incurred in instances where we have not been invoiced or otherwise notified of actual costs. Examples of areas in which subjective judgments may be required include costs associated with services provided by contract organizations for preclinical development, clinical trials and manufacturing of clinical materials. We account for expenses associated with these external services by determining the total cost of a given study based on the terms of the related contract. We accrue for costs incurred as the services are being provided by monitoring the status of the trials and the invoices received from our external service providers. In the case of clinical trials, the estimated cost normally relates to the projected costs of treating the patients in our trials, which we recognize over the estimated term of the trial according to the number of patients enrolled in the trial on an ongoing basis, beginning with patient enrollment. As actual costs become known to us, we adjust our accruals. To date, the number of clinical trials and related research service agreements has been relatively limited and our estimates have not differed significantly from the actual costs incurred. We expect, however, as clinical trials for clevudine, Racivir and R7128 advance, that our estimated accruals for clinical and research services will be more material to our operations in future periods.

Stock-based Compensation

We account for stock-based compensation arrangements in accordance with the provisions of SFAS 123R. SFAS 123R requires companies to recognize stock compensation expense for awards of equity instruments based on grant-date fair value of those awards (with limited exceptions). We adopted SFAS 123R using the modified prospective method, which results in recognition of compensation expense for all share-based awards granted or modified after October 1, 2006 as well as all unvested awards outstanding at the date of adoption. The cost is recognized as compensation expense over the life of the instruments, based upon the grant-date fair value of the equity or liability instruments issued. Prior to October 1, 2006, we accounted for stock-based employee compensation arrangements in accordance with the provisions of Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25) and related interpretations and had adopted the pro forma disclosure option for stock-based employee compensation under SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS No. 123). In accordance with EITF-96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, equity instruments granted to consultants are periodically valued and recorded as stock compensation expense as the equity instrument vests.

Recently Issued Accounting Standards

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements* (SFAS 157). This standard defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles and expands disclosures about fair value measurements. SFAS 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years. The adoption of SFAS 157 is not expected to have a material impact on us.

On February 15, 2007, the Financial Accounting Standards Board (FASB) issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities, including an amendment of FASB Statement No. 115* (SFAS 159). SFAS 159 permits companies to choose to measure many financial instruments and

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certain other items at fair value that are not currently required to be measured at fair value and establishes presentation and disclosure requirements designed to facilitate comparisons between companies that choose different measurement attributes for similar types of assets and liabilities. SFAS 159 is effective for fiscal years beginning after November 15, 2007. The adoption of SFAS 159 is not expected to have a material impact on us.

In June 2007, the EITF reached a consensus on Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities* (*EITF 07-3*). Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities should be deferred and capitalized. Such amounts should be recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided. This Issue is effective for financial statements issued for fiscal years beginning after December 15, 2007, and earlier application is not permitted. This consensus is to be applied prospectively for new contracts entered into on or after the effective date. The adoption of EITF 07-3 is not expected to have a material impact on us.

In December 2007, the EITF reached a consensus on Issue No. 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). The EITF concluded on the definition of a collaborative arrangement and that revenues and costs incurred with third parties in connection with collaborative arrangements would be presented gross or net based on the criteria in EITF 99-19 and other accounting literature. Based on the nature of the arrangement, payments to or from collaborators would be evaluated and the terms, the nature of the entity s business, and whether those payments are within the scope of other accounting literature would be presented. Companies are also required to disclose the nature and purpose of collaborative arrangements along with the accounting policies and the classification and amounts of significant financial statement amounts related to the arrangements. Activities in the arrangement conducted in a separate legal entity should be accounted for under other accounting literature; however required disclosure under EITF 07-1 applies to the entire collaborative agreement. EITF 07-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years, and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. We are currently evaluating the requirements of EITF 07-1; however we do not believe that its adoption will have a significant impact on our financial statements.

In December 2007, the FASB issued SFAS No. 141R, *Business Combinations*, (SFAS 141R) which changes the accounting for business acquisitions. SFAS 141R requires the acquiring entity in a business combination to recognize all (and only) the assets acquired and liabilities assumed in the transaction and establishes the acquisition-date fair value as the measurement objective for all assets acquired and liabilities assumed in a business combination. Certain provisions of this standard will, among other things, impact the determination of acquisition-date fair value of consideration paid in a business combination (including contingent consideration); exclude transaction costs from acquisition accounting; and change accounting practices for acquired contingencies, acquisition-related restructuring costs, in-process research and development, indemnification assets, and tax benefits. SFAS 141R is effective for financial statements issued for fiscal years beginning after December 15, 2008. The adoption of SFAS 141R is not expected to have a material impact on us.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51*, (SFAS 160) which establishes new standards governing the accounting for and reporting of noncontrolling interests (NCIs) in partially owned consolidated subsidiaries and the loss of control of subsidiaries. Certain provisions of this standard indicate, among other things, that NCIs (previously referred to as minority interests) be treated as a separate component of equity, not as a liability; that increases and decrease in the parent s ownership interest that leave control intact be treated as equity transactions, rather than as step acquisitions or dilution gains or losses; and that losses of a partially owned consolidated subsidiary be allocated to the NCI even when such allocation might result in a deficit balance. This standard also requires changes to certain presentation and disclosure requirements. SFAS 160 is effective for financial statements issued for fiscal years beginning after December 15, 2008. The provisions of the standard are to be applied to all NCIs prospectively, except for the presentation and disclosure requirements, which are to be applied retrospectively to all periods presented. The adoption of SFAS 160 is not expected to have a material impact on us.

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ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We invest our excess cash in high quality, interest-bearing securities. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid mutual and money market funds, and high quality marketable debt instruments of corporations, government agencies and financial institutions with maturities of less than two years. If a 10% change in interest rates were to have occurred on September 30, 2008, this change would not have had a material effect on the fair value of our investment portfolio as of that date. In addition, the $20.0 million we borrowed during the twelve months ended 2008 has a fixed interest rate of 12%.

Foreign Currency Exchange Rate Risk

We have entered into some agreements denominated, wholly or partly, in foreign currencies, and, in the future, we may enter into additional, agreements denominated in foreign currencies. If the values of these currencies increase against the United States dollar, our costs would increase. To date, we have not entered into any contracts to reduce the risk of fluctuations in currency exchange rates. In the future, depending upon the amounts payable under any such agreements, we may enter into forward foreign exchange contracts to reduce the risk of unpredictable changes in these costs. However, due to the variability of timing and amount of payments under any such agreements, foreign exchange contracts may not mitigate the potential adverse impact on our financial results.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item is included in our Financial Statements and Supplementary Data listed in Item 15 of Part IV of this Annual Report on Form 10-K.

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 carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined under Rule 13a-15(e) promulgated under the Exchange Act), as of September 30, 2008. Based on that evaluation, our principal executive officer and principal financial officer concluded that these controls and procedures are effective to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported as specified in SEC rules and forms. There were no changes in these controls or procedures identified in connection with the evaluation of such controls or procedures that occurred during our last fiscal quarter, or in other factors that have materially affected, or are reasonably likely to materially affect, these controls or procedures.

Our disclosure controls and procedures are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms of the SEC. These disclosure controls and procedures include, among other things, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

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Management s Annual Report on Internal Control over Financial Reporting

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

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of our management and board of directors; and
- 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 financial statements.

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

Our management assessed the effectiveness of our internal control over financial reporting as of September 30, 2008. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework. Based on our assessment, our management believes that, as of September 30, 2008, our internal control over financial reporting is effective. In addition, no changes in our internal control over financial reporting have occurred during the three months ended September 30, 2008 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

The effectiveness of our internal control over financial reporting as of September 30, 2008 has been audited by Grant Thornton LLP, an independent registered public accounting firm, as stated in their report which is included in Item 15 of Part IV of this Annual Report on Form 10-K and incorporated by reference to this Item 9A.

ITEM 9B. OTHER INFORMATION

Not applicable.

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PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information regarding executive officers and directors required by this Item 10 will be included in the definitive Proxy Statement for our 2009 Annual Meeting, or 2009 Proxy Statement, under Election of Directors , Executive Officers of the Company and Governance of the Company and is incorporated herein by reference. Other information required by this Item 10 will be included in the 2009 Proxy Statement under Section 16(a) Beneficial Ownership Reporting Compliance and Code of Ethics and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Information About Executive and Director Compensation and Compensation Committee Interlocks and Insider Participation of the 2009 Proxy Statement.

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

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Stock Ownership of Certain Beneficial Owners and Management and Securities Authorized for Issuance Under Our Equity Incentive Plans of the 2009 Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Certain Relationships and Related Transactions and Board Determination of Independence of the 2009 Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Fees of Independent Registered Public Accounting Firm and Pre-Approval Policies and Procedures of the 2009 Proxy Statement.

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PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) (1) Financial Statements

The following documents are included on pages F-2 through F-35 attached hereto and are filed as part of this Annual Report on Form 10-K.

(a) (2) Financial Statement Schedules

Financial Statement Schedules have been omitted because they are either not applicable or the required information is included in the financial statements or notes thereto.

(a) (3) List of Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K. We are incorporating by reference to our previous SEC filings each exhibit that contains a footnote. For exhibits incorporated by reference, the location of the exhibit in the previous filing is indicated in parentheses.

Exhibit Number	Description
3.1**	Third Amended and Restated Certificate of Incorporation of the Registrant (Exhibit 3.1) (5)
3.2**	Second Amended and Restated Bylaws of the Registrant (Exhibit 3.2) (5)
4.1**#	Pharmasset, Ltd. 1998 Stock Plan, as amended (Exhibit 4.4) (3)
4.2**#	2007 Equity Incentive Plan (Exhibit 4.12) (3)
4.3**#	Form of agreement for awards under the 2007 Equity Incentive Plan (Exhibit 4.3) (5)
10.1**	Collaboration Agreement, dated October 29, 2004, between F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. and the Registrant (Exhibit 10.1) (4)
10.2**	License Agreement, dated June 23, 2005, between Bukwang Pharm. Co., Ltd. and the Registrant (Exhibit 10.2) (4)
10.3**	Memorandum of Understanding, dated June 23, 2005, between The University of Georgia Research Foundation, Inc., Yale University and the Registrant (Exhibit 10.3) (1)
10.4**	Exclusive Patent and Know How License Agreement, dated April 24, 2003, by and between Primagen Holding B.V. and the Registrant (Exhibit 10.4) (4)

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Exhibit Number	Description
10.5**	Non-Exclusive Sublicense Agreement, dated August 26, 2005, between Apath, L.L.C. and the Registrant (Exhibit 10.5) (4)
10.6**	License Agreement, dated March 1, 1999, among Pharmasset, Ltd., Dr. Raymond F. Schinazi, Dr. Mahmoud H. el Kouni and Dr. Fardos N. M. Naguib (Exhibit 10.6) (1)
10.7**	License and Consulting Agreement, dated March 1, 1999, among Pharmasset, Ltd., Dr. Raymond F. Schinazi and Dr. Craig L. Hill (Exhibit 10.7) (1)
10.8**	License Agreement, dated December 30, 1998, between Emory University and Pharmasset, Ltd. (Exhibit 10.8) (1)
10.9**	License Agreement, dated December 8, 1998, between Emory University and Pharmasset, Ltd. (Exhibit 10.9) (1)
10.10**	License Agreement, dated February 10, 2006, between RFS Pharma LLC and the Registrant (Exhibit 10.10) (4)
10.11**	First Amendment to License Agreement, dated February 13, 2006, by and between RFS Pharma LLC and the Registrant (Exhibit 10.11) (1)
10.12**	Second Amendment to License Agreement, dated as of August 29, 2003, between Emory University and Pharmasset, Ltd. (Exhibit 10.12) (1)
10.13**	Termination and Reinstatement Agreement, dated as of June 9, 1999, between Emory University and Pharmasset, Ltd. (Exhibit 10.13) (1)
10.14**	Supplemental Agreement to the License Agreement, dated as of March 26, 2004, between Emory University and Pharmasset, Ltd. (Exhibit 10.14) (1)
10.15**#	Employment Agreement, dated as of June 15, 2004, between the Registrant and Peter Schaefer Price (Exhibit 10.15) (1)
10.16**	Lease, dated as of May 18, 2005, between 300 CRA LLC and the Registrant (Exhibit 10.18) (1)
10.17**	Mutual Termination of Lease Agreement, dated as of February 7, 2006, between C.S. Family, LLC and the Registrant (Exhibit 10.19) (1)
10.18**	Settlement Agreement and Mutual General Release, dated as of February 14, 2006, among the Registrant, Raymond F. Schinazi and the other signatories thereto (Exhibit 10.20) (1)
10.19**#	Form of Indemnity Agreement for Directors and Officers (Exhibit 10.21) (3)
10.20**#	Consulting Agreement, dated June 28, 2005, between Michael K. Inouye and the Registrant (Exhibit 10.22) (1)
10.21**#	Form of Change of Control Severance Agreement (Exhibit 10.23) (2)
10.22**#	Severance Agreement, dated as of January 5, 2007, between the Registrant and Abel De La Rosa, Ph.D. (Exhibit 10.24) (2)
10.23	Venture Loan and Security Agreement dated September 30, 2007 by and between the Registrant and Horizon Technology Funding V LLC
10.24	Manufacturing Services Agreement dated August 8, 2008 between Pharmasset, Inc. and Boehringer Ingelheim Chemicals, Inc.
10.25	License Agreement dated August 8, 2008 between Pharmasset, Inc. and Boehringer Ingelheim Chemicals, Inc.

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Exhibit Number	Description
10.26	Secured Promissory Note, dated as of October 5, 2007, between the Registrant and Horizon Technology Funding Group V LLC (Exhibit 10.1) (6)
10.27	Secured Promissory Note, dated as of March 28, 2008, between the Registrant and Horizon Technology Funding Group V LLC (Exhibit 10.1) (7)
10.28	Placement Agency Agreement, dated as of July 14, 2008, between the Registrant, Morgan Stanley & Co. Incorporated and the other placement agents named therein (Exhibit 10.1) (8)
10.29	Form of Investor Purchase Agreement for the follow-on common stock offering (Exhibit 10.2) (8)
23.1	Consent of Grant Thornton LLP
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

** Filed Previously
Portions of the Exhibit were omitted and filed separately with the Secretary of the SEC pursuant to an order of the SEC granting our application for confidential treatment filed pursuant to Rule 406 under the Securities Act.
Portions of the exhibits have been omitted pursuant to a confidential treatment request and this information has filed separately with the SEC.

Management contract or compensatory plan or arrangement.

(1) Filed as an Exhibit to our Registration Statement on Form S-1 filed with the SEC on May 8, 2006.
(2) Filed as an Exhibit to our Registration Statement on Form S-1/A filed with the SEC on January 17, 2007.
(3) Filed as an Exhibit to our Registration Statement on Form S-1/A filed with the SEC on March 2, 2007.
(4) Filed as an Exhibit to our Registration Statement on Form S-1/A filed with the SEC on April 24, 2007.
(5) Filed as an Exhibit to our Form 10-K filed with the SEC on December 31, 2007.
(6) Filed as an Exhibit to our Form 8-K filed with the SEC on October 11, 2007.
(7) Filed as an Exhibit to our Form 8-K filed with the SEC on March 28, 2008.
(8) Filed as an Exhibit to our Form 8-K filed with the SEC on July 15, 2008.

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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.

PHARMASSET, INC.

December 11, 2008 By: /s/ P. Schaefer Price
P. Schaefer Price

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 and on the dates indicated.

Each person, in so signing also makes, constitutes, and appoints Kurt Leutzinger and Paul Lubetkin as his true and lawful attorney-in-fact, with full power of substitution, in his name, place, and stead, to execute and cause to be filed with the Securities and Exchange Commission any or all amendments to this report.

Name	Title	Date
/s/ P. Schaefer Price **P. Schaefer Price**	Director, President and Chief Executive Officer (Principal Executive Officer)	December 11, 2008
/s/ Kurt Leutzinger **Kurt Leutzinger**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	December 11, 2008
/s/ G. Steven Burrill **G. Steven Burrill**	Chairman of the Board of Directors	December 11, 2008
/s/ William J. Carney **William J. Carney**	Director	December 11, 2008
/s/ Fredric D. Price **Fredric D. Price**	Director	December 11, 2008
/s/ Elliot F. Hahn **Elliot F. Hahn**	Director	December 11, 2008
/s/ Michael K. Inouye	Director	December 11, 2008

Michael K. Inouye		
/s/ Robert F. Williamson III	Director	December 11, 2008
Robert F. Williamson III		
/s/ Herbert J. Conrad	Director	December 11, 2008
Herbert J. Conrad		

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INDEX TO FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders

Pharmasset, Inc.

We have audited the accompanying balance sheets of Pharmasset, Inc. (the Company) as of September 30, 2008 and 2007, and the related statements of operations and comprehensive net loss, redeemable stock and warrants, stockholders equity (deficit), and cash flows for each of the three years in the period ended September 30, 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 Pharmasset, Inc. as of September 30, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended September 30, 2008 in conformity with accounting principles generally accepted in the United States of America.

As described in Note 2 to the financial statements, Pharmasset, Inc. adopted Financial Accounting Standards Board Interpretation No. 48 Accounting for Uncertainty in Income Taxes an interpretation of FASB No. 109 as of October 1, 2007 and Statement of Financial Accounting Standard No. 123(R) Share Based Payment as of October 1, 2006.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Pharmasset Inc. s internal control over financial reporting as of September 30, 2008, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO*)* and our report dated December 1, 2008 expressed an unqualified opinion.

/s/ Grant Thornton LLP

Philadelphia, Pennsylvania

December 11, 2008

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders

Pharmasset, Inc.

We have audited Pharmasset, Inc. s (the Company) internal control over financial reporting as of September 30, 2008, based on criteria established in *Internal Control Integrated Fram*ework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company 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 Annual 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, Pharmasset, Inc. maintained, in all material respects, effective internal control over financial reporting as of September 30, 2008, based on criteria established in *Internal Control Integrated Framework* issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Pharmasset, Inc. as of September 30, 2008 and 2007, and the related statements of operations and comprehensive net loss, redeemable stock and warrants, stockholders equity (deficit), and cash flows for each of the three years in the period ended September 30, 2008 and our report dated December 1, 2008 expressed an unqualified opinion.

/s/ Grant Thornton LLP

Philadelphia, Pennsylvania

December 11, 2008

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PHARMASSET, INC.

BALANCE SHEETS

	As of September 30, 2008	2007
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 63,073,103	$ 68,745,694
Short-term investments	497,310	1,252,113
Amounts due under collaborative agreements	1,169,690	919,110
Prepaid expenses and other assets	1,008,083	783,311
Total current assets	65,748,186	71,700,228
EQUIPMENT AND LEASEHOLD IMPROVEMENTS:		
Laboratory, office furniture and equipment	3,362,846	2,462,647
Leasehold improvements	1,836,553	1,836,553
	5,199,399	4,299,200
Less accumulated depreciation and amortization	(2,432,325)	(1,437,080)
Total equipment and leasehold improvements, net	2,767,074	2,862,120
OTHER ASSETS	466,809	1,282,051
TOTAL	$ 68,982,069	$ 75,844,399
LIABILITIES AND STOCKHOLDERS EQUITY		
CURRENT LIABILITIES:		
Current portion of long-term debt	$ 2,651,592	$
Current portion of capital lease obligation	41,641	159,440
Accounts payable	2,466,052	3,281,600
Accrued expenses	6,182,417	5,513,407
Deferred rent	124,463	124,462
Deferred revenue	1,857,136	1,857,136
Total current liabilities	13,323,301	10,936,045
DEFERRED RENT	79,793	204,256
NON CURRENT PORTION OF CAPITAL LEASE OBLIGATION		41,641
DEFERRED REVENUE	3,868,965	5,726,131
LONG-TERM DEBT, net	16,522,665	
Total liabilities	33,794,724	16,908,073
COMMITMENTS AND CONTINGENCIES		
STOCKHOLDERS EQUITY		
Common Stock, $0.001 par value, 100,000,000 shares authorized, 23,340,498 and 21,232,991 shares issued and outstanding at September 30, 2008, and September 30, 2007, respectively	23,340	21,233
Warrants to purchase 116,183 shares of common stock for $12.05 per share, with 66,390 exercisable starting September 30, 2007, and 49,793 shares exercisable starting March 28, 2008	1,140,114	526,720
Additional paid-in capital	145,818,439	115,518,201
Accumulated other comprehensive (loss) income	(2,604)	4,405
Accumulated deficit	(111,791,944)	(57,134,233)

Total stockholders equity	35,187,345	58,936,326
TOTAL	$ 68,982,069	$ 75,844,399

See notes to financial statements.

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PHARMASSET, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE NET LOSS

	Years Ended September 30,		
	2008	2007	2006
REVENUES:	$ 1,857,166	$ 22,009,458	$ 5,424,614
COSTS AND EXPENSES:			
Research and development	42,995,459	20,318,910	10,497,703
General and administrative	13,289,321	9,210,623	7,911,545
Total costs and expenses	56,284,780	29,529,533	18,409,248
OPERATING LOSS	(54,427,614)	(7,520,075)	(12,984,634)
INVESTMENT INCOME	1,986,276	2,470,563	1,658,977
INTEREST EXPENSE	(2,216,373)	(15,136)	
LOSS BEFORE INCOME TAXES	(54,657,711)	(5,064,648)	(11,325,657)
PROVISION FOR INCOME TAXES			
NET LOSS	(54,657,711)	(5,064,648)	(11,325,657)
REDEEMABLE PREFERRED STOCK ACCRETION		1,775,684	1,110,973
NET LOSS ATTRIBUTABLE TO COMMON STOCKHOLDERS	$ (54,657,711)	$ (6,840,332)	$ (12,436,630)
COMPREHENSIVE NET LOSS:			
NET LOSS	$ (54,657,711)	$ (5,064,648)	$ (11,325,657)
UNREALIZED GAIN (LOSS) ON AVAILABLE-FOR-SALE INVESTMENTS	(7,009)	2,100	(56,465)
COMPREHENSIVE NET LOSS:	$ (54,664,720)	$ (5,062,548)	$ (11,382,122)
NET LOSS ATTRIBUTABLE TO COMMON STOCKHOLDERS PER SHARE:			
BASIC	$ (2.51)	$ (0.46)	$ (1.19)
DILUTED	$ (2.51)	$ (0.46)	$ (1.19)
WEIGHTED AVERAGE SHARES OUTSTANDING:			
BASIC	21,808,283	14,990,472	10,462,369
DILUTED	21,808,283	14,990,472	10,462,369

See notes to financial statements.

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PHARMASSET, INC.

STATEMENTS OF REDEEMABLE STOCK AND WARRANTS

FOR THE YEARS ENDED SEPTEMBER 30, 2008, 2007 AND 2006

	Series B Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Series D Redeemable Convertible Preferred Stock		Series R Redeemable Convertible Preferred Stock		Series R-1 Warrants		Redeemable Common Stock		Tota Redeem Stock A Warra
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Number	Amount	Shares	Amount	
ANCE September 005 Restated	367,999	$ 624,577	366,606	$ 1,995,888	2,505,686	$ 11,918,403	400,000	$ 3,726,838	470,588	$ 264,000	213,307	$ 979,078	$ 19,508
tion of mable preferred to redemption		266		552		1,040,052		70,103					1,110
tion of mable common to redemption												211,173	211
ANCE September 006	367,999	624,843	366,606	1,996,440	2,505,686	12,958,455	400,000	3,796,941	470,588	264,000	213,307	1,190,251	20,830
tion of mable common to redemption												729,508	729
ation of Series arrants									(470,588)	(264,000)			(264
tion of mable rtible preferred to total ption value		756		1,562		1,570,307		203,059					1,775
ent of dividends form of on stock						(1,186,871)							(1,186
n of excess nd accretion to ed earnings						(562,892)							(562
ersion of mable rtible preferred into common	(367,999)	(625,599)	(366,606)	(1,998,002)	(2,505,686)	(12,778,999)	(400,000)	(4,000,000)					(19,402
ersion of mable common into common											(213,307)	(1,919,759)	(1,919
ANCE September 008 and 2007	$		$		$		$		$		$		$

See notes to financial statements.

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PHARMASSET, INC.

STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT)

FOR THE YEARS ENDED SEPTEMBER 30, 2008, 2007 AND 2006

	Warrants		Series A Convertible Preferred Stock		Series D-1 Warrants		Common Stock		Additional Paid-in	Accumulated Other Comprehensive			Total Stockhold
	Shares	Amount	Shares	Amount	Number	Amount	Shares	Amount	Capital	Series A Issuable	Income (Loss)	Accumulated Deficit	Equity (Deficit
LANCE September 2005 Restated			2,584,545	$ 2,585	1,254,960	$ 5,411,932	10,158,452	$ 10,158	$ 43,363,456	$ 300,719	$ 58,770	$ (37,479,482)	$ 11,668,
rcise of stock ons							132,934	133	338,669				338,8
k compensation									477,226				477,2
ance of Series A vertible preferred k			55,177	55					300,664	(300,719)			
retion of emable preferred k to redemption e												(1,110,973)	(1,110,9
retion of emable common k to redemption e												(211,173)	(211,
ealized gain on lable-for-sale stments											(56,465)		(56,4
loss												(11,325,657)	(11,325,6
LANCE September 2006			2,639,722	2,640	1,254,960	5,411,932	10,291,386	10,291	44,480,015		2,305	(50,127,285)	(220,
ration of Series warrants									264,000				264,0
rcise of stock ons							531,369	531	1,500,741				1,501,2
k compensation									2,284,778				2,284,7
retion of emable preferred k to redemption e												(1,775,684)	(1,775,6
retion of emable common k to redemption e												(729,508)	(729,5
ment of dividends e form of mon stock							131,864	132	1,186,644				1,186,7
version of vertible preferred k into common k			(2,639,722)	(2,640)			4,192,377	4,193	19,400,912				19,402,4
version of Series warrants into mon stock					(1,254,960)	(5,411,932)	822,689	823	5,411,047				
version of emable common k into common k							213,306	213	1,919,541				1,919,7

rn of excess dend accretion to ned earnings									562,892	562,8
proceeds from al public offering				5,050,000	5,050	39,070,523				39,075,5
ealized loss on lable-for-sale stments								2,100		2,1
of warrants in nection with debt ncing	66,390	526,720								526,7
loss									(5,064,648)	(5,064,6
LANCE September 2007	66,390	526,720		21,232,991	21,233	115,518,201		4,405	(57,134,233)	58,936,3
rcise of stock ons				657,507	657	2,641,741				2,642,3
k compensation restricted shares ed						3,590,798				3,590,7
proceeds from stered direct ring				1,450,000	1,450	24,067,699				24,069,1
ealized loss on lable-for-sale stments								(7,009)		(7,0
nt of warrants in nection with debt ncing	49,793	613,394								613,3
loss									(54,657,711)	(54,657,7
LANCE September 2008	116,183	$ 1,140,114		23,340,498	$ 23,340	$ 145,818,439	$	$ (2,604)	$ (111,791,944)	$ 35,187,3

See notes to financial statements.

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PHARMASSET, INC.

STATEMENTS OF CASH FLOWS

	Years Ended September 30,		
	2008	2007	2006
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (54,657,711)	$ (5,064,648)	$ (11,325,657)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation	506,015	403,125	351,016
Amortization	489,230	489,230	311,532
Non-cash stock compensation	3,590,799	2,284,778	477,226
Loss on disposal of fixed assets			8,227
Non-cash interest expense	404,221		
Changes in operating assets and liabilities:			
Amounts due under collaborative agreements, prepaid expenses and other assets	(446,587)	(1,337,622)	(700,178)
Accounts payable	(815,548)	2,571,119	397,637
Accrued expenses	836,711	3,290,479	(1,709,970)
Deferred rent	(124,462)	(124,462)	453,180
Deferred revenue	(1,857,166)	(1,584,844)	(2,876,167)
Net cash (used in) provided by operating activities	(52,074,498)	927,155	(14,613,154)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Proceeds from maturities or sale of investments	750,000		10,800,000
Purchase of equipment and leasehold improvements	(900,199)	(437,010)	(2,332,500)
Net cash provided by (used in) investing activities	(150,199)	(437,010)	8,467,500
CASH FLOWS FROM FINANCING ACTIVITIES:			
Borrowings of long-term debt	20,000,000		
Proceeds from exercise of stock options	2,642,398	1,621,272	338,802
Principal payments on capital lease obligations	(159,440)	(112,438)	
Proceeds from issuance of common stock, net of issuance costs, of $1,813,351 and $1,548,101 paid during 2008 and 2007, respectively	24,069,148	40,684,399	
Payments related to purchase of common stock		(120,000)	
Offering costs paid			(1,452,332)
Net cash provided by (used in) financing activities	46,552,106	42,073,233	(1,113,530)
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	(5,672,591)	42,563,378	(7,259,184)
CASH AND CASH EQUIVALENTS Beginning of period	68,745,694	26,182,316	33,441,500
CASH AND CASH EQUIVALENTS End of period	$ 63,073,103	$ 68,745,694	$ 26,182,316
SUPPLEMENTAL DISCLOSURES:			
Cash paid during the period for:			
Interest	$ 1,812,152	$ 15,136	$
Noncash transactions:			
Deferred compensation Series A convertible preferred shares issuable	$	$	$ (300,719)
Accretion of redeemable convertible preferred stock to redemption value	$	$ 1,775,684	$ 1,110,973
Accretion of redeemable common stock to redemption value	$	$ 729,508	$ 211,173
Fixed assets purchased on account	$	$	$ 164,977
Unrealized (loss) gain on available-for-sale investments	$ (7,009)	$ 2,100	$ (56,465)

Conversion of redeemable convertible preferred stock, redeemable common stock, and convertible preferred stock into common stock	$	$ 21,324,999	$
Exercise and conversion of Series D-1 warrants into common stock	$	$ 5,411,932	$
Capital lease obligations incurred	$	$ 313,520	$
Dividends paid on the Series D preferred stock in the form of common stock	$	$ 1,186,871	$
Warrants granted in connection with debt financing	$ 613,394	$ 526,720	$

See notes to financial statements.

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS

1. BACKGROUND

Description of Business Pharmasset, Inc. (Pharmasset or the Company) is a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. The Company s primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The Company currently has three clinical-stage product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America and Europe. R7128, an oral treatment for chronic HCV infection, has completed Phase 1 clinical trials in combination with Pegasys® plus Copegus® through a strategic collaboration with F. Hoffmann-La Roche Ltd and Hoffmann- La Roche Inc. (collectively, Roche). Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial. The Company has also identified proprietary, next generation HCV development candidates that are being evaluated for advancement into clinical development. One of these compounds, PSI-7851, was recently nominated as a lead candidate and has advanced into preclinical safety studies required for submission of an IND application with the FDA or an equivalent foreign regulatory filing. PSI-7851is being developed as part of the Company s research and development efforts to identify compounds that might be used in proprietary combination treatment for HCV. The Company s research and development efforts focus on a class of compounds known as nucleoside analogs, which act to inhibit the natural enzymes required for viral replication. The Company is subject to risks common to companies in the pharmaceutical industry including, but not limited to, product development risks, protection of proprietary intellectual property, compliance with government regulations, dependence on key personnel, the need to obtain additional financing, uncertainty of market acceptance of products, and product liability. (See Part I, Item 1A. Risk Factors for additional information).

Basis of Presentation The Company was incorporated as Pharmasset, Ltd. on May 29, 1998 under the laws of Barbados. The Company redomiciled under the laws of Delaware on June 8, 2004, as Pharmasset, Inc., and Pharmasset, Ltd. was discontinued on June 21, 2004. Pharmasset, Inc., then-existing as a Georgia corporation incorporated on June 5, 1998 and the only subsidiary of Pharmasset, Ltd., was merged with and into the Delaware corporation on July 23, 2004.

Initial Public Offering On May 2, 2007, the Company completed its initial public offering (IPO) of 5,050,000 shares of its common stock (including the underwriters exercise of a portion of their over-allotment option) at a public offering price of $9.00 per share. Net cash proceeds from the IPO were $40.7 million after deducting offering costs paid during fiscal 2007 and $39.1 million after deducting offering costs paid in fiscal 2006.

In connection with the IPO, the outstanding shares of the Company s Series B, Series C, Series D and Series R redeemable convertible preferred stock, the Series A convertible preferred stock, and the redeemable common stock were converted into 4,405,683 shares of common stock as of May 2, 2007. In addition, holders of the Series D redeemable convertible preferred stock were entitled to receive quarterly dividends at a rate equal to 7.5% per annum of the purchase price per share. Such dividends accrued from February 4, 2006 through May 2, 2007 and were paid out in the form of 131,864 shares of common stock. The Company s Series D-1 warrants were also exercised in full in connection with the IPO on a net exercise basis, which resulted in the Company issuing 822,689 shares of common stock to the warrant holders (See Note 9).

Reverse Stock Split On March 1, 2007, the Company s board of directors approved a 1.0 for 1.5 reverse stock split of the Company s outstanding common stock which became effective on April 19, 2007. All common share and per common share amounts in the accompanying financial statements and notes to the financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split.

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates The preparation of the Company s financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents Cash and cash equivalents represent cash and highly liquid investments purchased within three months of the maturity date and consist primarily of mutual and money market funds.

Investments The Company invests available cash primarily in mutual and money market funds, bank certificates of deposit and investment-grade commercial paper, corporate notes, and government securities. All investments are classified as available-for-sale and are carried at fair market value with unrealized gains and losses recorded in accumulated other comprehensive (loss) profit. For purposes of determining realized gains and losses, the cost of securities sold is based on specific identification.

Deferred Offering Costs The Company defers specific incremental costs directly attributable to planned public stock offerings until such offerings are completed. The deferred offering costs are then applied against the proceeds from the offering.

Deferred Financing Costs Costs incurred in connection with debt offerings are deferred (and included in prepaid expenses and other current assets and other (long-term) assets on the balance sheet), and amortized as interest expense over the term of the related debt using the effective interest method. The amortization expense is included in interest expense in the statements of operations and comprehensive net (loss) income.

Equipment and Leasehold Improvements Equipment and leasehold improvements are recorded at cost and are depreciated using the straight-line method over the following estimated useful lives of the assets: computer equipment three years; laboratory and office equipment seven years; and leasehold improvements over the lesser of the estimated life of the asset or the lease term. Expenditures for maintenance and repairs are expensed as incurred. Capital expenditures, which improve and extend the life of the related assets, are capitalized.

Intangible Assets Intangible assets consist of a technology license which gives the Company the right to sublicense certain technology to contract manufacturing organizations for the purpose of manufacturing an active pharmaceutical ingredient on behalf of the Company. The technology license is being amortized on a straight-line basis over an estimated useful life of five years. The estimated useful life of five years was determined based on the consideration of several factors including the nature of the asset, its expected use, length of the agreement and the period over which benefits are expected to be received from the use of the asset. Intangible Assets are included in Other Assets on the Balance Sheets.

Impairment of Long-Lived Assets The Company continually evaluates whether events or circumstances have occurred that indicate the estimated remaining useful lives of long-lived assets may require revision or that the carrying value of these assets may be impaired. To determine whether assets have been impaired, the estimated undiscounted future cash flows for the estimated remaining useful life of the respective assets are compared to the carrying value. To the extent that the undiscounted future cash flows are less than the carrying value, a new fair value of the asset is required to be determined. If such fair value is less than the current carrying value, the asset is written down to its estimated fair value.

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Fair Value of Financial Instruments The carrying amounts of cash and cash equivalents, amounts due under collaborative agreements, accounts payable, and accrued expenses approximate fair value because of their short-term nature. Investments at September 30, 2008 and 2007 are classified as available-for-sale securities and carried at fair market value. The fair value of the Company s debt as of September 30, 2008 approximates the carrying value. The fair value is based on management s estimate of current rates available to the Company for similar debt with the same remaining maturity.

Concentrations of Credit Risk, Suppliers and Revenues The Company s financial instruments that potentially subject it to concentrations of credit risk are cash and cash equivalents, and investments. The Company invests cash that is not currently being used in operations in accordance with its investment policy. The policy allows for the purchase of low-risk, investment grade debt securities issued by the United States government and very highly-rated banks and corporations, subject to certain concentration limits. The policy allows for maturities that are not longer than two years for individual securities and an average of one year for the portfolio as a whole.

The Company relies on certain materials used in its development process, some of which are procured from a single source. The failure of a supplier, including a subcontractor, to deliver on schedule could delay or interrupt the development process and thereby adversely affect the Company s operating results.

During each of the years ended September 30, 2008, 2007 and 2006, the Company derived a majority of its revenue from one customer (See Note 6).

Revenue Recognition The Company recognizes revenues in accordance with the Securities and Exchange Commission (SEC) Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition* (*SAB No. 104*). SAB No. 104 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectibility is reasonably assured. For arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets, the Company follows the guidance of Emerging Issues Task Force (EITF) No. 00-21, *Revenue Arrangements with Multiple Deliverables*, or EITF No. 00-21. In accordance with SAB No. 104 and EITF No. 00-21, the elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the collaborator and whether there is objective and reliable evidence of the fair value of the undelivered obligation(s). The consideration received is allocated among the separate units either on the basis of each unit s fair value or using the residual method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company s revenues are primarily related to its collaboration agreements, and these agreements provide for various types of payments to the Company, including non-refundable upfront license fees, research and development payments, and milestone payments.

Where the Company has continuing performance obligations under the terms of a collaborative arrangement, non-refundable upfront license payments received upon contract signing are recorded as deferred revenue and recognized as revenue as the related activities are performed. The period over which these activities are to be performed is based upon management s estimate of the development period. Changes in management s estimate could change the period over which revenue is recognized. Payments for research funding are recognized as revenues as the related research activities are performed.

The Company recognizes revenue from milestone payments when earned, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) the

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Company does not have ongoing performance obligations. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment is non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved to achieve the milestone; and the amount of the milestone appears reasonable in relation to the effort expended, the other milestones in the arrangement and the related risk associated with the achievement of the milestone. Any amounts received under the agreements in advance of performance, if deemed substantive, are recorded as deferred revenue and recognized as revenue as the Company completes its performance obligations.

Where the Company has no continuing involvement under a collaborative arrangement, the Company records nonrefundable license fee revenues when the Company has the contractual right to receive the payment, in accordance with the terms of the license agreement, and records milestones upon appropriate notification to the Company of achievement of the milestones by the collaborative partner.

Deferred revenues associated with a non-refundable payment received under a collaborative agreement that is terminated prior to its completion result in an immediate recognition of the deferred revenues.

Research and Development Expenses Research and development expenses consist primarily of salaries and related personnel expenses, fees paid to external service providers, costs of preclinical studies and clinical trials, drug and laboratory supplies, costs for facilities and equipment and the costs of intangibles that are purchased from others for use in research and development activities, such as in-licensed product candidates, that have no alternative future uses. Research and development expenses are included in operating expenses when incurred. Reimbursements received from the Company s collaborators for third-party research and development expenses incurred by the Company on their behalf are recorded as a contra-expense. Amounts due from collaborators for reimbursement of research and development expenses are recorded on the balance sheets as Amounts due under collaborative agreements.

Stock-Based Compensation On October 1, 2006, the Company adopted Statement of Financial Accounting Standards (SFAS) No. 123R, *Share-Based Payment* (SFAS 123R). This Statement is a revision of SFAS No. 123 Accounting for Stock-Based Compensation (SFAS 123) an supersedes Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees (APB 25) and its related implementation guidance. SFAS 123R requires companies to recognize stock compensation expense for awards of equity instruments to employees based on grant-date fair value of those awards (with limited exceptions). The Company adopted SFAS 123R using the modified prospective method, which results in recognition of compensation expense for all share-based awards granted or modified after October 1, 2006 as well as all unvested awards outstanding at the date of adoption. The cost is recognized as compensation expense over the life of the instruments, based upon the grant date fair value of the equity or liability instruments issued. The adoption of SFAS 123R resulted in stock compensation expense and therefore an increase in the loss before income taxes of $1,552,690, or $0.10 per share during the year ended September 30, 2007. In accordance with EITF-96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, equity instruments granted to consultants are periodically valued and recorded as stock compensation expense as the equity instrument vests.

Stock-based compensation expense is included in both research and development expenses and in general and administrative expenses in the statements of operations and comprehensive net loss. Since the Company s stock was not publicly traded prior to April 27, 2007, the expected volatility was calculated for each date of grant based on the peer method. The Company identified companies that trade publicly within the pharmaceutical industry that have similar SIC codes, employee count and revenues. The Company had chosen the weekly high price volatility for these companies for a period of five years. Effective October 1, 2006, the Company has used the weekly high price for these companies for a period of six years to coordinate with the expected term calculated pursuant to SAB 107 issued by the SEC.

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Prior to October 1, 2006, the Company elected to follow APB 25, and related interpretations to account for its stock-based employee compensation plans, and had adopted the pro forma disclosure option for stock-based compensation issued to employees under SFAS 123. The table below presents a summary of the pro forma effects to reported net loss prior to October 1, 2006 as if the Company had elected to recognize stock-based compensation costs based on the fair value of the options granted as prescribed by SFAS 123.

	Year Ended September 30, 2006
Net loss attributable to common stockholders as reported	$ (12,437)
Add: stock based compensation expense included in reported net loss	477
Deduct: stock-based compensation expense determined under fair value method	(1,484)
Pro forma net loss	$ (13,444)
Net loss per share as reported:	
Basic and diluted	$ (1.19)
Pro forma net loss per share:	
Basic and diluted	$ (1.29)

Income Taxes The Company accounts for income taxes under the asset and liability method. The Company provides deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company s financial statement carrying amounts and the tax bases of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that is expected to be realized.

On October 1, 2007, the Company adopted Financial Accounting Standards Board (FASB) Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement No. 109* (FIN 48). FIN 48 prescribes a comprehensive model for how a company should recognize, measure, present, and disclose in its financial statements uncertain tax positions that the company has taken or expects to take on a tax return (including a decision whether to file or not to file a return in a particular jurisdiction). Under FIN 48, the financial statements reflect expected future tax consequences of such positions presuming the taxing authorities full knowledge of the position and all relevant facts.

As a result of the adoption of FIN 48, there were no changes to the Company s deferred tax assets as of October 1, 2007. The total amount of unrecognized tax benefits at October 1, 2007 was $126,000, all of which would favorably impact the Company s effective tax rate if recognized. Since the unrecognized tax benefit has not been utilized on the Company s tax returns, there is no liability recorded on the balance sheets. The Company does not have any interest or penalties accrued related to tax positions at adoption of FIN 48. In the event the Company determines that accrual of interest or penalties are necessary in the future, the amount will be presented as a component of income taxes.

Preferred Stock Accretion Prior to the conversion of all of the Company s redeemable convertible preferred stock into common stock in May 2007 when the Company completed its IPO, the Company used the interest method to increase the carrying amount of its redeemable convertible preferred stock on each balance sheet date, so that the carrying amount, initially the fair value of the security on the date of issue, would equal the redemption amount at the earliest redemption date. These periodic increases to the carrying amount also used the

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

interest method to include amounts representing dividends not currently declared or paid, but which will be payable under the redemption features had they been still accrued and unpaid at the redemption date (See Note 9).

Comprehensive Net Income (Loss) Components of comprehensive income (loss) include net income (loss) and unrealized gain (loss) on available-for-sale securities, net of tax. Comprehensive income (loss) is represented in the statements of operations and comprehensive net income (loss).

Net Income (Loss) Per Common Share Basic net income (loss) per common share is calculated by dividing net income(loss) attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net income (loss) per common share is calculated by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares and other dilutive securities outstanding during the period. Dilutive potential common shares resulting from the assumed exercise of outstanding stock options and warrants are determined based on the treasury stock method.

	Years Ended September 30,		
	2008	2007	2006
	(In thousands, except per share amounts)		
Numerator:			
Net loss attributable to common stockholders	$ (54,658)	$ (6,840)	$ (12,437)
Denominator:			
Weighted average common shares outstanding used in calculation of basic net loss per share	21,808	14,990	10,462
Effect of dilutive securities:			
Common stock options			
Common stock warrants			
Preferred stock			
Preferred stock warrants			
Weighted average common shares outstanding used in calculation of diluted net loss per share	21,808	14,990	10,462
Net loss attributable to common stockholders per share:			
Basic	$ (2.51)	$ (0.46)	$ (1.19)
Diluted	$ (2.51)	$ (0.46)	$ (1.19)

The following table summarizes the securities outstanding at the end of each period with the potential to become common stock that have been excluded from the computation of diluted net income (loss) attributable to common stockholders per share, as their effect would have been anti-dilutive.

	Years Ended September 30,		
	2008	2007	2006
	(In thousands)		
Preferred stock			9,991
Preferred stock warrants			1,151

Common stock warrants	116	66	
Options to purchase common stock	2,372	2,101	2,376
Total	2,488	2,167	13,518

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Segment Reporting Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker, or decision-making group, in making decisions regarding resource allocation and assessing performance. The Company, which uses financial information in determining how to allocate resources and assess performance, has determined that it operates in one segment, which focuses on developing nucleoside analog drugs for the treatment of viral infections.

Recently Issued Accounting Standards In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements* (SFAS 157). This standard defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles and expands disclosures about fair value measurements. SFAS 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007 and interim periods within those fiscal years. The adoption of SFAS 157 is not expected to have a material impact on the Company.

On February 15, 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities, including an amendment of FASB Statement No. 115* (SFAS 159). SFAS 159 permits companies to choose to measure many financial instruments and certain other items at fair value that are not currently required to be measured at fair value and establishes presentation and disclosure requirements designed to facilitate comparisons between companies that choose different measurement attributes for similar types of assets and liabilities. SFAS 159 will be effective for fiscal years beginning after November 15, 2007. The adoption of SFAS 159 is not expected to have a material impact on the Company.

In June 2007, the Emerging Issues Task Force reached a consensus on Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services Received for Use in Future Research and Development Activities* (EITF 07-3). Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities should be deferred and capitalized. Such amounts should be recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided. This issue effects financial statements issued for fiscal years beginning after December 15, 2007, and earlier application is not permitted. This consensus is to be applied prospectively for new contracts entered into on or after the effective date. The adoption of EITF 07-3 is not expected to have a material impact on the Company.

In December 2007, the EITF reached a consensus on Issue No. 07-1, Accounting for Collaborative Arrangements (EITF 07-1). The EITF concluded on the definition of a collaborative arrangement and that revenues and costs incurred with third parties in connection with collaborative arrangements would be presented gross or net based on the criteria in EITF 99-19 and other accounting literature. Based on the nature of the arrangement, payments to or from collaborators would be evaluated and the terms, the nature of the entity s business, and whether those payments are within the scope of other accounting literature would be presented. Companies are also required to disclose the nature and purpose of collaborative arrangements along with the accounting policies and the classification and amounts of significant financial statement amounts related to the arrangements. Activities in the arrangement conducted in a separate legal entity should be accounted for under other accounting literature; however required disclosure under EITF 07-1 applies to the entire collaborative agreement. EITF 07-1 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years, and is to be applied retrospectively to all periods presented for all collaborative arrangements existing as of the effective date. The Company is currently evaluating the requirements of EITF 07-1; however, it does not believe that its adoption will have a significant impact on its financial statements.

In December 2007, the FASB issued SFAS No. 141R, Business Combinations, (SFAS 141R) which changes the accounting for business acquisitions. SFAS 141R requires the acquiring entity in a business

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

combination to recognize all (and only) the assets acquired and liabilities assumed in the transaction and establishes the acquisition-date fair value as the measurement objective for all assets acquired and liabilities assumed in a business combination. Certain provisions of this standard will, among other things, impact the determination of acquisition-date fair value of consideration paid in a business combination (including contingent consideration); exclude transaction costs from acquisition accounting; and change accounting practices for acquired contingencies, acquisition-related restructuring costs, in-process research and development, indemnification assets, and tax benefits. SFAS 141R is effective for financial statements issued for fiscal years beginning after December 15, 2008. The adoption of SFAS 141R is not expected to have a material impact on the Company.

In December 2007, the FASB issued SFAS No. 160, Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51, (SFAS 160) which establishes new standards governing the accounting for and reporting of noncontrolling interests (NCIs) in partially owned consolidated subsidiaries and the loss of control of subsidiaries. Certain provisions of this standard indicate, among other things, that NCIs (previously referred to as minority interests) be treated as a separate component of equity, not as a liability; that increases and decrease in the parent s ownership interest that leave control intact be treated as equity transactions, rather than as step acquisitions or dilution gains or losses; and that losses of a partially owned consolidated subsidiary be allocated to the NCI even when such allocation might result in a deficit balance. This standard also requires changes to certain presentation and disclosure requirements. SFAS 160 is effective for financial statements issued for fiscal years beginning after December 15, 2008. The provisions of the standard are to be applied to all NCIs prospectively, except for the presentation and disclosure requirements, which are to be applied retrospectively to all periods presented. The adoption of SFAS 160 is not expected to have a material impact on the Company.

3. RELATED PARTY TRANSACTIONS

Agreements related to Dr. Raymond Schinazi, a founder and former director Dr. Schinazi is one of the Company s founders and served as a director of the Company from 1998 until June 2005 and as an executive director of the Company from 1998 until June 2004. As of September 30, 2008, he and his affiliates beneficially owned 10.7% of the Company s capital stock. In February 2006, the Company entered into several agreements with Dr. Schinazi, which are described below.

Settlement Agreement The Company settled a disagreement that arose between Dr. Schinazi and the Company related to several issues by entering into a settlement agreement and mutual general release dated as of February 14, 2006, which provides for a mutual general release of claims by him, the Company and certain of its existing stockholders. Pursuant to this settlement agreement, the Company also entered into a license agreement with RFS Pharma LLC for a molecule called dioxolane thymine, or DOT, and a mutual termination of lease agreement with C.S. Family, LLC, which is 50% owned by Dr. Schinazi, each described in more detail below. Dr. Schinazi is the founder and majority stockholder of RFS Pharma LLC and is a named inventor of DOT. Additionally, this settlement agreement provides for certain amendments to the Company s stockholders agreement to, among other things, facilitate the transfer of 1.3 million shares of the Company s common stock that Dr. Schinazi owns to two affiliated entities, one of which is a trust of which he is the trustee and one of which is a limited partnership, of which he is a manager of its general partner. The settlement agreement also requires the Company to reimburse Dr. Schinazi for up to $100,000 of legal fees incurred by him in connection with the negotiation of the transactions contemplated by this settlement agreement.

License Agreement with RFS Pharma LLC As of February 10, 2006, the Company entered into a license agreement with RFS Pharma LLC to pursue the research, development and commercialization of an antiviral

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

nucleoside analog product candidate called DOT. Under this agreement, the Company paid to RFS Pharma LLC an upfront payment of $400,000 and the Company may also pay up to an aggregate of $3.9 million in future milestone payments related to development and regulatory events, royalties on future sales, and expense reimbursements in specified circumstances. Additionally, this license agreement provides for specified amounts of DOT drug substance to be purchased by the Company from RFS Pharma LLC for up to $82,000. The Company may terminate the license agreement on a country-by-country basis and/or product-by-product basis or in its entirety at any time upon 30 days advance written notice to RFS Pharma LLC prior to the launch of any licensed product, or upon 180 days advance written notice to RFS Pharma LLC following the launch of any licensed product. Additionally, upon a material breach of this agreement by either party, if the breaching party fails to cure the material breach during a 90-day period after notice of the breach has been provided, then the non-breaching party may terminate the agreement on a country-by-country or product-by-product basis with respect to the country(ies) and licensed product(s) to which the breach relates.

Operating Lease and Mutual Termination of Lease Agreement In 1998, the Company entered into an operating lease for office and laboratory space in Tucker, Georgia through October 31, 2008 with C.S. Family, LLC as the lessor, an entity with which Dr. Schinazi is affiliated. For the twelve months ended December 31, 2005 (unaudited), the Company had paid a total of $237,604 to the lessor under this agreement. The Company completed its relocation from Georgia to New Jersey in late 2005 and no longer maintains any operations in Georgia. Effective February 7, 2006, the Company entered into a Mutual Termination of Lease Agreement with the lessor, pursuant to which the Company paid $1.4 million (in addition to the balance of its security deposit and including repairs to the facilities) as full and final payment for and satisfaction of all amounts and other obligations due under the operating lease.

License Agreements with Emory University In 1998, the Company entered into various license agreements with Emory University to pursue the research, development and commercialization of various licensed compounds (including Racivir and DFC) and related technologies. The Company and Emory University will share in the proceeds, if any, received by the Company related to the development, sublicensing and commercialization of the licensed compounds, including milestone payments, fees, and royalties. Dr. Schinazi is an employee of Emory University and a named inventor of Racivir, DFC and certain of the other licensed compounds and related technologies and may receive a percentage of the milestone payments, fees and royalties paid by the Company to Emory University. In connection with several of these license agreements, the Company issued to Emory University 179,973 shares of redeemable common stock. Such amount was expensed to the statements of operations and comprehensive net loss for the year ended December 31, 1998 and the 179,973 shares of redeemable common stock were converted into 179,973 shares of common stock on May 2, 2007 when the Company completed the IPO.

Consulting Agreement In June 2005, the Company entered into a consulting agreement with Michael K. Inouye, a member of the Board of Directors. During the years ended September 30, 2008, 2007 and 2006, the Company paid $0, $0, and $9,700, respectively, to Mr. Inouye.

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NOTES TO FINANCIAL STATEMENTS (Continued)

4. INVESTMENTS

Available-for-sale investments as of September 30, 2008, consist of a corporate bond that matures on January 26, 2009. The following table summarizes the fair value, gross unrealized holding gain (loss), and cost basis as of September 30, 2008 and 2007.

	Fair Value	Gross Unrealized Holding Gain (Loss)	Cost
September 30, 2008			
Corporate Bond	$ 497,310	$ (2,604)	$ 499,914
September 30, 2007			
Corporate Bonds	$ 1,252,113	$ 4,405	$ 1,247,708

5. ACCRUED EXPENSES

Accrued expenses consisted of the following:

	As of September 30,	
	2008	2007
	(In thousands)	
Accrued compensation	$ 1,161	$ 790
Accrued accounting fees		69
Accrued legal fees	984	700
Accrued license fees		1,195
Accrued clinical trial expenses	3,367	2,309
Other accrued expenses	670	450
	$ 6,182	$ 5,513

6. CONTRACT REVENUE AGREEMENTS

The following is a reconciliation between cash payments received and receivable under contract revenue agreements and contract revenues reported:

	Years Ended September 30,		
	2008	2007	2006
		(In thousands)	
Cash received/receivable	$	$ 20,425	$ 2,548
Deferred		(375)	(2,500)
Amortization	1,857	1,959	5,377

Revenues	$ 1,857	$ 22,009	$ 5,425

The Company recorded revenues from the collaboration agreement with Roche comprising 100%, 99.8% and 39.3% of total revenues during the fiscal years ended September 30, 2008, 2007 and 2006. The Company recorded revenues from the collaboration agreement with Incyte Corporation comprising 0.0%, 0.0% and 59.8% of total revenues during the fiscal years ended September 30, 2008, 2007 and 2006, respectively. No other customer accounted for 10% or more of the Company s total revenues in the periods presented herein.

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NOTES TO FINANCIAL STATEMENTS (Continued)

Roche In October, 2004, the Company entered into a collaboration and license agreement with Roche to develop PSI-6130, PSI-6130 pro-drugs and chemically related nucleoside polymerase inhibitors for all indications, including the treatment of chronic HCV infections. Roche paid the Company an up-front payment of $8.0 million and has agreed to pay future research and development costs. The up-front payment was recorded as deferred revenue and is being amortized over the estimated development period. Roche has also agreed to make milestone and commercialization payments to the Company for PSI-6130 and its pro-drugs, the lead nucleoside compound of the collaboration, assuming successful development and marketing in Roche s territories. The portion of the above payments recorded as deferred revenue on the Company s balance sheets as of September 30, 2008 and 2007 was $5.7 million and $7.6 million, respectively.

In addition, the Company will receive royalties paid as a percentage of total annual net product sales, if any, and the Company will be entitled to receive one time performance payments should net sales from the product exceed specified thresholds.

The Company granted Roche worldwide rights, excluding Latin America and Korea, to PSI-6130 and its related compounds. The Company retained certain co-promotion rights in the United States. The Company will be required to pay Roche royalties on net product sales, if any, in the territories the Company has retained. Roche will fund research related to the collaboration. Roche will fund and the Company will be responsible for preclinical work, the IND filing, and the initial clinical trial, and Roche may manage other preclinical studies and clinical development. Roche has reimbursed the Company for $5.1 million, $4.2 million, and $4.7 million during the fiscal years ended September 30, 2008, 2007 and 2006, respectively, under this agreement.

The agreement will terminate once there are no longer any royalty or payment obligations. Additionally, Roche may terminate the agreement in whole or in part by providing six months written notice to the Company. Otherwise, either party may terminate the agreement in whole or in part in connection with a material breach of the agreement by the other party that is not timely cured. In the event of termination, Roche must assign or transfer to the Company all regulatory filings, trademarks, patents, preclinical and clinical data related to this collaboration.

In conjunction with the agreement, Roche purchased 400,000 shares of the Company s Series R redeemable convertible preferred stock and received warrants to purchase up to an additional 470,588 shares of Series R-1 redeemable convertible preferred stock for $4.0 million. These shares and warrants were initially recorded at fair value for financial reporting purposes. The 400,000 shares of Series R redeemable convertible preferred stock were converted into 266,666 shares of the Company s common stock on May 2, 2007 when the Company completed the IPO, and the related warrants expired without exercise on October 26, 2006.

Incyte Corporation In September 2003, the Company entered into a collaborative and license agreement with Incyte to develop and commercialize DFC for the treatment of HIV. The Company received an upfront payment of $6.25 million as a license fee, partial reimbursement for past development study and patent costs and in-process research and development. The upfront payment and related license and other direct costs had been amortized over the estimated time to Food and Drug Administration (FDA) approval of the drug, which coincided with the period over which the Company was to provide advisory services related to the development and regulatory approval of the drug.

On April 3, 2006, Incyte announced its decision to discontinue its development of DFC. Along with its decision, Incyte terminated the collaborative and license agreement it entered into with Pharmasset and returned its rights related to DFC to the Company. Since the upfront payment noted above was non-refundable, the termination of the collaborative and license agreement by Incyte resulted in immediate recognition of the

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

remaining deferred revenue (relating to this upfront payment) as revenues. The Company has analyzed the preclinical and clinical data on DFC generated by Incyte. A path for the further development of DFC has not yet been identified.

Under the agreement, the Company was to have received milestone payments and royalties on sales of the approved product. Incyte was responsible for all clinical development, patent and commercialization costs. As a result of this termination, the Company will no longer be eligible to receive milestone payments or royalties from Incyte with respect to DFC, and the Company will be solely responsible for any additional expenses that it may incur in connection with the development of DFC.

7. IN-LICENSE AGREEMENTS

Boehringer Ingelheim Chemicals, Inc. On August 8, 2008, the Company entered into a manufacturing services agreement with Boehringer Ingelheim Chemicals, Inc. (BICI) for the manufacture of clinical supplies of the active pharmaceutical ingredient (API) of clevudine. In addition to covering the clinical supply of the API, the Manufacturing Services Agreement also contains terms related to any eventual commercial manufacture and supply of the API by BICI. The Manufacturing Services Agreement has an initial term of five years and at the Company s option may be extended for an additional three years, and under certain circumstances, may be terminated by either the Company or BICI in advance of the expiration of its term. The Company also entered into a license agreement with BICI pursuant to which BICI granted the Company a non-exclusive, worldwide, perpetual, royalty-free license, with the right to sublicense to contract manufacturing organizations solely for the purpose of manufacturing the API on behalf of the Company, to use and practice certain BICI technology related to the manufacture of the API (the License). The Company agreed that in exchange for the License, and in addition to certain cash payments it will pay to BICI, the Company will, for a period of time after one or more products incorporating the API have been approved for commercialization by the FDA, source a certain minimum amount of its commercial requirements for the API exclusively from BICI.

Bukwang Pharmaceutical Company Ltd. In June 2005, the Company entered into a collaboration and license agreement with Bukwang Pharm. Co., Ltd. (Bukwang) to develop and commercialize clevudine. Bukwang granted the Company exclusive rights to develop, manufacture, and market clevudine in North America, Europe, Central and South America, the Caribbean, and Israel. Bukwang retained rights to the rest of the world, excluding those Asian territories which were licensed to Eisai Company Ltd. (Eisai) in November 2004.

The Company paid Bukwang an up-front payment of $6.0 million, which was included in research and development expenses in the nine months ended September 30, 2005. The Company accrued an additional $1.0 million payment in September 2007 upon the initiation of Phase 3 registration studies of clevudine, and may pay up to $23.0 million in additional milestone payments related to development, regulatory and commercialization events, and future royalties on net sales. The up-front and milestone payments to date have been expensed as incurred as no alternative use exists. The Company has the right to use the clinical data generated by Bukwang or Eisai, as well as all historical data collected by the prior licensee, Triangle Pharmaceuticals (acquired by Gilead Sciences in 2003) or Gilead Sciences. The Company will be responsible for conducting any future clinical trials, regulatory filings, and the commercialization of clevudine in its territories. Bukwang and Eisai are responsible for all ongoing clinical trials, regulatory filings, and the commercialization of clevudine in their respective territories. The Company s collaboration and license agreement with Bukwang will terminate once there are no longer any royalty obligations. The Company may terminate the agreement by providing six months written notice to Bukwang. In addition, either party may terminate the agreement if the other party commits a material breach of the agreement that is not timely cured. In the event of termination at will by the Company or for the

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Company s breach, the Company must license or transfer to Bukwang all regulatory filings, trademarks, patents, preclinical and clinical data related to this agreement. In the event of termination for a breach by Bukwang, Bukwang must license or transfer to the Company all patents, know-how, and manufacturing processes related to this agreement.

On June 23, 2005, the Company, along with the University of Georgia Research Foundation, Inc., (UGARF), and Yale University (Yale), signed a memorandum of understanding with regard to the patents and technology related to clevudine that had been exclusively licensed to Bukwang, and which the Company currently sublicenses from Bukwang. The memorandum of understanding provides that UGARF and Yale will grant the Company a license to these patents and technology in the event that the primary license with Bukwang is terminated, provided that the reason for such termination does not relate to any breach of the Company s sublicense by the Company or on the Company s behalf.

University of Georgia Research Foundation, Inc., Emory University and UAB Research Foundation, Inc. On December 30, 1998, Emory University (Emory University) granted to the Company an exclusive, worldwide license to make, have made, use, import, offer for sale and sell medical products based on a compound now known as DFC, including certain of its analogs and derivatives. In September 2003, the Company sublicensed the rights to DFC in certain territories to Incyte, under a collaboration and license agreement described in Note 6. On February 19, 1999, the Company issued 66,667 shares of its redeemable common stock to Emory University. The fair value was expensed in the statements of operations and comprehensive net loss for the year ended December 30, 1999. In addition, the Company agreed to pay Emory University a certain percentage of milestone payments and royalties that the Company receives from Incyte.

On December 8, 1998, Emory University granted the Company an exclusive, worldwide license pursuant to a license agreement (Racivir License Agreement) to make, have made, use, import, offer for sale and sell drug products based on a specified range of mixtures of ( ) FTC and (+) FTC (enriched FTC), which includes the mixture that the Company is developing as Racivir. As part of the consideration for this agreement, the Company issued to Emory University 66,667 shares of redeemable common stock, and agreed to pay Emory University royalties as a percentage of net product sales. The Company subsequently issued to Emory University an additional 13,307 shares of redeemable common stock pursuant to an anti-dilution provision in the agreement. The Company may also pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments. The agreement will expire upon the expiration of all licensed patents.

In a license agreement relating to emtricitabine that Emory University entered into with Triangle Pharmaceuticals, now Gilead Sciences, Inc., or Gilead, in 1996 (Emory/Gilead License Agreement), Emory University previously had granted a right of first refusal to Gilead that is applicable to any license or assignment relating to enriched FTC (which includes Racivir). The terms of this right of first refusal contains an exception permitting Emory University to license or assign its rights in respect of enriched FTC to any of the inventors (which included two of the founders of the Company) or to any corporate entity formed by or on behalf of the inventors for purposes of clinically developing enriched FTC so long as the licensee agrees in writing to be bound by the terms of Gilead s right of first refusal to the same extent as Emory University. The Company s license to Racivir was granted to the Company by Emory University pursuant to this exception and therefore the Company is bound by the terms of Gilead s right of first refusal to the same extent as Emory University.

Under the above license agreements with Emory University regarding DFC and Racivir, the Company is obligated to make minimum royalty payments to Emory University if a new drug registration of a compound resulting from the licensed technology is obtained and the compound is subsequently commercialized. These minimum royalty payments would begin in the second year following a New Drug Application (NDA)

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PHARMASSET, INC.

NOTES TO FINANCIAL STATEMENTS (Continued)

Registration, and continue until the tenth year. The Company may also make up to $1.0 million in marketing milestone payments under each of the two license agreements to Emory University if any products are commercialized and sold.

In March 2004, the Company entered into a supplemental agreement with Emory University in which it and Emory University agreed that, prior to any commercialization of enriched FTC by the Company, or by any licensee or assignee of the Company s rights under the Racivir License Agreement, the Company and Emory University would adhere strictly to the terms of the right of first refusal granted to Gilead in the Emory/Gilead License Agreement and offer to Gilead the same terms and conditions under which the Company, its licensee or assignee, propose to commercialize enriched FTC. Therefore, before the Company could enter into a commercialization agreement for Racivir with a third party or commercialize Racivir on its own, it would be required to offer Gilead the opportunity to be its commercialization partner on the same terms in which the Company intends, or its prospective partner intends, to commercialize Racivir. It is uncertain whether a third party would be willing to negotiate the terms of a commercialization agreement with the Company knowing that Gilead can take their place as licensee by accepting the negotiated terms and exercising its right of first refusal.

In 1998 and 2004, the Company entered into various license agreements in addition to those described above with UGARF, Emory University and the University of Alabama at Birmingham Research Foundation, Inc. (collectively, the Universities) to pursue the research, development and commercialization of certain human antiviral, anticancer and antibacterial applications and uses of certain specified technologies. Under each of these agreements, the Universities have granted an exclusive right and license under the related patents to the Company. The Company and the Universities will share in any proceeds received by the Company related to internal development or sublicensing of the specified technologies, including milestone payments, fees, and royalties.

In April 2002, the license agreement between UGARF, Emory University, and the Company dated June 16, 1998 was selectively modified to terminate certain technologies and related rights and obligations.

8. VENTURE LOAN AND SECURITY AGREEMENT

On September 30, 2007, the Company entered into a Loan Agreement that allowed the Company to borrow up to $30.0 million in $10.0 million increments (Loan Agreement). The Company borrowed the first and second $10.0 million increments by signing two Secured Promissory Notes (Notes) on October 5, 2007 and March 28, 2008, respectively, and is currently negotiating to borrow an additional $3.3 million under the Loan Agreement. The Notes bear interest at 12% and are to be repaid over a 45-month period with the first 15 monthly payments representing interest only followed by 30 equal monthly payments of principal and interest. The principal monthly repayments on the first $10.0 million begin on March 1, 2009 and end on August 1, 2011. The principal monthly repayments on the second $10.0 million begin on August 1, 2009 and end on January 1, 2012. Total principal repayments of the two Notes amount to $2.7 million in fiscal 2009, $7.6 million in fiscal 2010, $8.2 million in fiscal 2011, and $1.5 million in fiscal 2012. Prepayment of the loans made pursuant to the Loan Agreement is subject to penalty and substantially all of the Company s tangible and intangible assets (except for intellectual property) are collateral for the Loan Agreement.

Under the Loan Agreement, the Company agreed that in the event its market capitalization is below $90.0 million for 15 consecutive days in which the principal market for its common stock is open for trading to the public, the Company will be required to repay 50% of the then outstanding principal balance of the loans. The Company further agreed that in the event its market capitalization is below $40.0 million for 15 consecutive days in which the principal market for its common stock is open for trading to the public, the Company will be required to repay all of the then outstanding principal balance of the loans.

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In conjunction with entering into the Loan Agreement, the Company granted warrants to the lender to purchase shares of the Company s common stock (See Note 9). Since these warrants were granted in conjunction with entering into the Loan Agreement and with the intention of executing promissory notes, the relative fair value of the warrant was recorded as equity and deferred interest as the warrants became exercisable and the deferred financing costs and debt discount are being amortized over the term of the promissory notes using the effective interest method.

9. STOCKHOLDERS EQUITY (DEFICIT), REDEEMABLE STOCK CONVERSIONS, AND WARRANTS

Common Stock As of September 30, 2008, the Company had 100,000,000 shares of common stock authorized with a par value of $0.001 and the Company had reserved 2,371,861 shares of common stock for issuance upon the exercise of outstanding common stock options. Also, 650,795 shares of the Company s common stock were reserved for future grants of stock options (or other similar equity instruments) under the Company s 2007 Equity Incentive Plan as of September 30, 2008. In addition, 116,183 shares of the Company s common stock were reserved for future exercise of outstanding warrants as of September 30, 2008.

During fiscal 2007, 13,333 shares of common stock were purchased at a fair value of $9.0 per share. Such shares were immediately retired.

Registered Direct Public Offering On July 21, 2008, the Company completed a registered direct public offering of 1,450,000 shares of its common stock to a select group of institutional investors at a price of $17.85 per share, resulting in $24.1 million in net proceeds after deducting placement agent fees and offering expenses. The Company intends to use the net proceeds from the sale of the shares for general corporate purposes, which may include, but are not limited to, the acquisition of assets or businesses that are complementary to its existing business, the funding of clinical trials and the funding of in-licensing agreements for product candidates, additional technologies or other forms of intellectual property.

Initial Public Offering On May 2, 2007, the Company completed an IPO of 5,050,000 shares of its common stock (including the underwriters exercise of a portion of their over-allotment option) at a public offering price of $9.00 per share. Net cash proceeds from the IPO were $40.7 million after deducting offering costs paid during fiscal 2007 and $39.1 million after deducting additional offering costs paid in fiscal 2006.

Redeemable Stock Conversions In conjunction with the completion of the IPO on May 2, 2007, and pursuant to the amended and restated by-laws of the Company, all outstanding shares of redeemable convertible preferred stock (Series B, C, D and R See Note 10) were converted into an aggregate of 2,432,569 shares of common stock as follows:

Preferred Stock Series	Amount of Common Shares
Series B	245,331
Series C	250,120
Series D	1,670,452
Series R	266,666
	2,432,569

In addition, holders of the Series D redeemable convertible preferred stock (See Note 10) were entitled to receive quarterly dividends at a rate equal to 7.5% per annum of the purchase price per share. Such dividends accrued from February 4, 2006 through May 2, 2007, the closing date of the IPO, and were paid out in the form

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of 131,864 shares of common stock. Also, all outstanding shares of redeemable common stock and Series A convertible preferred stock were converted into 213,306 and 1,759,808 shares of common stock, respectively on May 2, 2007.

Warrants In conjunction with entering into a Loan Agreement (See Note 8), the Company granted a warrant to the lender to purchase up to 149,377 shares of the Company s common stock at a price of $12.05. The warrants are immediately exercisable (as of September 30, 2007) for 66,390 shares of common stock and warrants to purchase an additional 49,793 shares of common stock became exercisable on March 28, 2008, the date the Company executed a second promissory note with the lender in the amount of $10.0 million. The warrants expire seven years from the date of grant or upon a change of control as defined in the Loan Agreement. The fair value of the warrants were calculated using the Black-Scholes warrant-pricing methodology and the relative fair values were recorded as equity and deferred interest as the warrants became exercisable.

During fiscal 2007, the Series D-1 warrants originally granted in August 2004 (see Note 10) were exercised in full in connection with the IPO on a net exercise basis, which resulted in the Company issuing 822,689 shares of common stock to the warrant holders. Warrants to purchase up to 470,588 shares of Series R-1 redeemable convertible preferred stock granted in conjunction with Roche s purchase of 400,000 shares of the Company s Series R redeemable convertible preferred stock expired without exercise on October 26, 2006.

Preferred Stock Accretion Preferred stock accretion was $1,775,684 and $1,110,973 during the years ended September 30, 2007 and 2006, respectively. The accretion recorded during 2007 includes $1.0 million of accretion to bring the carrying amounts of the redeemable convertible preferred stock to their redemption values as of May 2, 2007, the date the Company completed the IPO and converted all of its redeemable convertible preferred stock outstanding into common stock.

10. REDEEMABLE STOCK AND WARRANTS

During the fiscal year ended September 30, 2007, the Series D-1 Warrants were exercised in full, and the Series R-1 Warrants expired without exercise. Also, the Series A Convertible Preferred Stock, the Series B, C, D and R redeemable convertible preferred stock, and the redeemable common stock were converted into common stock on May 2, 2007, the date the Company completed its IPO (See Note 9).

Following are descriptions of the Series A Convertible Preferred Stock, the Series B, C, D and R redeemable convertible preferred stock, the Series D-1 and R-1 Warrants, and the redeemable common stock.

Series A Convertible Preferred Stock The Company authorized 3,200,000 shares of Series A convertible preferred stock (Series A Preferred Stock). Series A Preferred Stock was convertible into common stock at the option of each holder, and automatically upon the earlier of the completion of a qualifying underwritten public offering of the Company s common stock, at an initial conversion ratio of one-to-one, subject to certain anti-dilution adjustments, or upon the vote of the holders of two-thirds of the shares of all preferred stock and the holders of two-thirds of the shares of Series D redeemable convertible preferred stock (Series D Preferred Stock). Holders of shares of Series A Preferred Stock had voting rights equal to the number of shares of common stock into which such shares were convertible. Shares of Series A Preferred Stock were not entitled to dividends unless declared by the board of directors. In the event the Company was liquidated, holders of Series A Preferred Stock were entitled to receive, prior to and in preference to the holders of common stock and redeemable common stock, an amount equal to the amount paid in plus any declared and unpaid dividends.

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NOTES TO FINANCIAL STATEMENTS (Continued)

The Series A Preferred Stock was issued at various times between February 1999 and September 2000 for an aggregate purchase price of approximately $5,630,000.

Series B and C Redeemable Convertible Preferred Stock The Company authorized 2,300,000 shares of Series B redeemable convertible preferred stock (Series B Preferred Stock) and 1,357,798 shares of Series C redeemable convertible preferred stock (Series C Preferred Stock). Series B Preferred Stock and Series C Preferred Stock were convertible into common stock at the option of each holder, and automatically upon the completion of a qualifying underwritten public offering of the Company s common stock, at an initial conversion ratio of one-to-one, subject to certain anti-dilution adjustments, or upon the vote of the holders of two-thirds of the shares of all preferred stock and the holders of two-thirds of the shares of Series D Preferred Stock. The stockholders agreement provided that, on or after August 4, 2009, outstanding shares were redeemable at the option of the holders of a majority of the shares of all preferred stock and a majority of the shares of the Series D Preferred Stock. The shares of Series B and C Preferred Stock were redeemable at an amount equal to the amount paid in, plus declared and unpaid dividends thereon. The redemption rights terminated upon a qualifying underwritten public offering of the Company s common stock.

The holders of shares of Series B and C Preferred Stock had voting rights equal to the number of shares of common stock into which such preferred shares were then convertible. Holders of Series B and C Preferred Stock were entitled to dividends, on an as-if converted basis, if the board of directors declared dividends on the common stock. In the event the Company was liquidated, holders of Series B and C Preferred Stock were entitled to receive, prior to and in preference to the holders of common stock, redeemable common stock and Series A, R, D-1 and R-1 Preferred Stock, an amount equal to the initial amount paid in plus any declared and unpaid dividends. Series B and C Preferred Stockholders were also entitled to receive a pro rata portion of the amounts paid to common stockholders, on an as-if converted basis. Holders of Series B and C Preferred Stock had a right of first refusal on new shares issued by the Company, pro rata on a fully diluted basis, and on the resale of shares by certain stockholders.

The Series B Preferred Stock was issued in June 1999 for an aggregate purchase price of approximately $3,910,000. The Series C Preferred Stock was issued in February 2001 for an aggregate purchase price of approximately $7,399,999. As of September 30, 2006, $755 and $1,563 remained to be accreted for Series B and Series C Preferred Stock, respectively, over the period remaining to potential future redemption.

Series D Redeemable Convertible Preferred Stock The Company authorized 7,843,380 shares of Series D redeemable convertible preferred stock (Series D Preferred Stock). Series D Preferred Stock was convertible into common stock at the option of each holder, and automatically upon the completion of a qualifying underwritten public offering of the Company s common stock, at an initial conversion ratio of one-to-one subject to certain anti-dilution adjustments, or upon the vote of the holders of two-thirds of the shares of all preferred stock and the holders of two-thirds of the shares of Series D Preferred Stock. The stockholders agreement provided that, on or after August 4, 2009, outstanding shares were redeemable at the option of the holders of a majority of the shares of all preferred stock and the holders of a majority of the shares of Series D Preferred Stock. The shares of Series D Preferred Stock were redeemable at an amount equal to the amount paid in, plus declared and unpaid dividends thereon. The redemption rights terminated upon a qualifying underwritten public offering of the Company s common stock.

The holders of shares of Series D Preferred Stock had voting rights equal to the number of shares of common stock into which such preferred shares were then convertible. Holders of Series D Preferred Stock were entitled to dividends, on an as-if converted basis, if the board of directors declares dividends on the common stock. The holders of Series D Preferred Stock were also entitled to receive quarterly dividends at a rate equal to

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NOTES TO FINANCIAL STATEMENTS (Continued)

7.5% per annum of the purchase price per share for the Series D Preferred Stock. Such dividends began to accrue on the Series D Preferred Stock commencing on February 4, 2006, and thereafter accrued quarterly, whether or not such dividends were declared and whether or not there were profits, surplus or other funds of the Company legally available for the payment of dividends. In the event the Company was liquidated, holders of Series D Preferred Stock were entitled to receive, prior to and in preference to the holders of common stock, redeemable common stock and Series A, R, R-1 and D-1 Preferred Stock, an amount equal to the initial amount paid in plus any declared and unpaid dividends. Series D Convertible Preferred Stockholders were also entitled to receive a pro rata portion of the amounts paid to common stockholders, on an as-if converted basis. Holders of Series D Preferred Stock had a right of first refusal on new shares issued by the Company, pro rata on a fully diluted basis, and on the resale of shares by certain stockholders. The Series D Preferred Stock was issued in August 2004 for an aggregate purchase price of approximately $40,001,238. As of September 30, 2006, $3,175,028 remained to be accreted for Series D Preferred Stock over the period remaining to potential future redemption including future accrual of dividends.

Series D-1 Warrants In conjunction with the Series D financing in August 2004, the Company authorized the issuance of Series D-1 warrants to purchase 1,254,960 shares of Series D-1 convertible preferred stock (Series D-1 Preferred Stock) at an exercise price of $0.10 per share. Series D-1 warrants became exercisable August 4, 2006 and expired August 4, 2009. Series D-1 warrants were subject to earlier termination pursuant to the completion of either a qualifying underwritten public offering of the Company s common stock or a qualifying merger or acquisition on or before the expiration date. The fair value of these warrants on the effective date of the Series D financing was estimated using the Black-Scholes option-pricing methodology.

If the warrants were exercised, the Series D-1 Preferred Stock was convertible into Common Stock at the option of the Holder and automatically upon the completion of a qualifying underwritten public offering of the Company s common stock, at an initial conversion ratio of one-to-one subject to certain anti-dilution adjustments, or upon the vote of the holders of two-thirds of the shares of all preferred stock and the holders of two-thirds of the shares of Series D Preferred Stock. The par value of the Series D-1 Preferred Stock was $0.001.

The holders of shares of Series D-1 Preferred Stock have voting rights equal to the number of shares of common stock into which such preferred shares were then convertible. Holders of Series D-1 Preferred Stock were entitled to dividends, on an as-if converted basis, if the board of directors declared dividends on the common stock. In the event the Company was liquidated, holders of Series D-1 Preferred Stock were entitled to receive, prior to and in preference to the holders of common stock and redeemable common stock, an amount equal to the initial amount paid in plus any declared and unpaid dividends. Series D-1 Preferred Stockholders were also entitled to receive a pro rata portion of the amounts paid to common stockholders, on an as-if converted basis.

Series R Redeemable Convertible Preferred Stock The Company authorized 400,000 shares of Series R redeemable preferred stock (Series R Preferred Stock). Series R Preferred Stock was convertible into common stock at the option of the holder, and automatically upon the completion of a qualifying underwritten public offering of the Company s common stock, at an initial conversion ratio of one-to-one subject to certain anti-dilution adjustments or upon the vote of the holders of two-thirds of the shares of all preferred stock and the holders of two-thirds of the shares of Series D Preferred Stock. The stockholders agreement provided that, on or after August 4, 2009, outstanding shares were redeemable at the option of the holders of a majority of all preferred stock and a majority of the Series D Preferred Stock. The shares of Series R Preferred Stock were redeemable at an amount equal to the amount paid in, plus declared and unpaid dividends thereon. The redemption rights terminated upon a qualifying underwritten public offering of the Company s common stock.

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NOTES TO FINANCIAL STATEMENTS (Continued)

The holders of shares of Series R Preferred Stock had voting rights equal to the number of shares of common stock into which such preferred shares were then convertible. Holders of Series R Preferred Stock were entitled to dividends, on an as-if converted basis, when the board of directors declared dividends to holders of common stock. In the event the Company was liquidated, holders of Series R Preferred Stock were entitled to receive, prior to and in preference to the holders of common stock and redeemable common stock, an amount equal to the initial amount paid in plus any declared and unpaid dividends. The Series R Preferred Stock was issued in October 2004 for an aggregate purchase price of $4,000,000. As of September 30, 2006, $203,059 remained to be accreted for Series R Preferred Stock over the period remaining to potential future redemption.

Series R-1 Warrants In conjunction with the issuance of Series R Preferred Stock in October 2004, the Company issued warrants to purchase 470,588 shares of Series R-1 redeemable convertible preferred stock (Series R-1 Preferred Stock) at an exercise price of $12.75 per share. Series R-1 Warrants became exercisable October 26, 2004 and expired October 26, 2006. These warrants were accounted for as a separate component of redeemable stock with a carrying value equal to their fair market value on the effective date of the Series R financing, which was estimated using the Black-Scholes option-pricing methodology.

Redeemable Common Stock In connection with various license agreements entered into in 1998, the Company issued to Emory University and University of Georgia Research Foundation Inc. 179,973 and 33,334 shares, respectively, of redeemable common stock (See Note 7). Redeemable common stock was redeemable at the option of the holder, at fair market value as determined by an independent appraisal. These redemption rights terminated upon the completion of a registered public offering of the Company s common stock. The carrying value of the redeemable common stock was adjusted to an estimate of its fair market value for financial reporting purposes each quarter. This estimate was made by taking into consideration such variables as the valuations attained by other comparable biotechnology companies in recent initial public offerings; the judgment of investment bankers as to the probability of executing a successful initial public offering; the liquidation preferences of the Company s preferred stock; the balance of the Company s cash, cash equivalents and short term investments; and the present value of the Company s product candidates as estimated, when available, from the market value of publicly traded companies developing comparable product candidates, and when this was not available, by a discounted cash flow analysis based on cost and revenue estimates provided by management, third party clinical research organizations and marketing consultants, using discount rates provided by an independent appraiser.

11. STOCK COMPENSATION

The Company s 1998 Stock Plan (1998 Plan), as amended, was originally adopted by its board of directors during 1998 and subsequently amended in 2000, 2004 and 2006. A maximum of 3,517,015 shares of the Company s common stock are authorized for issuance under the 1998 Plan. The purpose of the 1998 Plan is to provide an incentive to officers, directors, employees, independent contractors and to other persons who provide significant services to the Company. Upon the closing of the IPO, which occurred on May 2, 2007, the Company adopted the 2007 Equity Incentive Plan (2007 Plan). Upon the adoption of the 2007 Plan, no additional awards will be issued under the 1998 Plan and the shares remaining for future grant under the 1998 Plan were transferred to the 2007 Plan. As of September 30, 2008, 650,795 shares of the Company s common stock were reserved for future grants of stock options, stock appreciation rights, restricted stock, deferred stock, restricted stock units, performance shares, phantom stock and similar types of stock awards as well as cash awards. Options granted under the 2007 Plan may be either incentive stock options, as defined under Section 422 of the Code or nonstatutory stock options. Options granted under the 2007 Plan shall be at per share exercise prices equal to the fair value of the shares on the dates of grant. The 2007 Plan will terminate in fiscal 2017 unless it is extended or terminated earlier pursuant to its terms.

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NOTES TO FINANCIAL STATEMENTS (Continued)

Stock Options The assumptions used and weighted-average information for employee and director grants for the years ended September 30, 2008, 2007 and 2006 are as follows:

	Years Ended September 30,		
	2008	**2007**	**2006**
Risk free interest rate	4.01%	4.55%	4.78%
Expected dividend yield	0.0%	0.0%	0.0%
Expected lives (years)	6.03	5.94	5.00
Expected volatility	56.76%	54.33%	53.10%
Weighted-average fair value of options granted	$ 8.33	$ 2.79	$ 1.98

Generally, stock options granted under these plans have a contractual life of ten years and vest pro rata over a four year term. A summary of the Company s stock option activity during the year ended September 30, 2008 is as follows:

	Number of Shares	**Weighted Average Exercise Price**
Outstanding September 30, 2007	2,101,273	$ 4.01
Granted	904,600	$ 14.67
Exercised	(616,846)	$ 4.28
Forfeited	(17,166)	$ 8.83
Outstanding September 30, 2008	2,371,861	$ 7.97
Exercisable September 30, 2008	1,117,609	$ 4.31

The range of exercise prices of stock options outstanding at September 30, 2008 was $1.50 to $32.00. The weighted average remaining contractual life of stock options outstanding at September 30, 2008 was 7.62 years. The total intrinsic value of options exercised during the year ended September 30, 2008 was $9,119,449. The Company recognized compensation expense of $2,758,062, $1,552,690, and $454,078 during the years ended September 30, 2008, 2007 and 2006, related to stock options issued to non-employees and employees. As of September 30, 2008 and 2007, $6,821,109 (including $5,981,822 resulting from the adoption of SFAS 123R) and $3,500,662 (including $1,977,912 resulting from the adoption of SFAS 123R), respectively, of deferred stock-based compensation expense related to employee stock options remained unamortized. The unamortized amount of $5,981,822 as of September 30, 2008 has a weighted-average period of approximately 1.55 years to be recognized.

Outstanding as of September 30, 2008				**Exercisable as of September 30, 2008**	
Number of Options	**Exercise Price**	**Weighted Average Remaining Contractual Life (in Years)**	**Weighted Average Exercise Price**	**Number of Options**	**Weighted Average Exercise Price**
73,334	$ 1.50 $ 2.99	0.66	$ 1.50	73,334	$ 1.50
1,211,741	$ 3.00 $ 4.49	6.97	$ 3.46	849,766	$ 3.31
37,167	$ 4.50 $ 5.99	8.31	$ 5.46	19,678	$ 5.44
54,602	$ 6.00 $ 7.49	3.56	$ 6.47	54,602	$ 6.47
100,417	$ 7.50 $10.49	8.53	$ 8.98	77,729	$ 8.97

739,600	$ 10.50	$15.00	9.09	$	13.69	15,000	$ 13.67
154,000	$ 15.01	$29.99	9.70	$	19.36	27,500	$ 19.24
1,000	$ 30.00	$45.00	9.31	$	32.00		$

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NOTES TO FINANCIAL STATEMENTS (Continued)

As of September 30, 2008, there were 2,261,090 options outstanding that were either vested or expected to vest in the future, of which 1,117,609 options were currently exercisable, with weighted average exercise prices of $7.77 and $4.31 per share, aggregate intrinsic values of $27,585,839 and $17,487,784, and weighted average remaining contractual terms of 7.56 and 6.35 years, respectively.

Restricted Stock During the fiscal year ended September 30, 2008, the Company issued a total of 40,666 shares of restricted stock to its non-employee directors and to a non-employee (consultant). The restricted stock issued to each non-employee Director vests on July 16, 2009, as long as the director continues to serve on the Company s Board of Directors on that date. The restricted stock issued to the non-employee (consultant) vests quarterly over a four year period. As of September 30, 2008, holders were vested in 11,666 of the 40,666 restricted shares outstanding, leaving a total of 29,000 restricted shares unvested as of year end.

With regard to the restricted stock granted to the non-employee Directors, the fair value of the restricted stock issued was determined using the closing price of the Company s common stock as reported on the Global Market of The NASDAQ Stock Market LLC (NASDAQ) on the date of grant and is recognized as stock-based compensation expense evenly over the vesting period. The weighted average fair value of these shares as of the grant date was $20.01 per share.

With regard to the restricted stock granted to the non-employee (consultant), stock-based compensation expense equal to the fair value of the restricted shares that vest is recorded on a quarterly basis over the vesting period. The fair value of each of the restricted shares that vest is equal to the fair value of a share of the Company s common stock as of each vesting date.

The Company recognized compensation expense of $175,644 during the year ended September 30, 2008 related to restricted stock issued to its non-employee directors and to the non-employee (consultant). Unrecognized compensation expense for the restricted shares granted to the non-employee directors was $274,442 at September 30, 2008. This amount will be recognized over the remaining vesting period of the restricted shares.

Valuation of Privately-Held Company Stock Options Issued as Compensation During the years ended September 30, 2008, 2007 and 2006, the Company granted stock options to employees and directors at exercise and purchase prices deemed by the board of directors to be equal to the fair value of the common stock at the time of grant. Prior to January 1, 2006, the fair value of the common stock at the time of grant was determined by the board of directors at each stock option measurement date based on a variety of factors, including the Company s financial position and historical financial performance, the status of developments within the Company, the composition and ability of the current research and development and management team, an evaluation and benchmark of the Company s competitors, the current climate in the marketplace, the illiquid nature of the common stock, arm s length sales of the Company s capital stock (including redeemable convertible preferred stock), the effect of the rights and preferences of the preferred stockholders, and the prospects of a liquidity event, among others. In preparation for the Company s planned initial public offering, a retrospective analysis of the fair value of the common stock at option grant dates during 2005 using the methodology favored by the guidelines of the American Institute of Certified Public Accountants (AICPA) titled *Valuation of Privately-Held Company Equity Securities Issued as Compensation* was performed by management. The methodology developed at that time has subsequently been applied by management to the valuation of all employee stock options granted since 2005 through April 11, 2007, the date on which the last options were granted prior to April 27, 2007 when the Company s stock began trading on NASDAQ. The Company has not relied on an independent appraiser for stock option valuations because the Company used a methodology developed in accordance with AICPA guidelines and relied on the experience of management and

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NOTES TO FINANCIAL STATEMENTS (Continued)

members of its board of directors. Factors taken into consideration by this methodology include the judgment of management as to the probability of executing a successful initial public offering; the liquidation preferences of the Company s preferred stock; the net balance of the Company s cash, cash equivalents and short term investments; and the present value of the Company s product candidates as estimated, when available, from the market value of publicly traded companies developing comparable product candidates, and when this was not available, by a discounted cash flow (DCF) analysis based on cost and revenue estimates provided by third party clinical research organizations, marketing consultants and management and using discount rates provided by an independent appraiser.

The application of the Company s methodology for determining the fair value of the Company s common stock at each issuance date from January 1, 2006 through April 11, 2007 is discussed below:

Between May 24, 2006 and July 10, 2006, the Company granted 447,400 options to employees and members of the Company s board of directors. The Company s technology value as a private company was based on clevudine alone due to the early stage of development of R7128 and Racivir. A DCF analysis of clevudine was used due to the absence of a comparable program with an identifiable public market value. The value of the Company s common stock to a private investor was then calculated by adding this private technology value to the Company s net cash balance and subtracting the liquidation preference payments that would be made to the holders of the Company s preferred stock out of the proceeds of a private sale of the Company prior to any participation in the proceeds by holders of the Company s common stock. This process resulted in an estimate of the value of the Company s common stock as a private company of $3.87 per share, which the Company s board of directors deemed to be the appropriate fair value at which to set the exercise price of the options issued at that time. The theoretical value of the Company s common stock had it been publicly traded at that time was calculated by applying a premium, based on published academic research, to the Company s private technology value, to account for the value of the liquidity of a publicly traded stock, and adding the Company s net cash balance. No subtraction was made for liquidity preferences, since all the preferred stock was convertible to common stock upon an IPO. This process resulted in an estimate of the theoretical public price of the Company s common stock, based on clevudine alone, of $8.30 per share. The fair value of the Company s common stock used for financial reporting purposes was a weighted average of the private and public values, with the weights equal to the probability of executing a successful initial public offering versus a private sale of the Company, as estimated by management with the advice of investment bankers based on the recent experience of other biotechnology companies, market conditions and stockholder support for an initial public offering at that time. During this period, the probability of an IPO was considered to be 50%, resulting in a fair value of the Company s common stock for financial reporting purposes of $6.09 per share.

On November 7, 2006, the Company granted 317,067 options to employees and members of the Company s board of directors. The methodology used to determine the fair value of the Company s common stock at that time was the same as that described above, so only variations in its application are discussed below. The estimated value of the Company s common stock as a private company increased to $4.02 per share, based on the increase in the value of clevudine as it moved closer to market and the announcement of additional favorable clinical data that supported an increase in the revenue projection contained in the Company s DCF analysis. This increase in clevudine s value was partly offset by a reduction in the Company s net cash balance. The theoretical public price of the Company s common stock, based on clevudine alone, was estimated to be $8.75 at that time and the probability of an IPO was considered to be 50%, resulting in a weighted average fair value for financial reporting purposes of $6.38 per share.

From January 1, 2007 through April 11, 2007, the Company granted 147,500 options to employees and to a member of the Company s board of directors. The methodology used to determine the fair values of the

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Company s common stock during this time was the same as that described above, so only variations in its application are discussed below. The estimated value of the Company s common stock as a private company increased to amounts ranging from $4.02 to $5.63 per share, based on the increase in the value of the R7128 program as it advanced through Phase 1 clinical trials based on the valuation of a publicly traded company with an HCV program at a similar stage of development. The theoretical public price of the Company s common stock, based on clevudine and R7128, ranged from $8.84 to $11.28 during this time and the probability of an IPO was considered to be 90%, resulting in weighted average fair values for financial reporting purposes ranging from $6.53 to $10.71 per share.

During the year ended September 30, 2006, the Company granted 11,333 options to non-employees that are accounted for in accordance with EITF No. 96-18. The fair value of these awards on the initial grant date of $30,406 was estimated using the Black-Scholes option-pricing methodology.

12. INCOME TAXES

Income tax expense was $0 during the years ended September 30, 2008, 2007 and 2006.

The reconciliation between the federal statutory rate of 34.0% and the Company s effective tax rate is as follows:

	Years Ended September 30,		
	2008	**2007**	**2006**
Federal tax	-34.0%	-34.0%	-34.0%
State tax	-3.9%	-4.0%	-4.0%
Change in valuation allowance	36.3%	28.9%	36.5%
Stock compensation	1.6%	8.8%	1.3%
Other	0.0%	0.3%	0.2%
Effective tax rate	0.0%	0.0%	0.0%

The Company was originally organized in 1998 as a Barbados limited company, Pharmasset, Ltd., under Section 10 of the International Business Companies Act of Barbados. The Company was subject to United States withholding tax of 5% under the United States-Barbados tax treaty for United States sourced royalties paid to a Barbados company.

Pharmasset Ltd. owned a Georgia subsidiary which conducted research and development in the United States under a contract research and development agreement with the Company. Prior to June 8, 2004, only the Georgia subsidiary was subject to United States income taxes. The Company became domesticated as a corporation under the laws of the State of Delaware on June 8, 2004 as Pharmasset, Inc., on a tax-free basis with a carryover of the tax basis of its assets, and Pharmasset, Ltd. was dissolved on June 21, 2004. A portion of the expenses incurred by Pharmasset, Ltd. prior to the domestication have been capitalized for tax purposes and are to be amortized to offset future taxable income, if any, in the United States and a portion of these losses can not be utilized in the United States. On July 23, 2004, the Georgia subsidiary was merged into the Company.

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NOTES TO FINANCIAL STATEMENTS (Continued)

Deferred tax assets and liabilities are determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse. The components of the deferred taxes consist of the following:

	As of September 30,	
	2008	2007
	(in thousands)	
Deferred tax assets:		
Capitalized research and development	$ 1,219	$ 1,538
Net operating loss carryforwards	30,308	9,553
Payments received in collaborations	2,176	2,882
Licensing agreements	1,999	2,175
Stock compensation	684	449
Accrued liabilities	100	123
Research and development tax credits	138	138
Deferred rent	78	125
Depreciation	156	62
Gross deferred tax assets	36,858	17,045
Valuation allowance	(36,858)	(17,045)
Net deferred tax asset	$	$

As of September 30, 2008, the Company s unrecognized tax benefits ($126,000 as of October 1, 2007) have not significantly changed. The Company does not expect any significant changes to the unrecognized tax benefits within 12 months of the reporting date.

The IRS could challenge tax positions taken by the Company for the periods for which there are open tax years. The Company is open to challenge for the periods of 2005-2007 from federal and state jurisdictions, and from 1998-2004 for foreign jurisdictions.

As of September 30, 2008, the Company has United States federal net operating loss carryforwards of approximately $88.0 million available to offset future taxable income, if any. Of the federal net operating losses, $8.8 million was generated from windfall tax benefit stock option deductions. The tax benefit of this portion of the net operating loss will be accounted for directly to equity as additional paid in capital as the stock option related losses are utilized. As of September 30, 2008, the Company also had research and development tax credits of approximately $138,159 available to offset future tax liabilities. The loss carryovers and the research and development tax credits expire over a period of 2020 to 2029. The Barbados net operating losses effectively do not carry over as the Company does not anticipate conducting future business in that country. The Company established a full valuation allowance on its net deferred tax assets as it is more likely than not that such tax benefits will not be realized.

Utilization of the NOLs and research and development tax credit carryforwards may be subject to a substantial limitation under Section 382 of the Internal Revenue Code of 1986 due to changes in ownership of the Company that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. Since the Company s formation, the Company has raised capital through the issuance of capital stock on several occasions which, combined with the purchasing

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NOTES TO FINANCIAL STATEMENTS (Continued)

stockholders subsequent disposition of those shares, may have resulted in a change of control, as defined by Section 382. Due to the significant complexity and cost associated with a change in control study, and because there could be additional changes in control in the future, the Company has not formally assessed whether there has been one or more changes in control since the Company s formation. If the Company has experienced a change of control at any time since Company formation, utilization of its NOL or research and development credit carryforwards would be subject to the limitation rules under Section 382. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization which would reduce the Company s gross deferred tax assets.

13. COMMITMENTS AND CONTINGENCIES

On May 23, 2005, the Company entered into an operating lease for office and laboratory space through May 22, 2010, in Princeton, New Jersey. Monthly lease payments began May 23, 2005. The Company also leases office space in Durham, North Carolina. Monthly lease payments began May 1, 2007 and end on April 1, 2009. On February 7, 2006, the Company terminated its lease on its office and laboratory space in Atlanta, Georgia with a lease termination payment of $1,398,000 (see Note 3). The lessor was an entity with which Dr. Schinazi was affiliated. In January 2007, the Company entered into a capital lease for lab equipment with principal and interest payments of $14,044 due monthly through December 2008.

As of September 30, 2008, future payments under capital leases and minimum future payments under non-cancellable operating leases are as follows:

	September 30, 2008	
	Capital Lease	Operating Leases
	(In thousands)	
Fiscal 2009	$ 42	$ 835
Fiscal 2010		508
Total minimum payments required	42	$ 1,343
Less: Amounts representing interest		
Minimum future payments of principal	42	
Less: Current portion	(42)	
Long-term portion	$	

Rent expense under operating leases was $867,935, $777,939, and $811,513 during the years ended September 30, 2008, 2007 and 2006, respectively. Rent expense of $29,140 during the year ended September 30, 2006, was paid to C.S. Family, LLC, a related party.

We may pay up to an aggregate of $4.5 million in milestone payments and certain cost reimbursements if we reach milestones related to development and regulatory events under our license agreement with RFS Pharma LLC. We also agreed to pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments under our license agreement for DFC. Under our collaboration and license agreement with Bukwang, in the future we may pay up to an aggregate of $23.0 million in milestone payments related to development, regulatory and commercialization events. Under our license agreement with Emory University for Racivir, we agreed to pay Emory University up to an aggregate of $1.0 million in future marketing milestone payments. None of these potential future payments are included in our financial statements, as the payments are contingent on the achievement of milestones, which we have not yet achieved.

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NOTES TO FINANCIAL STATEMENTS (Continued)

14. EMPLOYEE SAVINGS PLAN

The Company maintains a contributory employee savings plan (401(k) Plan) for its employees. Under the 401(k) Plan, the Company matches certain employee contributions at the discretion of the board of directors. Expense under the 401(k) Plan was $141,888, $122,263, and $55,876, during the years ended September 30, 2008, 2007 and 2006, respectively. On January 11, 2006, the Company elected to implement a new 401(k) Plan which provides for, among other things, a discretionary employer match of 50 cents on every dollar contributed by each employee under the plan up to a maximum annual amount of 6% of such employee s salary up to a maximum annual match of $3,500 per employee, such discretionary match being made automatically unless action is taken by the compensation committee to cancel the match for a given year.

15. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following tables present unaudited quarterly financial data for the Company. The Company s quarterly results of operations for these periods are not necessarily indicative of future results of operations.

	Three Months Ended			
	Dec. 31, 2007	March 31, 2008	June 30, 2008	Sept. 30, 2008
	(in thousands, except per share data)			
Revenues:	$ 464	$ 464	$ 464	$ 464
Net income (loss)	$ (12,173)	$ (12,136)	$ (15,028)	$ (15,321)
Net income (loss) attributable to common stockholders	$ (12,173)	$ (12,136)	$ (15,028)	$ (15,321)
Net income (loss) per common share:				
Basic	$ (0.57)	$ (0.57)	$ (0.69)	$ (0.67)
Diluted	$ (0.57)	$ (0.57)	$ (0.69)	$ (0.67)

	Three Months Ended			
	Dec. 31, 2006	March 31, 2007	June 30, 2007	Sept. 30, 2007
	(in thousands, except per share data)			
Revenues:	$ 8,117	$ 5,464	$ 464	$ 7,964
Net income (loss)	$ 3,907	$ (1,457)	$ (5,862)	$ (1,653)
Net income (loss) attributable to common stockholders	$ 3,623	$ (1,744)	$ (7,067)	$ (1,653)
Net income (loss) per common share:				
Basic	$ 0.35	$ (0.16)	$ (0.40)	$ (0.08)
Diluted	$ 0.33	$ (0.16)	$ (0.40)	$ (0.08)

Basic and diluted net loss per common share are identical since common equivalent shares are excluded from the calculation as their effect is antidilutive, except for the quarter ended December 31, 2006.

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EXHIBIT INDEX

Exhibit Number	Description
10.23	Venture Loan and Security Agreement dated September 30, 2007 by and between the Registrant and Horizon Technology Funding V LLC
10.24	Manufacturing Services Agreement dated August 8, 2008 between Pharmasset, Inc. and Boehringer Ingelheim Chemicals, Inc.
10.25	License Agreement dated August 8, 2008 between Pharmasset, Inc. and Boehringer Ingelheim Chemicals, Inc.
23.1	Consent of Grant Thornton LLP
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Portions of this exhibit were omitted and filed separately with the Secretary of the SEC pursuant to a request for confidential treatment that has been filed with the SEC.