METABASIS THERAPEUTICS INC
Form 10-K
March 23, 2006

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

FOR ANNUAL AND TRANSITION REPORTS
PURSUANT TO SECTIONS 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the fiscal year ended December 31, 2005

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

For the transition period from to

Commission file number: 000-50785

METABASIS THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**33-0753322**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
11119 North Torrey Pines Road, La Jolla, CA	**92037**
(Address of principal executive offices)	(Zip Code)

(858) 587-2770

(Registrant s telephone number, including area code)

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

Title of Each Class	Name of Each Exchange on Which Registered
None	None

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

Common Stock, par value $0.001 per share

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

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

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 ý No o

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. o

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

Large accelerated filer o Accelerated filer o Non-accelerated filer ý

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

As of June 30, 2005, the last business day of the registrant s most recently completed second fiscal quarter, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was approximately $16.0 million, based on the closing price of the registrant s common stock on the Nasdaq National Market on June 30, 2005 of $3.15 per share. Shares of common stock held by executive officers, directors and 10% or greater stockholders of the registrant have been excluded in that such persons or entities may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of outstanding shares of the registrant s common stock, par value $0.001 per share, as of March 1, 2006 was 25,325,605.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement to be filed with the Securities and Exchange Commission within 120 days after the end of the registrant s fiscal year ended December 31, 2005 are incorporated by reference into Part III of this report.

METABASIS THERAPEUTICS, INC.

FORM 10-K ANNUAL REPORT

FOR THE YEAR ENDED DECEMBER 31, 2005

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PART I

Item 1. Business

Forward-Looking Statements

This annual report on Form 10-K contains forward-looking statements that are based on our management s beliefs and assumptions and on information currently available to our management. Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities, the effects of future regulation and the effects of competition. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as anticipates, believes, could, estimates, expects, intends, may, plans, potential, predicts, projects, or similar expressions.

Forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. We discuss these risks in greater detail in the Risk Factors section below and in our other filings with the Securities and Exchange Commission. Our actual results may differ materially from those anticipated in these forward-looking statements. Readers are cautioned not to place undue reliance on forward-looking statements. The forward-looking statements speak only as of the date on which they are made, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they are made.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel drugs to address some of the world s most widespread and costly chronic diseases involving pathways in the liver. These diseases include metabolic diseases such as diabetes, hyperlipidemia, a disease involving elevated levels of lipids such as cholesterol, and obesity, among others, and liver diseases such as hepatitis and primary liver cancer. We have established a broad and growing product pipeline targeting large markets with significant unmet medical needs. We have discovered all of our product candidates internally using our proprietary technologies.

We currently have the following four product candidates in clinical trials in descending order from our most advanced product, pradefovir:

Pradefovir, a product candidate for the treatment of hepatitis B that has successfully completed Phase II clinical trials and is scheduled to enter Phase III clinical trials in 2006. Pradefovir uses our HepDirect technology to target the active form of Hepsera, a marketed anti-viral drug indicated for the treatment of hepatitis B, selectively to the liver. The active form of Hepsera is known as adefovir. Hepsera delivers adefovir throughout the body, rather than selectively to the liver. We believe that Hepsera, which is indicated for the treatment of hepatitis B, is used at a suboptimal dose due to an increased risk of kidney toxicity at higher doses. Because pradefovir targets adefovir to the liver while limiting the amount that reaches other organs, we believe that higher liver levels of the active drug may be

achieved without causing kidney toxicity, thereby providing greater efficacy. In July 2004 Valeant Pharmaceuticals International, with whom we are collaborating with respect to the development of pradefovir and to whom we have licensed worldwide commercialization rights, commenced a 48 week dose-ranging Phase II clinical trial of pradefovir, the purpose of which was to evaluate safety and efficacy and select an appropriate dose for potential Phase III clinical trials. Based on the decision to initiate this Phase II clinical trial, we earned a $1 million milestone payment from Valeant. In the clinical trial, which was completed in 2005 and met its primary efficacy end-point, Valeant reported that pradefovir produced greater viral load reductions than Hepsera and was safe and well tolerated with no evidence of renal toxicity. Based on the promising results seen in the Phase II clinical trial and after discussions with the U.S. Food and Drug Administration, or FDA, Valeant has informed us that it intends to initiate the Phase III clinical trials for pradefovir in 2006. (Pradefovir was formerly called remofovir and before that, Hepavir B.)

CS-917, a product candidate for the treatment of type 2 diabetes that is currently in Phase II clinical trials. CS-917 is being developed in collaboration with Daiichi Sankyo Co., Ltd. In addition to having responsibility for clinical development of the drug, Daiichi Sankyo has worldwide commercialization rights. We have retained co-promotion rights for CS-917 in North America. We believe CS-917, which we discovered using our NuMimetic

technology, inhibits a metabolic pathway in the liver that is responsible for producing the sugar called glucose. In type 2 diabetic patients, this pathway produces excessive amounts of glucose, a process that contributes to high blood glucose levels which in turn may lead to morbidity and death. Daiichi Sankyo reports that results from a 14-day Phase II clinical trial and a 28-day Phase II clinical trial, both in type 2 diabetic subjects, demonstrated that CS-917 is capable of significantly lowering blood glucose levels. Based on the results of the 28-day clinical trial, we earned a $3.5 million milestone payment from Daiichi Sankyo. CS-917 is currently in a Phase IIb clinical trial designed to allow measurement of the regulatory endpoint hemoglobin A1c, a standard measure of long-term glucose control, after 3 months of dosing.

MB07133, a product candidate for the treatment of primary liver cancer that is currently in a Phase I/II clinical trial designed to evaluate safety and preliminary efficacy in a limited number of patients. MB07133 uses our HepDirect technology to target the active form of araC to the liver while decreasing levels of the active form of the drug in tissues outside of the liver. AraC is a marketed anti cancer drug used to treat leukemia. We believe MB07133 s unique liver-targeting property will enhance efficacy in the liver while minimizing the toxicities associated with araC therapy. MB07133 is currently being studied in patients with primary liver cancer to identify the maximum tolerated dose. Once this dose is identified, we plan to study MB07133 at that dose in a limited number of patients in order to evaluate its potential efficacy. We retain all rights to MB07133.

MB07803, a product candidate for the treatment of type 2 diabetes that is currently in a Phase I clinical trial. We consider MB078703 to be a second generation inhibitor of the metabolic pathway in the liver that is responsible for producing glucose and is designed to work by the same mechanism as CS-917. In early 2006 we began a Phase I clinical trial with MB07083 to assess its safety in healthy human volunteers. We retain all rights to MB07803.

In addition to these product candidates, we have a clinical development candidate, MB07811, which we have recommended for clinical development for the treatment of high cholesterol and possibly obesity. Recommendation for clinical development refers to an internal process involving our analysis of relevant pre-clinical data and selection of compounds suitable for clinical development by us. MB07811 is designed to act by controlling the expression of certain genes in the liver that are important for making or using cholesterol as well as genes involved in the control of energy expenditure. We plan to file an Investigational New Drug application, or IND, for MB07811 and to commence clinical trials of MB07811 in 2006 if the preclinical data is supportive and the proposed clinical trials are cleared by the FDA.

We have expertise in liver diseases and in the pathways and proteins residing in the liver that significantly contribute to certain metabolic diseases or that are important for transporting drugs into the liver, acting upon them and expelling them from the body. These processes are referred to as drug uptake, metabolism and excretion, respectively. With this knowledge, we developed proprietary technologies, including two which we called NuMimetic and HepDirect, which we have used to develop our current product candidates and which we expect to use to expand our product pipeline in the future.

We use our NuMimetic technology to discover molecules that bind effectively and specifically to certain regulatory sites, called nucleotide binding sites, residing on proteins called enzymes that control the output of cellular pathways involved in metabolic diseases, or metabolic pathways. We have developed a library of these unique molecules, known as nucleotide mimetics, and have used this library to discover compounds that we believe will lower glucose, cholesterol or lipid levels. We used our NuMimetic technology to discover CS-917 and MB07803, and we are also using it in certain of our advanced research programs, in which we have identified lead drug compounds and shown them to have efficacy in animal models. In addition to our internal programs that use the NuMimetic technology, we are using this technology in a collaboration with Merck & Co., Inc. to discover new treatments for metabolic diseases such as type 2 diabetes (by a different mechanism than CS-917 and MB07803), hyperlipidemia and a disease associated with fatty livers, known as non-alcoholic steatohepatitis, by inhibiting cholesterol and lipid production in the liver by activating a protein kinase in the liver known as AMPK.

We use our HepDirect technology to target drugs selectively to the liver, resulting in increased levels of the active form of the drug in the liver and decreased levels in non-liver tissues. We believe this liver-targeting property may significantly improve drug efficacy and safety when compared to non liver-targeting therapies. Our HepDirect technology can potentially be used to improve certain currently marketed drugs or applied to certain drug candidates, resulting in new, proprietary drugs that may then be marketed by us or by companies we collaborate with that have compounds that would benefit from this approach. Pradefovir and MB07133 use our HepDirect technology, as do several of our advanced research programs. In addition to our internal programs that use the HepDirect technology, we have collaborated with Merck to discover new treatments for hepatitis C by applying our HepDirect technology and other liver-targeting technology to certain compounds supplied by Merck.

Our research programs focus on metabolic diseases linked to pathways in the liver such as type 2 diabetes, hyperlipidemia and obesity, as well as liver diseases such as hepatitis C and liver fibrosis. Our goal is to expand our clinical development pipeline by continuing to recommend additional new drug compounds for clinical development. We believe that a broad product pipeline will provide strong growth potential and reduce our reliance on the success of any single product candidate. We may also in-license technologies and products to complement our internal discovery efforts. We believe our advanced research programs have the potential to yield additional clinical development candidates. Once we recommend a drug compound for clinical development, the clinical development candidate undergoes pre-clinical development including scale-up, toxicology and formulations development. Successful compounds would then enter human clinical testing.

Our advanced research programs include:

a program that has used our HepDirect and other liver-targeting technology in a collaboration with Merck to identify drugs to treat hepatitis C infection. The funded research phase of this collaboration has ended. Merck is currently evaluating and/or may evaluate drug compounds discovered under the research phase of the collaboration to determine if one or more will be recommended for clinical development,

a program using our NuMimetic technology in a collaboration with Merck to treat metabolic diseases such as type 2 diabetes (by a different mechanism than CS-917 and MB07803), hyperlipidemia and a disease associated with fatty livers, known as non-alcoholic steatohepatitis, by inhibiting cholesterol and lipid production in the liver, and

a program using our HepDirect technology to treat liver fibrosis by inhibiting the overproduction of collagen in the liver.

Our goal is to be a leading biopharmaceutical company developing and commercializing novel drugs. We intend to accomplish this goal by executing our strategy of

advancing the development of our product candidates and developing a broad product pipeline,

continuing to enhance our expertise in liver pathways and metabolism and our related intellectual property rights,

pursuing a diversified development and commercialization strategy for our product candidates,

establishing additional partnerships based on HepDirect or our other proprietary liver-targeting technologies, and

becoming a fully-integrated pharmaceutical company.

Disease Backgrounds

Liver diseases such as hepatitis B, hepatitis C, primary liver cancer and liver cirrhosis represent some of the most widespread and serious diseases in the world. Metabolic diseases such as type 2 diabetes, hyperlipidemia, obesity and non-alcoholic steatohepatitis are major healthcare problems worldwide, but are especially prevalent in the U.S. and Europe. We believe that these metabolic diseases can be treated by targeting metabolic pathways that reside in the liver, such as the pathways responsible for the production of glucose, cholesterol and fat molecules. As a group, liver and metabolic diseases represent one of the largest pharmaceutical markets with worldwide sales of drugs targeting these diseases exceeding $30 billion annually.

Liver diseases are generally poorly treated with current drug therapies. Moreover, these marketed drugs generally show significant limitations, including poor tolerability, safety risks or inadequate efficacy in certain patients. Some existing anti-viral and anti-cancer drugs are not effective against diseases of the liver due to the liver s inability to effectively convert them to their active forms. The use of existing drugs for the treatment of liver diseases is further limited in some cases by dose-limiting toxicities which may occur when high levels of the drug accumulate in tissues outside the liver.

In contrast to liver diseases, many more drugs are available for treating metabolic diseases either alone or in combination with other drugs. However, while effective drug therapies exist for some patients, most are inadequately treated or controlled.

Over 60% of patients treated for type 2 diabetes remain above the targeted levels for glucose set by the American Diabetes Association. In addition, over 80% of patients with coronary heart disease, which is associated with hyperlipidemia, remain above the targeted levels for cholesterol set by the National Cholesterol Education Program. Obese patients or patients with non-alcoholic steatohepatitis are even more poorly treated with few drugs on the market showing suitable efficacy and safety for these patients. As a result, we believe more effective drugs are needed to treat these diseases.

Our Pipeline

The following table summarizes our product candidates currently in clinical development, our clinical development candidate and our advanced research programs in descending order from our most advanced product candidate, pradefovir:

(1) None of our product candidates have received regulatory approval in the U.S. or in foreign countries.

(2) Phase III clinical trials expected to commence in 2006.

(3) Phase I clinical trials expected to commence in 2006.

(4) We are collaborating with Merck to apply our HepDirect™ and other liver-targeting technologies to certain compounds for the treatment of hepatitis C infection.

Pradefovir: A HepDirect prodrug of adefovir for the treatment of hepatitis B

Pradefovir is an oral product candidate that has successfully completed Phase II clinical trials to evaluate its potential to treat hepatitis B, a serious liver infection. Although several marketed drugs target hepatitis B, the disease remains poorly treated. One currently marketed hepatitis B drug is Hepsera, a non-liver specific prodrug of the antiviral compound adefovir. A prodrug is a drug to which a chemical modification has been made that renders it inactive until enzymes in the body convert it to its active form. Hepsera offers advantages over existing drugs because it is not associated with a high incidence of viral resistance, but toxicity issues limit the doses at which it can be administered and therefore its efficacy in treating this disease. Pradefovir, on the other hand, is designed using our proprietary HepDirect technology to deliver high concentrations of adefovir to the liver, while limiting the amount of adefovir generated outside of the liver, thereby potentially significantly reducing dose-related toxicities. In pre-clinical studies, pradefovir has been shown to result in higher levels of the active form of Hepsera, adefovir, in the liver without significantly increased levels of adefovir in the bloodstream or kidney. In clinical studies conducted to date, pradefovir has reduced hepatitis B virus levels to a greater extent than Hepsera at doses that are associated with lower circulating adefovir levels. In these studies, pradefovir also appeared to be safe and well tolerated. We are developing pradefovir in partnership with Valeant, to whom we licensed worldwide commercialization rights. Pradefovir was formerly called remofovir and before that, Hepavir B.

Hepatitis B

Hepatitis B is a viral disease that causes inflammation of the liver. Hepatitis B is transmitted by contact with the blood or other body fluids of an infected person. Hepatitis B infection is often difficult to diagnose because, depending upon the severity of the infection, patients can either be asymptomatic or experience only general flu-like symptoms such as fatigue, nausea or vomiting. Without appropriate treatment, continued inflammation of the liver leads to progressive scarring, or fibrosis, and eventually may lead to liver cancer, resulting in death.

Hepatitis B is the most common serious liver infection in the world. Over two billion people worldwide, or approximately one-third of the world s population, have been infected at some time with hepatitis B, and approximately 400 million of those people are chronic carriers of the virus. Approximately 1.2 million deaths per year worldwide are hepatitis B related. The Centers for Disease Control and Prevention reports that, in the U.S., over 1.2 million people are chronically infected with hepatitis B and nearly 80,000 new infections occur every year.

Sales of anti-viral drugs for the treatment of hepatitis B in the seven largest pharmaceutical markets, which are comprised of the U.S., France, Germany, Italy, Japan, Spain and the U.K., are expected to nearly triple between 2000 and 2010. There is also an opportunity for substantial additional growth from potential sales of anti-viral drugs for hepatitis B in emerging markets including Eastern Europe and Asia. These regions have some of the highest rates of chronic hepatitis B infection in the world. There are currently over 300 million people with chronic hepatitis B infection in these emerging markets, representing greater than 75% of the total chronic infections worldwide.

Current Treatments

In the U.S., until recently, there were three approved treatments for chronic hepatitis B: Intron A, Epivir-HBV, also referred to as Zeffix (lamivudine) and Hepsera. Each of these therapies has limitations in the treatment of patients with Hepatitis B. For example, Intron A is effective only in a small fraction of hepatitis B patients and is generally poorly tolerated. Patients taking Epivir-HBV or Zeffix can develop significant resistance to lamivudine, the drug s active ingredient. We believe that induction of viral resistance is also a significant issue for certain hepatitis B product candidates that are currently in late stage clinical development. Hepsera, on the other hand, shows limited propensity to induce virus mutations that are resistant to drug therapy and has proven effective against lamivudine-resistant strains of hepatitis B. However, potential kidney toxicities limit the level at which Hepsera can be dosed. In March 2005, a fourth drug called Baraclude™ (entecavir) was approved. To date, Baraclude has not been shown to induce significant viral resistance in drug naïve patients. However, based on clinical data, lamivudine resistant patients respond less effectively to Baraclude therapy and exhibit a higher rate of viral resistance.

Hepsera, lamivudine and Baraclude all decrease virus levels, as measured by hepatitis B DNA in the blood serum. Nevertheless, further decreases are desirable since these reductions are not considered sufficient to cure the infection in the majority of patients. In 2003, the New England Journal of Medicine reported that a three-fold higher dose (30 mg) of Hepsera led to a more than ten-fold greater reduction in hepatitis B DNA in the blood serum of patients and consistent trends toward improvement in all measures of liver injury. However, this higher dose caused elevation in markers of kidney toxicity that prevented further development at that dose. As a result, we believe the approved dose of Hepsera (10 mg) may be suboptimal for the reduction of virus levels.

Pradefovir

Pradefovir and Hepsera are both prodrugs of 9, -[2 (Phosphonomethoxy) ethyl] adenine (PMEA), or adefovir. When the prodrug is converted to adefovir in patients with hepatitis B, it acts in the liver and leads to decreased viral levels. Pradefovir is a HepDirect prodrug that after oral administration is absorbed rapidly after which it is taken up by the liver and converted to the active form, adefovir. Hepsera, on the other hand, is converted to adefovir throughout the bloodstream. As a result of this difference in distribution, higher dosing of pradefovir is possible due to the reduced systemic and renal adefovir levels, providing potentially improved efficacy relative to Hepsera in the treatment of hepatitis B, based on results of a Phase II clinical trial, which is further discussed in the clinical trials section below.

Clinical Trials

Under our agreement with Valeant, Valeant is responsible for conducting and reporting the results of clinical studies of pradefovir, and is responsible for making all regulatory filings related to the product, including submission of INDs and other regulatory submissions to the FDA. The following information is based on information provided to us by Valeant in connection with our agreement, or otherwise announced by Valeant.

Valeant has completed two single-dose Phase I clinical trials of pradefovir in 47 healthy volunteers. Pradefovir was safe and well tolerated at all dose levels studied. These clinical trials evaluated the pharmacokinetic profile of pradefovir, indicating that pradefovir appeared to be converted to its desired form, adefovir, in humans.

Pradefovir was also studied in two 28-day, randomized, placebo-controlled, double-blind, dose-escalation Phase I clinical trials designed to evaluate safety and preliminary efficacy in 80 hepatitis B patients in the U.S. and Taiwan.

The hepatitis B patients in the 28-day U.S. Phase I clinical trial were divided into groups that received 5, 10, 30 or 60 milligrams of pradefovir or a placebo administered orally once a day. The patients in the 28-day Taiwanese Phase I clinical trial were divided into groups that received 5, 10, 20 or 30 milligrams of pradefovir or a placebo administered orally once a day. In each of the dose groups evaluated, pradefovir was safe and well tolerated, and patients treated with pradefovir exhibited a statistically significant reduction, as determined by a p-value of less than 0.05, in hepatitis B virus levels compared to patients treated with a placebo. The reduction in median hepatitis B virus levels, which was determined by measuring viral DNA, and the overall distribution of adefovir throughout the body were consistent with results expected for our HepDirect technology based on pre-clinical studies.

Based on these initial results, in July 2004 Valeant commenced a 12-month dose-ranging Phase II clinical trial of pradefovir the purpose of which was to select appropriate doses for Phase III clinical trials. This Phase II clinical trial was fully enrolled as of November 2004 and 24 week interim results which showed evidence of safety and efficacy were first reported by Valeant in July 2005 and presented at the American Association for the Study of Liver Diseases, or AASLD, meeting in November 2005. Initial results of the completed Phase II clinical trial were announced by Valeant and Metabasis in March 2006, and detailed results of the completed Phase II clinical trial will be presented at the 41st Annual Meeting of the European Association for the Study of the Liver in April 2006 in Vienna, Austria.

The Phase II clinical trial conducted by Valeant was an open-label, randomized, multiple dose clinical trial with 242 patients enrolled at 21 sites in the United States, Taiwan, Singapore and South Korea. Approximately half of the patients had been previously treated ineffectively with other drugs. Patients that have been previously treated ineffectively are considered to be more difficult to treat. The Phase II clinical trial consisted of five treatment groups: pradefovir 5, 10, 20 and 30 mg administered once a day (called QD administration), and Hepsera 10 mg (QD), with an overall treatment duration of 48 weeks.

The data from the Phase II clinical trial showed that the patient group that received 30 mg (QD) pradefovir achieved a 5.54 log (10) drop in hepatitis B viral (HBV) DNA, a measure of viral load, from baseline as compared to a 4.19 log (10) drop in the 10 mg (QD) Hepsera (adefovir dipivoxil) group ($p<0.001$). Pradefovir at doses of 10 and 20 mg (QD) also showed a statistically significant greater reduction in viral load compared to Hepsera. The following chart illustrates these results:

Pradefovir Phase 2 Week 48 Results (all patients)

Mean Log(10) HBV DNA Decline From Baseline

(Intent-to-Treat Analysis)

Baseline Mean HBV DNA	Week 48	p-Value Compared to

	Dose	Number of Patients	(Log (10) copies/mL)	Mean Decline in HBV DNA	Hepsera Control
Hepsera	10 mg QD	50	8.0	-4.19	N/A
Pradefovir	5 mg QD	47	7.9	-4.09	0.83
	10 mg QD	49	7.9	-4.84	0.007
	20 mg QD	48	8.0	-4.89	0.007
	30 mg QD	**48**	**8.2**	**-5.54**	**<0.001**

The percentage of patients in the 30 mg (QD) pradefovir cohort achieving undetectable HBV DNA (<400 c/mL) was almost double that of patients receiving 10 mg (QD) of Hepsera. The percentage of patients with HBV DNA of less than 400 c/mL were 45 percent, 63 percent, 56 percent, and 71 percent for the pradefovir 5, 10, 20, and 30 mg (QD) groups, respectively, and 36 percent for the Hepsera group.

No patient demonstrated an increase in serum creatinine levels over baseline of greater than or equal to 0.5 mg/dL. Serum creatinine levels are a marker for renal toxicity that has been associated with higher doses of adefovir. Renal safety was comparable between all treatment groups. There were no serious adverse events related to treatment. The most frequently reported adverse events were similar across all treatment groups, including Hepsera. No dose-related trends regarding safety were identified and no events resulted in a patient being withdrawn prematurely from treatment.

Valeant has reviewed results from the Phase II clinical trial with the FDA and intends to initiate Phase III clinical trials in 2006.

Pre-clinical Studies

Together with Valeant, we conducted pre-clinical studies of pradefovir in rats, mice and monkeys. These studies showed that animals treated with an oral dose of pradefovir exhibited higher levels of adefovir and its biologically active form, adefovir diphosphate, in the liver and lower levels of adefovir and adefovir diphosphate in tissues outside of the liver, including the kidney and gastrointestinal tract, relative to animals treated with a similar dose of Hepsera. Results from one of these studies are depicted in the chart below, which shows the profile of adefovir diphosphate levels, measured by nanomoles per gram, over a 24 hour period in the livers and kidneys of rats administered an oral dose of either pradefovir or Hepsera at a level of 30 milligrams per kilogram.

CS-917: A gluconeogenesis inhibitor for the treatment of type 2 diabetes

CS-917 is an oral product candidate for type 2 diabetes that we discovered using our proprietary NuMimetic technology. Data generated to date indicate that CS-917 inhibits a metabolic pathway in the liver called gluconeogenesis, which is responsible for the excessive production of glucose by patients with type 2 diabetes. We believe that CS-917 is the first product candidate to be studied in human clinical trials that is designed to directly block this pathway. In pre-clinical studies and two completed clinical trials, CS-917 has shown a statistically significant reduction in elevated blood glucose levels of the type that characterize type 2 diabetes. CS-917 is being developed in partnership with Daiichi Sankyo, and we retain co-promotion rights in North America.

Diabetes

There are two forms of diabetes: type 1 (insulin-dependent, juvenile-onset diabetes) and type 2 (adult-onset diabetes). Approximately 90% of diabetes patients have type 2 diabetes. Elevated blood glucose levels in type 2 diabetic patients result from decreased glucose metabolism combined with increased glucose production. Decreased glucose metabolism arises from a relative

underproduction of the hormone insulin by the pancreas, along with a decrease in the sensitivity of the body s tissues, such as muscle, liver and fat, to insulin action. Increased glucose production is caused by increased synthesis of glucose by the gluconeogenesis pathway in the liver. Over time, the chronically elevated blood glucose levels in type 2 diabetics can lead to many long-term complications such as coronary heart disease, stroke, blindness, peripheral vascular disease, kidney disease and nerve damage. Diabetes is a leading cause of death in the U.S.

Type 2 diabetes afflicts over 170 million people worldwide, with over 18 million afflicted in the U.S. Global sales of oral diabetes drugs currently exceed $10 billion annually, with the U.S. accounting for over 65% of the total sales.

Current Treatments

The United Kingdom Prospective Diabetes Study, a landmark 20-year clinical study completed in 1996, demonstrated that stringent control of blood glucose levels reduces the risk of the serious complications associated with type 2 diabetes. As a result of this study, the American Diabetes Association now recommends that levels of hemoglobin A1c be maintained under 7% in type 2 diabetic patients. However, at present no single marketed drug is capable of lowering hemoglobin A1c levels into the targeted range for a sustained period of time in the majority of patients with type 2 diabetes.

Drugs from each of the three major classes of oral diabetes drugs not only exhibit limited efficacy, but also are associated with less than desired tolerability and significant mechanism-based side effects. These drug classes include:

insulin secretion enhancers, which lower glucose levels by inducing insulin secretion from the pancreas. This drug class has been associated with a significant risk of hypoglycemia,

insulin sensitizers, which lower glucose levels by enhancing insulin sensitivity. This drug class has been associated with fluid retention, weight gain, and a risk of congestive heart failure, and

hepatic glucose output inhibitors, which lower glucose levels by inhibiting liver glucose production. The only drug in this class is metformin, which, based on a study reported in the medical journal Diabetes, inhibits glucose production by the liver by only approximately 20-25%, even when administered at doses higher than the commonly prescribed daily dose. Therefore, a more effective hepatic glucose output inhibitor may improve efficacy over metformin. Metformin therapy has been associated with an increased risk of lactic acidosis in certain patient populations, especially patients with kidney dysfunction. In addition, metformin therapy can lead to transient gastrointestinal disturbances such as nausea, diarrhea and vomiting, which can compromise patient compliance.

Certain widely used insulin secretion enhancers and insulin sensitizers, but not metformin, are also associated with increased weight gain. Since weight gain is known to exacerbate diabetes, physicians often prescribe metformin as a first line therapy to obese patients, who according to a recent study published in the medical journal Diabetes & Endocrinology comprise more than 90% of newly diagnosed type 2 diabetic patients.

In the United Kingdom Prospective Diabetes Study, obese patients treated with maximum doses of metformin or an insulin secretion enhancer showed a steady rise in hemoglobin A1c levels above the targeted range at three years. Progressively fewer patients were able to maintain baseline hemoglobin A1c levels at six years and nine years, respectively.

Once treatment with a single oral drug fails to adequately control glucose levels, diabetic patients typically are treated with one or more additional oral drugs. It is estimated that more than 75% of type 2 diabetic patients will require multiple oral drug therapies to attain adequate glucose control and just over 30% of type 2 diabetic patients will ultimately advance to a stage that requires daily insulin injections. We believe that because of the limitations in currently marketed drugs, the diabetes market is receptive to new drugs, and new therapeutic approaches have the potential to experience rapid clinical acceptance.

CS-917

Studies show that the elevated blood glucose levels that characterize type 2 diabetic patients are correlated with the overproduction of glucose by the liver, which arises from an increased rate of flow through the gluconeogenesis pathway. We believe that CS-917 is the first product candidate to be studied in human clinical trials that is designed to directly block the gluconeogenesis pathway by inhibiting an enzyme called fructose-1,6-bisphosphatase, or FBPase. We believe that FBPase represents an important control point within this pathway and a suitable target for inhibiting the overproduction of glucose found in type 2 diabetic patients. Pharmaceutical companies have tried to find inhibitors of FBPase, but to our knowledge have thus far

failed to discover compounds of sufficient potency and specificity to be considered as product candidates. Using our NuMimetic technology, we have identified molecules that effectively bind to the nucleotide-binding site on FBPase and potently and specifically inhibit FBPase activity in animal models.

We believe that CS-917 may be effective across a broad patient population because glucose overproduction by the liver is common to all type 2 diabetics regardless of disease stage or body mass. Unlike insulin sensitizers and certain insulin secretion enhancers, CS-917 does not cause weight gain in animals and is therefore expected to be appropriate for effective treatment of obese diabetics. Studies also show that CS-917 is effective in animal models of lean diabetes and that glucose lowering occurs independent of insulin levels. Taken together these characteristics may make CS-917 useful:

in advanced diabetics, a patient population commonly resistant to therapies dependent on insulin production such as insulin sensitizers and insulin secretion enhancers,

in early stage diabetes, and

in prediabetics where CS-917 may be effective in preventing or delaying the onset of diabetes.

Clinical Trials

To date, our partner Daiichi Sankyo has completed a number of Phase I clinical trials of CS-917 in healthy volunteers as well as Phase I and Phase II clinical trials of CS-917 in type 2 diabetic patients.

Results from two Phase II clinical trials provide evidence that CS-917 is capable of significantly lowering blood glucose levels in humans. The first Phase II clinical trial completed involved treatment of 39 type 2 diabetic subjects with CS-917 or a placebo once daily for 14 days using a randomized, placebo-controlled, double-blind clinical trial design. The patients were divided into groups that received 50, 100, 200 or 400 milligrams of CS-917 or a placebo. Patients were dosed in the morning following a ten hour overnight fast and then fasted an additional six hours. The efficacy endpoint of the clinical trial was a comparison of cumulative glucose levels over the six-hour fasting period following administration on day 14 relative to baseline levels (which are cumulative glucose levels determined for the same period prior to clinical trial initiation) in patients treated with CS-917, as compared to the change from baseline levels in patients treated with a placebo. CS-917 appeared to be safe and well tolerated and the primary efficacy endpoint of the clinical trial, demonstration of a statistically significant reduction in these cumulative glucose levels as determined by a p-value of less than 0.05 in patients treated with the highest dose of CS-917, was achieved. A p-value of less than or equal to 0.05 is generally considered to signify a statistically significant result, which means a result is unlikely to occur by chance. Furthermore, the reduction in glucose levels seen on day 14 compared to baseline levels was greater in all groups treated with CS-917 than that seen in the placebo-treated groups.

In the second Phase II clinical trial, 146 type 2 diabetic subjects were treated with CS-917 or a placebo administered two or three times per day for 28 days using a randomized, placebo-controlled, double-blind clinical trial design. The primary efficacy endpoint of the clinical trial was the change from baseline in the plasma glucose level measured after an overnight fast, often called the fasting plasma glucose level, on the morning

of day 29 following the last dose on the evening of day 28, as compared to the change measured in the patients that received a placebo over the same time period. In each case, the group of patients who received CS-917 showed a statistically significant reduction in fasting plasma glucose levels compared to the corresponding dose group that received a placebo, as determined by a p-value of less than 0.05.

The results of clinical trials to date indicate that CS-917 may need to be administered more than once daily, although this has not been definitively determined.

The inhibition of gluconeogenesis can cause elevated levels of lactic acid, or lactate, which, if high and sustained, under certain conditions can lead to lactic acidosis, a serious and potentially fatal condition. However, metformin, which reduces liver glucose production through an unknown mechanism, also raises lactate above normal levels in about 4% of patients with no apparent adverse clinical consequences. In the 14-day Phase II clinical trial of CS-917, two patients treated with the highest dose of CS-917 (400 milligrams) exhibited lactate levels above the normal range on each day they received CS-917. Lactate levels in both patients returned to normal levels prior to administration of the next scheduled dose. In the 28-day Phase II clinical trial of CS-917, isolated instances of lactate elevation significantly above the normal range were seen in some patients in both CS-917- and placebo-treated groups over the course of the 28 days. No patient exhibited sustained lactate levels significantly above the normal range over a period of consecutive days during the clinical trial. However, one patient who received 200 milligrams of CS-917 twice a day was withdrawn from the clinical trial by the investigator on day 15 due to concerns over elevated lactate levels measured the previous day.

A larger and longer-term Phase II clinical trial designed to further evaluate the safety and effectiveness of CS-917 and to determine dosing levels for potential Phase III clinical trials was initiated in December 2004. In addition, a second clinical trial that involved administration of a relatively high dose of CS-917 to evaluate the timing of dose administration was also initiated at that time. Additional Phase I clinical trials evaluating concomitant administration of CS-917 with other drugs were also initiated, including a clinical trial evaluating the interaction of CS-917 with the marketed diabetes drug metformin.

In March 2005, we were notified by Daiichi Sankyo that two serious adverse events involving lactic acidosis had occurred in two patients in a Phase I clinical trial evaluating the interaction of CS-917 with metformin. The serious adverse events were resolved after medical intervention. After the adverse events occurred, the three clinical trials that were ongoing at that time were stopped by Daiichi Sankyo, while one Phase I clinical trial which did not combine CS-917 with metformin continued and was completed.

It was subsequently determined that the two patients that experienced the lactic acidosis had blood levels of metformin that were elevated compared to other patients in the clinical trial that received metformin before administration of CS-917. After CS-917 administration, when the two patients were being administered metformin and CS-917 the metformin blood levels increased significantly, into a range that is associated with lactic acidosis. CS-917 blood levels also rose higher than expected. A high blood level of metformin is believed to cause mitochondrial toxicity which can cause lactic acidosis. These dangerous levels are known to occur in patients with significant renal dysfunction who are inappropriately given metformin. Consequently, metformin is contraindicated for use in patients with significant renal dysfunction.

The reason for the unexpectedly high blood levels of both drugs in these two patients is unknown at this time. In July 2005, after completing a comprehensive review of the program and the events and data surrounding the two serious adverse events, we and Daiichi Sankyo concluded that the lactic acidosis observed in the two patients was likely due to the significantly increased blood levels of metformin described above which in turn likely led to mitochondrial toxicity. Subsequently, Daiichi Sankyo decided that Phase IIb clinical trials of CS-917 as a mono-therapy could safely resume with precautions to assure that patients do not take CS-917 in combination with metformin.

In February 2006, based on reports from Daiichi Sankyo, after submission of the proposed clinical trial protocol to the FDA and approval by the institutional review board, or IRB, a Phase IIb clinical trial of CS-917 was initiated. This Phase IIb clinical trial will allow measurement of the regulatory endpoint, the blood level of hemoglobin A1c. Daiichi Sankyo has conducted and will likely conduct additional studies combining CS-917 with other diabetes drugs to assess both the safety and eventually the potential for enhanced efficacy with the combination. However, further combination of CS-917 and metformin will be avoided unless additional data suggests that the elevation of metformin blood levels as seen in the two patients can be avoided through patient exclusion or through the administration of CS-917 at lower doses or through other means. Should CS-917 eventually be approved and combination with metformin remains an issue, the FDA may require additional measures be taken during marketing, such as prominent warning labels known as black-box warnings, physician education programs and/or other steps regarding concomitant use of CS-917 and metformin.

Pre-clinical Studies

Results from clinical trials of CS-917 are consistent with the glucose-lowering effect observed in pre-clinical studies we conducted with Daiichi Sankyo in several animal models of diabetes. Studies in rats showed that daily oral administration of CS-917 lowered blood glucose when dosed chronically, or over an extended period of time. Moreover, maximum glucose lowering in these studies was better than or equal to the glucose lowering effects of insulin sensitizers and insulin secretion enhancers. CS-917 also lowered glucose in both obese and lean diabetes animal models. Like metformin, but unlike the insulin sensitizers and certain insulin secretion enhancers, CS-917 induced no weight gain in treated animals relative to untreated animals.

Pre-clinical studies indicated that the combination of maximally effective doses of an insulin sensitizer with an FBPase inhibitor may result in greater efficacy than either drug alone. The following chart shows the results of a study in which we administered to an animal model of obese diabetes either no drug, referred to as control, or maximally effective doses of the insulin sensitizer troglitazone, CS-917 or a combination of troglitazone and CS-917. Blood glucose levels were monitored over three weeks, measured as milligrams per deciliter of blood, and shown to decrease similarly between animals treated with troglitazone and CS-917. The drug combination, however, led to near normalization of blood glucose levels, which is approximately 150 milligrams per deciliter:

In addition to troglitazone, which is no longer marketed because of safety concerns, we have evaluated the combination of FBPase inhibitors with other currently marketed insulin sensitizers with similar results.

Pre-clinical studies in diabetes animal models support the use of CS-917 in advanced diabetic patients. As in humans, animal models with diabetes show increased glucose production as they age and their diabetes worsens. Our studies demonstrated that these animals respond poorly to insulin sensitizers and insulin secretion enhancers. In contrast, these animals respond well to CS-917, indicating glucose-lowering effects in both advanced stage and early stage animal models of the disease.

In addition, Daiichi Sankyo has shown that chronic dosing of CS-917 decreases the insulin dose required to maintain a target glucose level in a mouse model of diabetes. Based on these studies and other pre-clinical data, including glucose-lowering effects in non-human primates and oral bioavailability data and toxicology results from studies in both rats and non-human primates, Daiichi Sankyo moved CS-917 into clinical trials in July 2001.

MB07133: A HepDirect prodrug for the treatment of primary liver cancer

MB07133 is an intravenously administered product candidate in a Phase I/II clinical trial designed to evaluate safety and preliminary efficacy in a limited number of patients with primary liver cancer. Few treatment options exist, and no drug has been approved for treatment of primary liver cancer. MB07133 uses our HepDirect technology to target the active form of araC to the liver while decreasing levels of the active form of the drug in tissues outside of the liver. AraC is a marketed anti cancer drug used to treat leukemia. AraC s anti-cancer activity is associated with its ability to be converted to its biologically active form, araCTP. Treatment with araC does not result in the generation of efficacious levels of araCTP in the liver due to the failure of araC to be converted to an intermediate form called araCMP. Using our HepDirect technology we

designed MB07133 to deliver araCMP to the liver thereby providing a means to treat primary liver cancer. We retain all rights to MB07133.

Primary Liver Cancer

Primary liver cancer is a malignancy originating in the liver that often kills patients within six months after diagnosis with less than 10% of patients surviving for five years or more. Metastatic liver cancer, on the other hand, originates in other organs and then progresses to the liver. In the U.S., the American Cancer Society reports that primary liver cancer is the ninth leading cause of cancer mortality in men and is the twelfth leading cause of cancer mortality in women. The American Cancer Society estimates that approximately 18,500 new cases of primary liver cancer will be diagnosed in the U.S in 2006. Primary liver cancer is responsible for over 500,000 deaths per year worldwide.

While the definitive cause of primary liver cancer is unknown, it is well-recognized that patients with chronic liver diseases such as hepatitis B, hepatitis C, alcoholic cirrhosis and iron overload are at high risk for developing liver cancer over a

30-year period. In the U.S., Europe and Japan, hepatitis C is considered to be one of the leading risk factors associated with primary liver cancer. The incidence of primary liver cancer in these countries is expected to increase over the next 10 to 15 years due to the large number of people previously infected with hepatitis C whose disease has or will advance to liver cirrhosis. In the U.S. alone, the National Institutes of Health projects a four-fold increase over this period in patients with chronic hepatitis C.

We believe that given the current and projected primary liver cancer incidence levels, and the cost of similar cancer therapeutics, an approved drug for primary liver cancer could present a substantial worldwide commercial opportunity.

Current Treatments

Treatment methods for patients with primary liver cancer are typically determined by the stage of the disease at diagnosis. Patients are generally classified as eligible for surgical tumor resection, inoperable and non-terminal, or terminal. According to the American Cancer Society, on average, over a ten-year period, over 16% of patients have been treated by surgical tumor resection. Additionally, over 50% of patients are inoperable and non-terminal and 26% of patients are terminal. Patients who undergo successful tumor resection have a future life expectancy of about five years, whereas all other patients have an average life expectancy of less than one year. Treatment for inoperable and non-terminal patients is dependent on many factors. Liver transplantation represents the only method that can cure the disease, but few transplants are possible due to the severe shortage in liver donors and the high cost. Other alternatives involve non-surgical therapies that use either radioactive microscopic beads (such as TheraSpheres) or chemotherapy (known as Transcatheter Arterial Chemoembolization (**TACE**)) injected through a catheter directly into the liver. Other treatments include regional tumor destruction and chemotherapy. However, we believe the disease remains poorly treated, and there are no currently approved drug therapies for primary liver cancer.

MB07133

MB07133 uses our HepDirect technology to target the active form of araC to the liver while decreasing levels of the active form of the drug in tissues outside of the liver. AraC is a marketed anti cancer drug used to treat leukemia. AraC is effective against leukemia but not solid tumors, including primary liver cancer, in large part because the enzymes required for conversion of araC to araCTP exist predominantly in leukemic cells and bone marrow cells. Conversion of araC to araCTP in bone marrow results in the dose-limiting toxicity that is traditionally associated with araC therapy.

Using our HepDirect technology, we developed MB07133, a product candidate that produces higher levels of araCTP in the liver with little to no araCTP produced in the bone marrow. MB07133 causes higher levels of araCTP in the liver because it effectively bypasses the first step in the metabolic pathway used to convert araC to araCTP, which otherwise requires an enzyme that is present only at relatively low levels in the liver. At the same time, MB07133 produces low levels of araCTP in the bone marrow because it is not readily converted to araCTP in bone marrow and blood. We believe that this change in distribution of araCTP will maximize MB07133 s potential therapeutic effect on liver tumors while minimizing its toxicity.

Clinical Trials

In September 2003 we initiated a Phase I/II clinical trial designed to evaluate the safety and preliminary efficacy of MB07133 in non-terminal patients with inoperable primary liver cancer tumors in the U.S., Hong Kong and Taiwan. The clinical trial is an open label, dose escalation Phase I/II clinical trial in patients with confirmed primary liver cancer tumors involving continuous intravenous infusion of MB07133 for seven days followed by a 21-day recovery period. Patients may receive infusions until treatment failure up to a total of six infusions of MB07133. The goal of this clinical trial is to establish the maximum tolerated dose. In addition to safety, we are monitoring changes in tumor size, physical well-being and changes in blood chemistry. Once the maximum tolerated dose is identified, we plan to study MB07133 at that dose in a limited number of patients in order to evaluate its potential efficacy.

Pre-clinical Studies

MB07133 has been studied in animals and shown to produce a significantly different distribution of araC and araCTP when compared to animals treated with araC alone. In one study, rats treated with MB07133 demonstrated significantly higher levels of araCTP in the liver and significantly lower levels of araC and araCTP in the blood and bone marrow, respectively, than rats treated with only araC. The following charts show the results achieved in this study:

In another study, MB07133 and araC were continuously infused into rats for two days, after which the levels of araCTP in the liver and bone marrow were determined. The MB07133-treated rats showed high levels of araCTP in the liver, whereas araCTP was not detected in the livers of animals treated with araC alone. The opposite was observed in bone marrow, where araCTP levels were high in the rats treated with araC alone and not detected in the MB07133-treated rats. The level of araCTP achieved in the liver with MB07133 in these studies is above the levels of araCTP shown to kill human primary liver cancer cells in culture.

The differences in liver and bone marrow araCTP levels produced by MB07133 as compared to araC alone result in significant improvement in animal toxicology. Mice treated for five days with araC alone produced a dose-dependent decrease in body weight and a dose-dependent loss of bone marrow cells, whereas mice treated for the same period with MB07133 showed no loss in weight or bone marrow cells except at the highest dose, where a partial decrease in bone marrow cells was noted. We believe these results suggest that relative to araC, MB07133 may be able to deliver therapeutically active levels of araCTP to human primary liver cancer tumors with less toxicity.

MB07803: A second-generation gluconeogenesis inhibitor for the treatment of type 2 diabetes

Like CS-917, MB07803 is an oral product candidate for type 2 diabetes that we discovered using our proprietary NuMimetic technology. MB07803 is designed to have the same mechanism of action as CS-917 - it blocks the gluconeogenesis pathway in the liver by inhibiting FBPase. MB07803 is targeted to the same market and to have advantages over current therapies that are similar to those expected with CS-917. We retain all rights to MB07803.

In April 2002, upon completion of the discovery research portion of our collaboration with Daiichi Sankyo, we began work on a program designed to discover and develop second generation gluconeogenesis inhibitors. The goal of the second generation program was to discover and develop compounds with pharmaceutical properties that were improved over those seen to date with CS-917. One or more of these improvements, if they are demonstrated in subsequent clinical trials, may give second generation compounds certain advantages over CS-917. Should CS-917 prove to be an important new therapy for type 2 diabetes we believe the second generation could expand the use of this class further.

In October 2002, we entered into an exclusive option agreement with Daiichi Sankyo, under which Daiichi Sankyo paid us a non-refundable $8.5 million option fee that gave Daiichi Sankyo the right to negotiate a new agreement for the discovery,

development and licensing of second generation gluconeogenesis inhibitors, and an option to license an additional back-up compound discovered during the option period. In August 2003, Daiichi Sankyo exercised its right under the option agreement to designate an additional back-up compound and chose not to exercise its option to negotiate a new agreement for the discovery, development and licensing of second generation gluconeogenesis inhibitors, at which time the option expired. As a result, Daiichi Sankyo has no rights to compounds discovered under the second generation program and therefore we may develop these compounds on our own or in collaboration with another company.

In 2004, we recommended MB07803 for clinical development from this second generation program and in February 2006, we initiated a Phase I clinical trial of MB07803.

MB07811: A compound for the treatment of hyperlipidemia and possibly obesity

We currently have a clinical development candidate, MB07811, which we have recommended for clinical development for the potential treatment of high cholesterol and possibly obesity. MB07811 is the outgrowth of our efforts to find ways to control the expression of certain genes in the liver that are important for making or using cholesterol as well as genes involved in the control of energy expenditure. MB07811 is currently undergoing pre-clinical development including scale-up, toxicology (animal studies) and formulations development. It is anticipated that, if these efforts are successful, we would then enter MB07811 into human clinical testing.

Hyperlipidemia is a disease characterized by an elevation of lipids, such as cholesterol or triglycerides, in the bloodstream. Patients with hyperlipidemia have a greater risk of suffering heart attacks and other forms of heart disease. Global sales of cholesterol and triglyceride reducers used to treat hyperlipidemia currently exceed $20 billion, with over 60% of these sales occurring in North America. A person is generally considered obese under National Institutes of Health guidelines if he or she is 30 pounds or more overweight for his or her age, height, sex and bone structure. Approximately 60 million adults in the U.S. suffer from obesity. Obesity significantly raises the risk of illness or death from serious medical conditions including hypertension, type 2 diabetes, cardiovascular disease, stroke and certain cancers. In the U.S., obesity-related costs exceed $75 billion per year.

We have discovered a series of compounds that exhibit high liver specificity in animals and data indicate that these compounds can lower cholesterol in animals without causing toxicities associated with previously discovered compounds in the same class. The most advanced compound from this series, MB07811, was recommended for clinical development in 2005. Data generated in numerous preclinical models across six species indicate that MB07811 may be able to effectively lower serum cholesterol. Data from tests in a primate model indicate that MB07811 may lower serum cholesterol as effectively as the most widely prescribed statin, Lipitor® (atorvastatin) (see Chart A below) and is additive with Lipitor (see Chart B below).

Chart A

Chart B

We plan to file an IND for MB07811 and to commence clinical trials of MB07811 in 2006 if additional preclinical data is supportive and the proposed clinical trials are cleared by the FDA. We retain all rights to MB07811.

Our Research Programs

We are expanding our product pipeline by using our proprietary technologies, our knowledge of liver diseases, and our expertise in pathways and proteins residing in the liver that significantly contribute to metabolic diseases. We have additional expertise in processes in the liver that are important for drug uptake, metabolism and excretion, all of which are important for targeting drugs to the liver with high specificity. We have used this knowledge to develop our proprietary NuMimetic and HepDirect technologies, which we use in several of our research programs. We also have expertise in structure-based drug design and we have developed novel computational methods useful for predicting drug binding effectiveness and specificity. These methods have aided our design and discovery of novel nucleotide mimetics. Our goal is to expand our clinical development pipeline by continuing to recommend additional compounds for clinical development.

Our advanced research programs include:

A viral enzyme inhibitor for the treatment of hepatitis C

Hepatitis C is a viral disease that causes inflammation of the liver that may lead to cirrhosis, primary liver cancer and other long-term complications. Roughly 3% of the world population has been infected with hepatitis C. In the U.S., nearly 4 million people are infected with hepatitis C, of whom 2.7 million are chronically infected.

We have had a collaboration with Merck to create liver-targeting prodrugs of certain compounds that Merck is supplying to us. These compounds target the hepatitis C virus residing in the liver. The funded research phase of this collaboration has ended. Merck is currently evaluating the drug compounds discovered during the collaboration to determine if one or more will be recommended for clinical development. Merck is solely responsible for conducting and funding all development work for compounds resulting from this collaboration and for commercializing any resulting products.

A nucleotide mimetic targeting a protein kinase for the treatment of type 2 diabetes, hyperlipidemia and non-alcoholic steatohepatitis

Non-alcoholic steatohepatitis results from fatty liver disease, a condition associated with type 2 diabetes and obesity, and can ultimately lead to liver fibrosis and later cirrhosis. Based on the number of obese people in the U.S., it is projected that over 6.0 million people currently suffer from non-alcoholic steatohepatitis.

Using our NuMimetic technology, we have discovered a highly potent and selective nucleotide mimetic that activates a protein kinase found in the liver known as AMPK, which regulates cholesterol and fat levels. We have shown in animal models that our lead compound from this research program can inhibit cholesterol and fat synthesis. We believe that this compound or a related compound using our NuMimetic

technology may be useful for the treatment of metabolic diseases such as type 2 diabetes (by a different mechanism than CS-917 and MB07803), hyperlipidemia (by a different mechanism than MB07811), and a disease associated with fatty livers, known as non-alcoholic steatohepatitis, by inhibiting cholesterol and lipid production in the liver. We have entered into a second collaboration with Merck to research, develop and commercialize novel small molecule therapeutics that activate AMPK.

A liver-specific collagen inhibitor for the treatment of liver fibrosis

Liver fibrosis is a life-threatening disease characterized by excessive scarring of the liver, typically caused by chronic hepatitis B or hepatitis C infections or alcoholism, which in turn results in compromised liver function, or cirrhosis. It is estimated that at least 25,000 deaths are caused by chronic liver disease and liver cirrhosis each year in the U.S., almost half of which are attributable to alcoholism.

Liver fibrosis involves an overproduction in the liver of a protein called collagen. This overproduction leads to changes in liver structure and function, and ultimately to liver failure. Using our HepDirect technology, we have developed compounds that target an enzyme controlling collagen production in the liver and showed in animal models of liver disease that our approach led to reduced liver fibrosis.

We retain worldwide commercialization rights to all of the compounds generated from our advanced research programs with the exception of the compounds covered under our collaborations with Merck.

Our Proprietary Technologies

We have developed proprietary technologies that we have used to develop our current product candidates and which we expect to help us expand our product pipeline in the future. Our NuMimetic technology encompasses know-how and compound libraries that are useful in the discovery of molecules that bind effectively and specifically to nucleotide binding sites on certain key enzymes controlling important metabolic pathways. We used this technology to identify CS-917 and MB07803 and may continue to use it to help discover product candidates in other areas. Our HepDirect technology is a proprietary technology used to target drugs to the liver. We applied this technology to develop pradefovir and MB07133 and will continue to use it in programs focused on the discovery of drugs for liver diseases such as hepatitis C and liver fibrosis as well as metabolic diseases.

NuMimetic Technology

The liver plays a central role in many metabolic diseases. Metabolic pathways that reside in the liver are responsible for much of the body s generation of products such as cholesterol, glucose and lipids. This production is normally dependent on an individual s nutritional and hormonal status. However, in individuals with metabolic diseases, these pathways are improperly controlled, leading to excessive production of cholesterol, glucose and lipids.

We are studying enzymes found in the liver that directly or indirectly control the flux, or rate of flow, through these pathways. We believe that many of these enzymes use compounds called nucleotides as a signal for switching flow on or off. While nucleotides are more typically known as a cell s primary chemical energy form and its building blocks for DNA synthesis, they are also recognized as important regulators of metabolic pathways.

We believe that certain nucleotide-binding enzymes represent important drug targets. Nucleotides that bind to these enzymes affect enzymatic activity and therefore the flux through certain metabolic pathways. Certain enzymes important to glucose, cholesterol and fat production and metabolism are known to contain a nucleotide-binding site. It is likely that successful drug compounds targeting these sites will need to exhibit both high binding affinity and high enzyme specificity. Over the past two decades, efforts to find such compounds by screening large compound libraries have failed in large part due to the physical characteristics of these sites.

We have extensively studied the structure of certain nucleotide-binding sites to determine the structural elements that are important for binding and specificity. Through these efforts, we have discovered proprietary compounds that bind to these sites and simulate the action of the natural nucleotides. We have generated large libraries of these compounds, which are known as nucleotide mimetics. These libraries and the know-how generated from our studies constitute our NuMimetic technology.

The following diagram illustrates how our NuMimetic technology works:

HepDirect Technology

Developing drugs to treat diseases of the liver has been a major challenge for the pharmaceutical industry. Although companies have worked for decades to develop drugs that treat chronic liver diseases, relatively few drugs are commercially available. In addition, currently marketed drugs approved for chronic liver diseases generally show poor tolerability, have significant safety risks or are ineffective in the majority of patients. We believe a primary reason for these limitations is that many drugs cannot be delivered to the liver in sufficient quantities to be effective without leading to serious toxicity in other tissues.

Our HepDirect technology addresses these problems by delivering high concentrations of the biologically active forms of target drugs to the liver while simultaneously reducing drug exposure in other tissues. We accomplish this process by making a simple chemical modification that renders the target drug biologically inactive and more readily available to cells. We refer to the modified drug as a HepDirect prodrug. The following diagram illustrates how a HepDirect prodrug works:

Administration of HepDirect prodrugs results in their distribution throughout the body. HepDirect prodrugs, unlike most other prodrug classes, are generally stable in the blood and tissues outside the liver. Because of the limited capacity of non-liver tissues to metabolize and convert HepDirect prodrugs to their active forms, distribution into these tissues leads to rapid reappearance of the prodrugs into the blood stream and ultimately diffusion of the prodrugs from the blood into the liver. In the liver, HepDirect prodrugs are metabolized by an enzyme expressed predominantly in the liver (CYP3A4) which converts the prodrug to the biologically active form of the target drug. Because HepDirect prodrugs are metabolized primarily in the liver, higher target drug levels are achieved in the liver while target drug levels outside of the liver are diminished.

Our HepDirect technology is broadly applicable to a wide variety of drugs. In some cases, the technology may enable the use of drugs that are otherwise ineffective or poorly effective in a particular liver disease due to the drug s failure to achieve therapeutic levels in the liver or due to the inability to administer doses that achieve therapeutic levels as a consequence of drug-related toxicities outside of the liver.

We have shown that our HepDirect technology can deliver compounds with anti-viral, anti-cancer, or anti-fibrotic activity, and we are continuing to use this technology to discover innovative new products for treating liver diseases, and to deliver compounds that affect pathways in the liver responsible for metabolic diseases. For example, we are using this technology and other liver-targeting technologies in a collaboration with Merck in which we are creating prodrugs of certain compounds to target the hepatitis C virus residing in the liver. The funded research phase of this collaboration has ended. Merck is currently evaluating the drug compounds discovered under the research phase of the collaboration to determine if one or more will be recommended for clinical development.

Other Technologies

We have developed other proprietary technologies useful for discovering new candidates for treating diseases. These include additional proprietary methods for targeting the liver and structure-based drug design technologies. We continue to develop and refine our capabilities for identifying important new drugs.

Our Business Strategy

Our goal is to be a leading biopharmaceutical company developing and commercializing novel drugs. Important elements of our business strategy include:

Advancing the development of our product candidates. We currently have four product candidates in clinical trials, pradefovir for the treatment of hepatitis B, CS-917 and MB07803 for the treatment of type 2 diabetes and MB07133 for the treatment of primary liver cancer. We were responsible for the discovery and initial development of each of these product candidates. Valeant and Daiichi Sankyo are primarily responsible for further clinical development of pradefovir and CS-917, respectively. We participate on joint development teams, and we retain significant commercial interest in both product candidates, including North American co-promotion rights for CS-917. We are solely responsible for the development of, and have all rights to, both MB07803 and MB07133.

Continuing to develop a broad product pipeline. We are aggressively seeking to expand our pipeline of product candidates. Our goal is to expand our clinical development pipeline by continuing to recommend new drug compounds for clinical development. In 2005, we recommended the clinical development of MB07811, a clinical development candidate for the treatment of high cholesterol and possibly obesity. In addition, we have entered into a collaboration with Merck to create liver-targeting prodrugs of certain compounds that Merck is supplying to us. These compounds target the hepatitis C virus residing in the liver. We also have an advanced research program for the treatment of type 2 diabetes (by a different mechanism than CS-917 and MB07803) and the treatment of hyperlipidemia (by a different mechanism than MB07811) which is covered under our AMPK collaboration with Merck. These advanced research programs may yield additional drug compounds for clinical development. We retain worldwide commercialization rights to MB07811and all of the compounds generated from our advanced research programs, with the exception of compounds covered by our collaborations with Merck. Using our internal drug discovery capabilities and our HepDirect, NuMimetic and other proprietary technologies, we intend to discover and develop new drug compounds for the treatment of metabolic diseases, liver diseases and certain other diseases linked to pathways in the liver. In addition, at the appropriate time, and as resources allow, we may seek to expand our product pipeline by acquiring products or

businesses or in-licensing technologies that we believe are a strategic fit with our business and complement our existing product candidates and research programs.

Continuing to enhance our expertise in liver pathways and metabolism and related intellectual property rights. Our near-term strategy is to continue to develop proprietary drugs and technologies for the potential treatment of metabolic diseases, cancer and certain other diseases linked to pathways in the liver. We have extensive expertise in liver diseases, as well as pathways and proteins residing in the liver that significantly contribute to certain metabolic diseases or that are important for drug uptake, metabolism and excretion. We intend to continue to invest in our know-how and capabilities, including our HepDirect, NuMimetic and other technologies. Our expertise in this area gives us a competitive advantage for continuing to build a broad product pipeline. We will continue to pursue comprehensive intellectual property protection of our technologies and product candidates when appropriate.

Pursuing a diversified development and commercialization strategy for our product candidates. We have implemented a development and commercialization strategy that combines collaborative partnerships with our own internal product development and commercialization efforts. The revenues from license fees, milestone payments and research funding associated with these arrangements, combined with reduced clinical development expenses, will allow us to better manage our resources and focus on building new opportunities. At the same time, as appropriate, we retain rights that allow us to participate in the commercialization of our product candidates. This strategy is designed to develop and distribute our products as broadly and as effectively as possible while still allowing us to establish our own sales and marketing infrastructure as appropriate. For example, with CS-917, we have a strategic alliance whereby Daiichi Sankyo is responsible for conducting clinical trials, but we have retained an option to co-promote CS-917 in North America, while with MB07133 and MB07803, we are solely responsible for development of the product candidate and have retained all rights. Merck is responsible for conducting future clinical trials under our AMPK collaboration while we have retained the option to co-promote any resulting products in the United States. Our goal for future collaborations is to seek to establish them after we have demonstrated high value for the subject candidate, a strategy which we believe will allow us to retain greater control over development, participation and commercialization.

Establishing additional partnerships based on HepDirect or our other proprietary liver-targeting technologies. Our HepDirect and other proprietary technologies can help overcome some of the challenges faced in developing drugs for liver and metabolic diseases. We believe these technologies are broadly applicable to a wide variety of drug targets. We may partner these technologies with other biopharmaceutical companies whose products would benefit from improved liver-targeting. For example, in 2003 we entered into a collaboration with Merck to discover new treatments for hepatitis C. We created liver-targeted versions of certain compounds provided by Merck that target the hepatitis C virus residing in the liver. The funded research portion of this collaboration was recently completed. Merck is currently evaluating the drug compounds discovered under the research phase of the collaboration to determine if one or more will be recommended for clinical development.

Becoming a fully-integrated pharmaceutical company. We plan to become a fully-integrated pharmaceutical company. In time and as resources allow, we expect to rely less on collaborative arrangements with other

pharmaceutical companies and more on our own internal development, marketing and sales capabilities. We have relied and continue to rely on our partners for the development of our first two product candidates, pradefovir and CS-917. In contrast, we have managed the early clinical development of MB07133 and MB07803 entirely on our own. Still, we have not built an extensive and expensive infrastructure for this effort. Instead, we have relied on a network of consultants and contract research organizations to carry out this development program. We are expanding our internal infrastructure and intend to continue to do so over time as our pipeline expands and we further develop products internally.

Strategic Alliances

In some cases, we use strategic alliances and collaborative partnerships with pharmaceutical and biotechnology companies to augment our internal drug discovery and development capabilities, and to assist the commercialization of our products globally. The revenues from license fees, milestone payments and research funding associated with these arrangements, combined with clinical development expenses assumed by our partners, have allowed us to better manage our resources and focus on building new opportunities. We have generally structured our alliances and partnerships to license specific products, rather than technology, or to apply our technology to a partner s product, and we intend to continue this practice in the future.

Valeant

In October 2001, we entered into a development and license agreement with Valeant for the development and commercialization of pradefovir. Under the agreement, we granted Valeant exclusive worldwide rights to develop and commercialize pradefovir during the term of the agreement. We also agreed that, for so long as Valeant is continuing to develop or commercialize pradefovir, neither we nor our affiliates will develop or commercialize chemically similar compounds that use our HepDirect technology. We further agreed that if Valeant determines that further development of pradefovir is not desirable, Valeant will have the right to substitute one of these compounds, if available, for pradefovir (or the compound that is then under development by Valeant under our agreement). Valeant paid us a license fee of $2 million under the agreement and will be obligated to make milestone payments to us upon the occurrence of specified development, regulatory and commercial milestones. Valeant will pay royalties to us on sales, if any, of products licensed to Valeant under the agreement for the longer of (1) ten years from the first commercial sale or (2) the term of any valid patent right of pradefovir. If all development, regulatory and commercial milestones are achieved, and including the $2 million license fee, we may be entitled to payments which total up to $20 million, plus royalties. In addition, Valeant is solely responsible for conducting and funding all development work, although a joint development committee composed of representatives of Valeant and Metabasis is responsible for overseeing those development efforts. In the third quarter of 2002, Valeant initiated clinical testing of pradefovir for the treatment of hepatitis B. As of December 31, 2005, we had received $2 million in milestone payments under the agreement.

During the first five years of the agreement, if we decide to develop with a third party a compound using our HepDirect technology (other than the compound licensed to Valeant) for the treatment of hepatitis B in humans, Valeant will have a right of first participation to obtain rights in the compound. If Valeant exercises its right of first participation, we have agreed to negotiate in good faith during a limited negotiation period regarding the terms upon which we would grant Valeant those rights. These terms would include an upfront payment, research funding, development and regulatory milestone payments and royalty payments on sales of products, all of which are specified in the development and license agreement. If Valeant does not exercise its right of first participation or we are unable to negotiate the terms on which we would grant Valeant these rights, we may develop the compound with the third party. In addition, under the agreement, Valeant has a ten-year option to obtain an exclusive license to develop and commercialize any other HepDirect compound that we own or control that contains a certain anti-viral drug owned and controlled by Valeant and a five-year option to enter into additional collaborative arrangements with us relating to the application of our HepDirect technology to drug compounds for the treatment of hepatitis B that Valeant has a right to commercialize.

The term of the development and license agreement will continue until all of Valeant s royalty payment obligations have expired, unless the agreement is earlier terminated. The agreement may be terminated entirely or on a country by country basis by either party only for material breach of the other party which remains uncured.

Daiichi Sankyo

In April 1997, we established a multi-year research, development and commercialization collaboration with Daiichi Sankyo to discover, develop and commercialize FBPase inhibitors for the treatment of diabetes. The discovery research portion of the collaboration was extended in February 2000 and March 2001 and ended in April 2002. Under this agreement, our drug discovery efforts were fully funded by Daiichi Sankyo. Daiichi Sankyo had the right to select compounds discovered during the discovery period and is responsible for conducting and funding the clinical development of any compound selected for development. Daiichi Sankyo has exclusive, worldwide commercialization rights to products developed under the agreement. Daiichi Sankyo selected CS-917 as a clinical candidate in 1999 and initiated Phase I clinical trials of CS-917 in July 2001. A joint development committee composed of members from both Daiichi Sankyo and Metabasis oversees clinical development. Compounds that Daiichi Sankyo develops during the five-year period following completion of the drug discovery phase of the collaboration, which target type 1 or type 2 diabetes and act by direct suppression of hepatic gluconeogenesis by inhibiting FBPase, are also subject to the collaboration agreement.

As part of the collaboration, Daiichi Sankyo paid us license fees and sponsored research totaling $20.3 million over the five-year discovery research portion of the collaboration and made an investment of $7.3 million in our Series A preferred stock. As of December 31, 2005, Daiichi Sankyo had made three milestone payments totaling $6.5 million and is obligated to make additional payments based on the achievement of future clinical and regulatory milestones. If all clinical and regulatory milestones are achieved, and including the $20.3 million in license fees and sponsored research, the $7.3 million investment in our Series A preferred stock and the $8.5 million option fee referred to below, we may be entitled to payments which total up to $54.5 million. In addition, Daiichi Sankyo will pay us a royalty on net sales, in countries where we have not exercised our co-promotion rights, of any product developed under the collaboration

agreement for the longer of (1) ten years from the first commercial sale or (2) the term of any valid patent right of a product. In keeping with our partnering strategy, we have the option to co-promote CS-917 or any other product developed under the collaboration in North America on terms and conditions to be negotiated after we exercise the option. We have the contractual right to exercise our co-promotion option for CS-917 prior to the filing of a New Drug Application, or NDA, for CS-917.

In October 2002, we entered into an exclusive option agreement with Daiichi Sankyo, under which Daiichi Sankyo paid us a non-refundable $8.5 million option fee that gave Daiichi Sankyo the right to negotiate a new agreement for the discovery, development and licensing of second generation gluconeogenesis inhibitors, and an option to license an additional back-up compound discovered during the option period. In August 2003, Daiichi Sankyo exercised its rights under the option agreement to designate an additional back-up compound, which Daiichi Sankyo will have the option to license only in the event that the development of CS-917 and the current back-up compound are discontinued. Daiichi Sankyo has the right to terminate development of CS-917 and the current back-up compound and to substitute the additional back-up compound for CS-917 and the current back-up compound under the terms of our collaboration agreement. Also in August 2003, Daiichi Sankyo chose not to exercise its option to negotiate a new agreement for the discovery, development and licensing of second generation gluconeogenesis inhibitors, at which time the option expired. As a result, Daiichi Sankyo has no rights to MB07803, and we may therefore develop MB07803 on our own or in collaboration with another company. Because MB07803 may be directly competitive with CS-917 should they both be developed and because Daiichi Sankyo has no commercial or other rights to MB07803, the information that Metabasis receives from Daiichi Sankyo regarding CS-917 has been reduced.

The term of our collaboration agreement, including the license of the additional back-up compound under our option agreement, will continue until all of Daiichi Sankyo s royalty payment obligations have expired, unless the agreement is earlier terminated. The agreement may be terminated by either party only for material breach which remains uncured or for bankruptcy of the other party. In addition, on a country-by-country basis, we will be entitled to regain rights to CS-917 from Daiichi Sankyo if it does not diligently develop and market CS-917 in a particular country.

Merck

In December 2003, we entered into a collaboration agreement with Merck to discover new treatments for hepatitis C. Under this collaboration, we are creating liver-targeting prodrugs of certain compounds that Merck is supplying to us. These compounds target the hepatitis C virus residing in the liver. The research term of the collaboration was initially for one year and in January 2005, was extended for an additional year through December 2005. At the same time, the scope of the technology that we apply to the Merck compounds was expanded. As part of this collaboration, Merck paid us an upfront fee of $500,000 and research support totaling $2.7 million during 2004 and 2005. Merck is also obligated to pay pre-clinical and clinical milestone payments if specified development and regulatory events occur and royalties on sales of products resulting from the collaboration. If all pre-clinical and clinical milestones are achieved, and including the $500,000 upfront fee and the $1.4 million in research support for each of the first two research years, we may be entitled to payments which total up to $93.3 million, plus royalties. Merck is solely responsible for conducting and funding all development work for compounds resulting from the collaboration and for commercializing any resulting products.

During the initial one-year research term we agreed to work exclusively with Merck on research and development of compounds using our HepDirect technology for hepatitis C, except that our agreement with Merck allowed us to continue our internal hepatitis C research program during that time. Until the first anniversary of the date of our agreement, Merck had an option to extend this exclusivity period by paying us an exclusivity fee of $3.0 million. In January 2005, Merck informed us that it did not wish to exercise this option. The funded research phase of this collaboration has ended. Merck is currently evaluating the drug compounds discovered under the research phase of the collaboration to determine if one or more will be recommended for clinical development.

In addition, for a specified period following the effective date of the agreement, Merck has an exclusive option to obtain a license to develop and commercialize certain compounds from our internal program to discover antiviral compounds to treat hepatitis C. The parties have agreed upon the principal financial terms of any such license. If Merck exercises its option, the parties have agreed to negotiate in good faith during a limited negotiation period a separate written agreement that includes these financial terms, as well as other commercially reasonable terms to be negotiated by the parties. If Merck does not exercise its option to license a development candidate from our internal program before its expiration, or if, despite good faith negotiations, the parties do not enter into a separate written license agreement before the expiration of the negotiation period, then we retain all rights to that candidate including the right to license to another strategic partner.

The term of the collaboration agreement will continue until all of Merck s royalty payment obligations have expired, unless the agreement is earlier terminated. The agreement may be terminated by either party for material breach or insolvency of the other party. Merck also has the right to terminate the agreement without cause at any time after the end of the research term upon 90 days advance written notice to us.

In June 2005, we entered into a collaboration agreement with Merck to research, develop and commercialize novel small molecule therapeutics with the potential to treat several metabolic diseases including type 2 diabetes, hyperlipidemia and obesity by activating AMPK. As part of this collaboration, Merck paid an initial non-refundable license fee of $5.0 million in July 2005 and agreed to provide research support funding of a minimum of $2.1 million each year during the three-year research term. The three-year research term is subject to renewal for one additional year upon the parties mutual agreement. Our level of research activities, and the minimum research support funding, may be increased during the term upon mutual agreement of both parties. Merck is also obligated to pay milestone payments if specified preclinical and clinical development and regulatory events occur and to pay royalties on sales of any product resulting from this collaboration. We would also have the option to co-promote any such product in the United States. If all pre-clinical and clinical milestones are achieved on multiple indications, then including the $5.0 million initial, non-refundable license fee and the minimum $6.3 million in research support funding, we may be entitled to payments which total up to $74.3 million, plus royalties. Merck is solely responsible for conducting and funding all development work for compounds resulting from this collaboration.

The term of the collaboration agreement will continue until all of Merck s royalty payment obligations have expired, unless the agreement is earlier terminated. The agreement may be terminated by either party for material breach or insolvency of the other party. Merck also has the right to terminate the agreement without cause at any time after the end of the twenty-first month following the effective date upon 90 days advance written notice to us.

Sicor

As part of our June 1999 corporate restructuring, we agreed to pay Sicor Inc., now an indirect wholly-owned subsidiary of Teva Pharmaceutical Industries Ltd., a 2% royalty on our direct sales of products that would infringe one of our patents, patent applications, discoveries or inventions in existence as of our corporate restructuring, and 10% of any royalties we receive from licenses of these patents, patent applications, discoveries or inventions. We also agreed to pay Sicor a 1% royalty on our direct sales of products that use, contain or are based on our trade secrets, know-how and other proprietary rights in existence as of our corporate restructuring that are not covered by the 2% royalty, and 5% of any royalties we receive from licenses of these trade secrets, know-how and other proprietary rights that are not covered by the 10% royalty. Some or all of our current product candidates and drug compounds from our research programs may be subject to these royalty provisions.

Intellectual Property

Our success will depend in large part on our ability to:

obtain and maintain patent and other legal protections for the proprietary technology, inventions and improvements we consider important to our business,

prosecute and defend our patents,

preserve our trade secrets, and

operate without infringing the patents and proprietary rights of third parties.

We intend to continue to seek appropriate patent protection for our lead compounds, our proprietary technologies and their uses by filing patent applications in the U.S. and selected other countries. We intend for these patent applications to cover, where possible, claims for composition of matter, medical uses, processes for preparation and formulations.

As of February 1, 2006, we owned a total of 30 issued U.S. patents, 17 pending U.S. utility applications, and seven pending U.S. provisional applications. In foreign countries, as of the same date, we owned a total of 118 issued patents, five allowed applications and 171 pending applications.

Of the above applications and patents, we co-own one pending U.S. utility application, 18 foreign pending applications and one foreign allowed application with Daiichi Sankyo. We co-own one pending U.S. utility application, one pending U.S.

provisional application, and one foreign pending application with Merck. As of the same date, we held rights to a total of four in-licensed U.S. patents and 16 in-licensed foreign patents.

We believe we have a strong intellectual property position, including 13 issued U.S. patents, 23 pending U.S. applications, 76 foreign issued patents, five foreign allowed and 165 foreign pending applications that relate to proprietary technologies and compounds used in our current business. Our currently issued patents that relate to proprietary technologies and compounds used in our current business will expire between 2018 through 2021. The remaining currently issued patents that relate to our proprietary technologies and compounds that are no longer a primary focus of our current business will expire between 2006 and 2020.

Although we believe our rights under patents and patent applications provide a competitive advantage, the patent positions of pharmaceutical and biotechnology companies are highly uncertain and involve complex legal and factual questions. We may not be able to develop patentable products or processes, and may not be able to obtain patents from pending applications. Even if patent claims are allowed, the claims may not issue or, in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us. Any patents or patent rights that we obtain may be circumvented, challenged or invalidated by our competitors.

We also rely on trade secrets, proprietary know-how and continuing innovation to develop and maintain our competitive position, especially when we do not believe that patent protection is appropriate or can be obtained. Our policy is to require each of our employees, consultants and advisors to execute a proprietary information and inventions agreement before they begin providing services to us. Among other things, this agreement obligates the employee, consultant or advisor to refrain from disclosing any of our confidential information received during the course of providing services and, with some exceptions, to assign to us any inventions conceived or developed during the course of these services. We also require confidentiality agreements from third parties that receive our confidential information.

The biotechnology and biopharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. As our current and potential product candidates and others based upon our proprietary technologies progress toward commercialization, the possibility of an infringement claim against us increases. While we attempt to be certain that our products and proprietary technologies do not infringe other parties patents and other proprietary rights, competitors or other parties may assert that we infringe on their proprietary rights.

We have conducted searches of U.S. and foreign patents, but cannot guarantee that the searches were comprehensive and therefore whether any of our product candidates or the methods of using, making or identifying our product candidates infringe the patents searched, or that other patents do not exist that cover our product candidates or these methods. There may also be pending patent applications related to these patents that are unknown to us and may prevent us from marketing our product candidates. Other product candidates that we may develop, either internally or in collaboration with others, could be subject to similar delays and uncertainties.

For a more detailed discussion of risks and uncertainties concerning intellectual property protection for our product candidates and proprietary technologies, see the section in Risk Factors entitled *Risks Related to Our Intellectual Property.*

Sales and Marketing

We do not currently have internal sales or marketing capabilities. In order to commercially market our product candidates if we obtain regulatory approval, we must either develop a sales and marketing infrastructure or collaborate with third parties with sales and marketing capabilities. We have granted Daiichi Sankyo and Valeant worldwide marketing and commercialization rights for CS-917 and pradefovir, respectively. However, we have retained a co-promotion option to directly market CS-917 in North America. In addition, at this point we have retained exclusive rights to MB07133, MB07803 and MB07811, as well as the compounds from our advanced research programs, with the exception of compounds that are covered by our collaborations with Merck.

We intend to make decisions regarding direct marketing of the product candidates for which we retain commercialization rights based on the data derived from our development and research programs in the future. If we proceed with direct marketing of any product candidates, we anticipate building a sales force designed to call on specialists that would be expected to prescribe the largest market share of the product candidate.

Competition

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Due to the high demand for treatments for liver and metabolic diseases, research is intense and new treatments are being sought out and developed by our competitors.

We are aware of many competitive products currently marketed or under development that are used to treat some of the diseases we have targeted. If CS-917 and/or MB07803 are ultimately determined safe and effective and approved for marketing, they may face significant competition from various formulations of metformin and products containing metformin. Metformin is a drug that, like CS-917 and MB07803, inhibits liver glucose production, albeit through an unknown mechanism. Because it does not cause weight gain, metformin is often prescribed as a first-line therapy to obese diabetic patients, who are reported to comprise more than 90% of newly diagnosed type 2 subjects. In addition, inexpensive generic forms of metformin are available. Accordingly, unless CS-917 and/or MB07803 demonstrate a significant benefit over metformin or demonstrate that they can be used in the patient population who do not tolerate and/or adequately respond to metformin treatment, the price required to effectively compete with the generic form of metformin may be so low that it becomes uneconomical for us or Daiichi Sankyo to market CS-917 or for us to market MB07803.

Other currently marketed drugs that may compete with CS-917 and/or MB07803 include, but are not limited to the following classes:

sulfonylureas increase the secretion of insulin by the pancreas, thereby lowering the level of the sugar glucose in the blood,

insulins mimic the naturally occurring hormone insulin made by the pancreas to control blood glucose levels,

peroxisome proliferator-activated receptor agonists - improve insulin sensitivity by activating certain genes involved in fat synthesis and carbohydrate metabolism,

incretin mimetics mimic the naturally occurring hormone incretin . Incretin reduces blood glucose levels by increasing the secretion of insulin from the pancreas, slowing absorption of glucose from the gut, and reducing the action of glucagon (glucagon is a hormone that increases glucose production by the liver),

alpha-glucosidase inhibitors - decrease the absorption of carbohydrates from the intestine, resulting in a slower and lower rise in blood glucose throughout the day,

glinides - stimulate the pancreas beta-cells to produce insulin, and

metformin combination therapies combines metformin with members of the above-mentioned classes, particularly sulfonylureas and PPARs.

In addition, many companies are developing novel therapies that target diabetes. These companies may develop and introduce products competitive with or superior to CS-917 and/or MB07803.

Currently approved treatments for hepatitis B in the U.S. that may compete with pradefovir are included in the following classes:

interferons - mimic the naturally occurring interferon . Interferon is an infection-fighting immune substance produced by the body,

nucleoside analogues - chemically engineered nucleoside compounds structurally similar to the building blocks of DNA and RNA that interferes with the replication of HBV, and

nucleotide analogues - chemically engineered nucleotide compounds structurally similar to the building blocks of DNA and RNA that interferes with the replication of HBV.

A competitor to pradefovir will be Hepsera (adefovir dipivoxil), which is a nucleotide analogue marketed in the U.S. by Gilead Sciences, Inc. Pradefovir and Hepsera are prodrugs of the same active drug, and therefore will directly compete. In order to effectively compete with Hepsera, pradefovir may have to be significantly more beneficial or less expensive than Hepsera. In addition, marketed products approved to treat HIV infections are being evaluated for their effectiveness in treating hepatitis B infections.

There are no currently approved drugs for primary liver cancer. However, a few companies are developing novel therapies specifically for primary liver cancer. In addition, companies are developing therapies for other solid tumors which may be efficacious in treating primary liver cancer. These companies may develop and introduce products competitive with or superior to MB07133.

If MB07811 is ultimately determined safe and effective and approved for marketing, it would compete with products marketed by several large pharmaceutical companies that currently comprise a very large share of the hyperlipidemia market. The major classes of hyperlipidemia drugs include, but are not limited to:

statins - reduce serum cholesterol levels by inhibiting a key enzyme involved in the biosynthesis of cholesterol,

fibrates reduce the amount of cholesterol and triglycerides (fatty substances) in blood,

nicotinic acid derivatives (NADs) - lower cholesterol and triglycerides. NADs decrease low density lipoproteins and increase high density lipoproteins,

cholesterol absorption inhibitors - inhibit the absorption of dietary and biliary cholesterol,

bile acid sequestrants bind with cholesterol-containing bile acids in the intestines and remove them in bowel movements, and

statin combination therapies - combine statins with members of the above-mentioned classes, particularly CAIs.

These large pharmaceutical companies are also developing novel therapies that target hyperlipidemia. These companies may develop and introduce products competitive with or superior to MB07811. Lipitor (atorvastatin; a statin marketed by Pfizer) is currently the best selling prescription medicine. In addition, generic statins (cholesterol-reducers) have recently been approved in the major pharmaceutical markets, which would also compete with MB07811.

In addition, many other companies are developing products for the treatment of the diseases we are targeting and if successful, these products could compete with our products. If we receive approval to market and sell any of our product candidates, we may compete with these companies and their products as well as others in varying stages of development.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, clinical trials, regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our competitors may succeed in developing technologies and therapies that are more effective, better tolerated or less costly than any which we are developing, or that would render our product candidates obsolete and noncompetitive. Our competitors may succeed in obtaining approvals from the FDA and foreign regulatory authorities for their products sooner than we do for ours. We will also face competition from these third parties in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, and in acquiring and in-licensing technologies and products complementary to our programs or advantageous to our business.

Manufacturing

Valeant and Daiichi Sankyo are responsible for all clinical and commercial manufacturing of pradefovir and CS-917, respectively. We rely on several suppliers to produce sufficient quantities of MB07133 and MB07803 for use in clinical studies and intend to rely on these or other suppliers to product sufficient quantities of MB07811 for use in future clinical studies. We currently intend to continue this practice for any future clinical trials and the possible large-scale commercialization of MB07133 and MB07803 and for any other potential products for which we retain significant development and commercialization rights. All of our current product candidates are small molecule drugs. These drugs are historically simpler and less expensive to

manufacture than biologic drugs. We believe our focus on small molecule drugs gives us a manufacturing advantage over companies that develop and manufacture biologic drugs.

Government Regulation and Product Approval

Our Product Candidates

Pradefovir, CS-917, MB07133, MB07803 and any other product candidates that we or our collaborators develop will require regulatory approval before they can be commercialized. Valeant and Daiichi Sankyo are responsible for clinical development and regulatory approval of pradefovir and CS-917, respectively, although we jointly oversee the clinical development of these product candidates through our participation in joint development committees. Although our collaborations with Merck have not yet yielded a product candidate, should either of them be successful, we will be dependent on Merck for clinical development and regulatory approval of any resulting product candidate. We are solely responsible for clinical development and regulatory approval of MB07133 and MB07803.

Product Regulation

Governmental authorities in the U.S. and foreign countries regulate, among other things, the pre-clinical and clinical testing, manufacturing, labeling, storage, record-keeping, advertising, promotion, export, marketing and distribution of drug products. In the U.S., pharmaceutical products are regulated by the FDA under the Federal Food, Drug, and Cosmetic Act, its implementing regulations and other federal laws and regulations. Both before and after the FDA approves a product, the manufacturer and the holder of the product approval are subject to comprehensive regulatory oversight. Violations of regulatory requirements at any stage, including the pre-clinical and clinical testing process, the NDA approval process, or the post-FDA-approval marketing of the product, may result in various adverse consequences. These adverse consequences may include a clinical hold on an ongoing study, the FDA s delay in approving or refusal to approve a product, suspension of manufacturing or withdrawal of an approved product from the market, seizure or recall of a product or the imposition of criminal or civil penalties against the manufacturer or the holder of the product approval. In addition, later discovery of previously unknown problems may result in restrictions on a product, its manufacturer, or the NDA holder, or market restrictions through labeling changes or product withdrawal. Also, new government requirements may be established that could delay or prevent regulatory approval of our products under development.

The steps required before a new drug may be approved for marketing in the U.S. generally include:

conducting appropriate pre-clinical laboratory tests and pre-clinical studies in animals in compliance with the FDA s Good Laboratory Practice, or GLP, requirements,

the submission of the results of these evaluations and studies to the FDA, along with manufacturing information and analytical data, in an IND for human clinical testing, which must become effective before human clinical trials may commence,

obtaining approval of institutional review boards, or IRBs, to introduce the product into humans in clinical studies,

conducting adequate and well-controlled human clinical trials to establish the safety and efficacy of the product, in compliance with FDA s Good Clinical Practice, or GCP requirements,

the submission of the results of pre-clinical studies, clinical studies, and adequate data on chemistry, manufacturing and control information to the FDA in an NDA, and

FDA review and approval of the NDA, including potential pre-approval inspections of manufacturing and testing facilities to assess compliance with the FDA s current Good Manufacturing Practice, or CGMP, requirements and other FDA regulations.

Pre-clinical studies generally include animal studies to evaluate the product s mechanism of action, safety and efficacy. Compounds must be produced according to applicable CGMP requirements, and pre-clinical safety tests must be conducted in compliance with FDA s GLP and similar international regulations. The results of the pre-clinical tests, together with manufacturing information and analytical data, are generally submitted to the FDA as part of an IND, which must become

effective before human clinical trials may be commenced. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA before that time requests an extension or raises concerns about the conduct of the clinical trials described in the application. The sponsor of the application and the FDA must resolve any outstanding concerns before clinical trials can proceed. Clinical trials involve the administration of the investigational product to healthy volunteers or to patients with the disease or disorder being tested, under the supervision of a qualified principal investigator, and must be conducted in accordance with good clinical practices and other requirements, including the informed consent of human test subjects. Clinical trials are conducted in accordance with protocols that detail many items, including:

the objectives of the study,

the parameters to be used to monitor safety, and

the efficacy criteria to be evaluated.

Each protocol must be submitted to the FDA as part of the IND. Further, each clinical study must be reviewed and approved by an IRB at each institution at which the study will be commenced, prior to the recruitment of subjects. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the drug into human subjects, the drug is tested in healthy volunteers or, on occasion, in patients, for safety and, as appropriate, for absorption, metabolism, distribution, excretion, pharmacodynamics, pharmacokinetics and other preliminary measures of efficacy. Phase II usually involves initial studies designed to identify doses of the drug that result in suitable efficacy, safety and tolerance in patients with the targeted disease. A clinical trial designed to generate efficacy data but that is not expected to satisfy FDA criteria for NDA approval is sometimes referred to as a Phase IIb study. Phase III clinical trials, commonly referred to as pivotal studies, are undertaken to provide proof of clinical efficacy and to provide sufficient evidence of safety to justify FDA approval, typically within an expanded and diverse patient population at multiple, geographically dispersed clinical study sites. Phase I, Phase II or Phase III testing may not show sufficient safety or efficacy within any specific time period, if at all, with respect to any products being tested. Furthermore, the sponsor, the FDA or the IRB may suspend clinical trials at any time on various grounds, including a finding that the healthy volunteers or patients are being exposed to an unacceptable health risk.

The results of the pre-clinical studies and clinical trials, together with detailed information on the manufacture and composition of the product, are submitted to the FDA as part of an NDA requesting approval for the marketing of the product. The cost of preparing and submitting an NDA is substantial.

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

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, an approvable letter followed by an approval letter. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require post approval testing and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling restrictions which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Once the NDA is approved, a product will be subject to certain post-approval requirements, including requirements for adverse event reporting and submission of periodic reports. Additionally, the FDA also strictly regulates the promotional

claims that may be made about prescription drug products. In particular, the FDA requires substantiation of any claims of superiority of one product over another including, in many cases, requirements that such claims be proven by adequate and well controlled head-to-head clinical trials. To the extent that market acceptance of our products may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively effect the sales of our products and/or our costs.

If the FDA s evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter.

The not approvable letter outlines the deficiencies in the submission and often requires additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, FDA may withhold approval of an NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

FDA approval of any application may entail many delays or never be granted. Moreover, if regulatory approval of a product is granted, the approval may include limitations on the uses or patient populations for which the product may be marketed. Further, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems occur following initial marketing. Finally, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, we or our collaborators may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or the conduct of additional pre-clinical studies and clinical trials.

Among the conditions for approval is the requirement that the prospective manufacturer s quality control, recordkeeping and manufacturing procedures conform to CGMP requirements enforced by the FDA through its facilities inspection program. In addition, product manufacturing facilities in California are subject to licensing requirements of the California Department of Health Services. These requirements must be followed at all times in the manufacture of the approved product, and manufacturing facilities are subject to inspection by the FDA and the California Department of Health, or other applicable governmental authorities, at any time. In complying with these requirements, manufacturers must continue to expend time, money and effort in the area of production and quality control to be certain of full compliance. The applicable requirements are complex, can be subject to differing interpretations and are subject to change without clear advance notice or guidance from the FDA. Any failure to comply with these requirements may subject manufacturers to, among other things, notices or letters detailing alleged deviations and demanding corrective actions, actions seeking fines and civil penalties, suspension or delay in product approvals, product seizure or recall, suspension of manufacturing, or withdrawal of product approval.

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

There are limitations on the timing of FDA s ability to approve an ANDA for a generic equivalent of a listed drug. In the event that the sponsor of the listed drug has properly informed FDA of patents covering its listed drug, applicants submitting an ANDA referencing that drug are required to certify whether they intend to market their generic products prior to expiration of those patents. If an ANDA applicant certifies that it believes one or more listed patents are invalid or not infringed, it is required to provide notice of its filing to the NDA sponsor and the patent

holder. If the patent holder then initiates a suit for patent infringement against the abbreviated NDA sponsor within 45 days of receipt of the notice, FDA cannot grant effective approval of the ANDA until either 30 months has passed or there has been a court decision holding that the patents in question are invalid or not infringed. A holding that a valid and enforceable listed patent is infringed will preclude approval of the ANDA until the expiration of that patent. If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then FDA cannot grant effective approval of the ANDA until those patents expire. Under Federal law, the term of a patent covering a new chemical entity can be extended by up to five years, for an effective patent life of up to 14 years after approval, based on restoration of part of the patent life lost during clinical testing and FDA review.

Federal law also provides for periods of non-patent exclusivity that also limit the timing of potential approval of an ANDA for a generic equivalent to a listed drug. These include a period of three years of non-patent exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which such three year period FDA cannot grant effective approval of an ANDA based on that listed drug. Federal law also provides a period of five years following approval of a drug containing no previously approved active ingredients, during which an ANDA for a generic equivalent cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval.

The first abbreviated new drug applicant submitting a substantially complete application certifying that listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days after a court decision of invalidity or non-infringement or after it begins marketing its product, whichever occurs first, during which subsequently submitted abbreviated NDAs cannot be granted effective approval. Similar non-patent exclusivity restrictions and patent certification requirements apply to so-called 505(b)(2) NDA applications which rely, in part or in whole, on data generated by or for parties other than the applicant to support an NDA approval.

FDA also imposes a number of complex requirements and restrictions on entities that advertise and promote prescription drugs, which include, among others, standards for and regulations of print and in-person promotion, product sampling, direct-to-consumer advertising, off-label promotion, industry sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act, and failure to abide by FDA requirements can result in penalties and other enforcement actions, including the issuance of warning letters or other letters objecting to violations and directing that deviations from FDA standards be corrected, total or partial suspension of production, and state and federal civil and criminal investigations and prosecutions.

Federal regulations and FDA policies prohibit a sponsor or investigator, or any person acting on behalf of a sponsor or investigator, from representing in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation. Prior to approval of a product candidate, any assertion that one of our product candidates is safe or effective for any purpose or that it is superior to any currently approved product could result in regulatory action by FDA and could delay approval of the product candidate.

A variety of Federal and state laws apply to the sale, marketing and promotion of pharmaceuticals that are paid for, directly or indirectly, by Federal or state health care programs, such as Medicare and Medicaid. The restrictions imposed by these laws are in addition to those imposed by the FDA and corresponding state agencies. Some of these laws significantly restrict or prohibit certain types of sales, marketing and promotional activities by pharmaceutical manufacturers. Violation of these laws can result in significant criminal, civil, and administrative penalties, including imprisonment of individuals, fines and penalties and exclusion or debarment from Federal and state health care and other programs. Many private health insurance companies also prohibit payment to entities that have been sanctioned, excluded, or debarred by Federal agencies. We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA and other agencies have broad regulatory and enforcement powers, including the ability to impose fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals, any one or more of which could have a material adverse effect upon us.

Other Regulations

We are also subject to regulation by the Occupational Health and Safety Administration and state and federal environmental protection agencies, and to regulation under the Toxic Substances Control Act. We may in the future be subject to additional federal, state or local regulations. The Occupational Health and Safety Administration or these environmental protection agencies may promulgate regulations that may affect our research and development programs. We cannot predict whether any agency will adopt any regulation which could limit or impede our operations.

Environmental and Safety Matters

We use hazardous chemicals, biological agents and various radioactive isotopes and compounds in our research and development activities. Accordingly, we are subject to regulations under federal, state and local laws regarding employee safety, environmental protection and hazardous substance control, and to other present and possible future federal, state and local regulations. We may also incur significant costs

complying with environmental laws and regulations adopted in the future.

Also, although we believe our current safety procedures for handling and disposing of hazardous materials comply with federal, state and local laws and regulations, we cannot entirely eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of these materials. In the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Employees

As of December 31, 2005, we employed 95 full-time employees, consisting of 72 employees in research, development and regulatory affairs and 23 in management, administration, finance, receiving and facilities. As of the same date, 35 of our employees had a Ph.D. or M.D. degree. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Scientific Advisory Board

We have established a scientific advisory board consisting of medical professors and industry experts with knowledge of our target markets. Our scientific advisors generally meet once a year as a group to assist us in formulating our research, development and clinical strategies. Some individual scientific advisors consult with and meet informally with us on a more frequent basis. We have entered into consulting agreements with all of our scientific advisors, but they are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

Corporate Information

We were incorporated in Delaware in April 1997 as a wholly owned subsidiary of Gensia Sicor Inc., now Sicor Inc., which became an indirect wholly owned subsidiary of Teva Pharmaceutical Industries Limited in January 2004. In December 1997, Sicor assigned to us specified assets and liabilities relating to its then existing business of discovering and developing proprietary pharmaceutical products. Although we established a new business plan, pursued new opportunities and discovered new products and technologies following our inception, many of the assets we obtained in the transfer served as a foundation upon which we built our technologies and know how. In June, 1999 we completed a corporate restructuring and management stock purchase in which we became an independent company. We have a wholly owned subsidiary, Aramed, Inc., which was transferred to us by Sicor and does not conduct an active business.

Available Information

We make available free of charge on or through our Internet website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports, as soon as practicable after we electronically file these materials with, or furnish them to, the Securities and Exchange Commission. The address of our website is http:/ /www.mbasis.com. The information contained in, or that can be accessed through, our website is not part of this annual report on Form 10-K.

Item 1A. Risk Factors

You should consider carefully the following information about the risks described below, together with the other information contained in this annual report on Form 10-K and in our other filings with the Securities and Exchange Commission, before you decide to buy or maintain an investment in our common stock. We believe the risks described below are the risks that are material to us as of the date of this annual report. If

any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.

Risks Related to our Business

We are dependent on the success of one or more of our current product candidates and clinical development candidate, and we cannot be certain that any of them will receive regulatory approval or be commercialized.

We have expended significant time, money and effort in the development of our four current product candidates, pradefovir, CS-917, MB07133 and MB07803, and our current clinical development candidate, MB07811. Clinical trials conducted to date in patients treated with pradefovir have provided evidence of efficacy as measured by various parameters that we believe to be clinically and statistically significant. However, no pivotal, adequate and well-controlled clinical investigations designed to provide clinical and statistically adequate proof of efficacy, or to provide sufficient evidence of safety to justify approval, have been completed with any of our products. All of our product candidates will require

additional development, clinical trials and regulatory clearances before they can be commercialized. Positive results from pre-clinical studies and early clinical trials do not necessarily mean later clinical trials will succeed. Our product development efforts may not lead to commercial drugs, either because our product candidates or clinical development candidates fail to be safe and effective in clinical trials or because we have inadequate financial or other resources to pursue our product candidates through the clinical trial and approval processes. If any of our product candidates fail to demonstrate safety or efficacy at any time or during any phase of development, we would experience potentially significant delays in, or be required to abandon, development of the product candidate.

We do not anticipate that any of our current product candidates or clinical development candidate will be eligible to receive regulatory approval and begin commercialization for a number of years, if at all. Even if we were ultimately to receive regulatory approval for these product candidates or clinical development candidates, we and/or our partners, as applicable, may be unable to commercialize them successfully for a variety of reasons. These include, for example, the availability of alternative treatments, lack of cost effectiveness, the cost of manufacturing the product on a commercial scale and the effect of competition with other drugs. The success of our product candidates or clinical development candidates may also be limited by the prevalence and severity of any adverse side effects. If we fail to commercialize one or more of our current product candidates or clinical development candidates, we may be unable to generate sufficient revenues to attain or maintain profitability, and our reputation in our industry and the investment community may be damaged.

If clinical trials of our product candidates do not produce successful results, we and our commercialization collaborators, as applicable, will be unable to commercialize these products.

To receive regulatory approval for the commercialization of pradefovir, CS-917, MB07133, MB07803 or any other product candidates that we may develop, adequate and well-controlled clinical trials must be conducted to demonstrate safety and efficacy in humans to the satisfaction of the FDA in the U.S. and other regulatory agencies elsewhere in the world. In order to support marketing approval, these agencies typically require successful results in one or more Phase III clinical trials, which our current product candidates have not yet reached and may never reach. Clinical testing is expensive, can take many years and has an uncertain outcome. Failure can occur at any stage of the testing. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent commercialization of our current or future product candidates, including the following:

clinical trials may produce negative or inconclusive results,

patient recruitment and enrollment in clinical trials may be slower than we anticipate,

costs of clinical trials may be greater than we anticipate,

our product candidates may cause undesirable side effects that delay or preclude regulatory approval or limit their commercial use or market acceptance if approved,

collaborators who are responsible for clinical trials of our product candidates may not devote sufficient resources to these clinical trials or conduct them in a timely manner, or

we may face delays in obtaining regulatory approvals to commence a clinical trial.

Success in pre-clinical testing and early clinical trials does not mean that later clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy despite having progressed through initial clinical testing. Our clinical experience with our product candidates is limited, and to date our product candidates have been tested in less than the number of patients that will likely need to be studied to gain regulatory approval. The data collected from clinical trials with larger patient populations may not demonstrate sufficient safety and efficacy to support regulatory approval of these product candidates.

The targeted endpoints for clinical trials of pradefovir and CS-917 have been, and will continue to be, primarily established by Valeant and Daiichi Sankyo, respectively. We are solely responsible for establishing the targeted endpoints for clinical trials of MB07133 and MB07803, as well as MB07811 should we initiate clinical trials of that clinical development candidate, as we currently expect. These targeted endpoints may be inadequate to demonstrate the safety and efficacy levels required for regulatory approvals. Even if we believe data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support marketing approval by the FDA or other regulatory agencies abroad. Further, pre-clinical and clinical data can be interpreted in different ways, and the FDA or other foreign regulatory agencies may interpret such data in different ways than us or our collaborators. Our failure to adequately demonstrate the safety and efficacy of our product candidates would prevent our receipt of regulatory approval, and ultimately the commercialization of these product candidates.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval or commercialization or have other significant adverse implications on our business.

Prior to receiving regulatory approval, undesirable side effects caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale.

For example, the inhibition of gluconeogenesis can cause elevated levels of lactic acid, or lactate, which, if high and sustained under certain conditions, could lead to lactic acidosis, a serious and potentially fatal condition. Certain pre-clinical animal studies have shown that CS-917 raises lactate levels two- to three-fold in some but not all animal models. Elevated lactate levels have also been observed in certain human clinical trials of CS-917. For example, in a 28-day Phase II clinical trial of CS-917, isolated instances of lactate elevation significantly above the normal range were seen in some patients in both CS-917 and placebo treated groups over the course of the 28 days. No patient exhibited sustained lactate levels significantly above the normal range over a period of consecutive days during the clinical trial. However, one patient who received 200 milligrams of CS-917 twice a day was withdrawn from the clinical trial by the investigator on day 15 due to concerns over consistently elevated lactate levels measured the previous day. Other incidences of elevated lactate levels have been observed and will likely occur in the future.

Our drugs could also exhibit adverse interactions with other drugs. For instance, in March 2005, we were notified by Daiichi Sankyo that two serious adverse events involving lactic acidosis had occurred in two patients in a Phase I clinical trial evaluating the interaction of CS-917 with metformin. The serious adverse events were resolved after medical intervention. The two patients were administered CS-917 in combination with metformin. At high blood levels, metformin is believed to cause mitochondrial toxicity, a cellular toxicity, which can cause lactic acidosis. These dangerous levels are known to occur in patients with significant renal dysfunction who are inappropriately given metformin. Consequently, metformin is contraindicated for use in patients with significant renal dysfunction. After the adverse events occurred, three clinical trials that were ongoing at the time were stopped while one Phase I clinical trial which did not combine CS-917 with metformin continued and was completed. It was subsequently determined that the two patients that experienced the lactic acidosis had blood levels of metformin that were elevated compared to other patients in the clinical trial that received metformin before administration of CS-917. After CS-917 administration, when the two patients were being administered metformin and CS-917, the metformin blood levels increased significantly into a range that is associated with mitochondrial toxicity and subsequent lactic acidosis. CS-917 blood levels also rose higher than expected.

The reason for the unexpectedly high blood levels of both drugs in these two patients is unknown at this time. In July 2005, after completing a comprehensive review of the program and the events and data surrounding the two serious adverse events, we and Daiichi Sankyo concluded that the lactic acidosis observed in the two patients was likely due to the significantly increased blood levels of metformin described above which in turn likely led to mitochondrial toxicity. Subsequently, Daiichi Sankyo decided that Phase IIb clinical trials of CS-917 could safely resume. In February 2006, based on reports from Daiichi Sankyo, after submission of the proposed clinical trial protocol to the FDA and approval by the IRB, a Phase IIb clinical trial of CS-917 was initiated. This Phase IIb clinical trial provides for measurement of the regulatory endpoint, HbA1c. Daiichi Sankyo has conducted and will likely conduct additional studies combining CS-917 with other diabetes drugs to assess both the safety and eventually the potential for enhanced efficacy with the combination. However, further combination of CS-917 and metformin will be avoided unless additional data suggests that the elevation of metformin blood levels as seen in the two patients can be avoided through patient exclusion or through the administration of CS-917 at lower doses or through other means. Should CS-917 eventually be approved and combination with metformin remains an issue, the FDA may require additional measures be taken during marketing, such as prominent warning labels known as black-box warnings, physician education programs and/or other steps regarding concomitant use of CS-917 and metformin.

In February 2006, we initiated Phase I clinical trials of our second-generation product candidate for diabetes, MB07803, which is intended to work by the same mechanism as CS-917.

It is also possible that CS-917 and MB07803 may cause other side effects. In certain pre-clinical studies, as expected based on the mechanism of these compounds, fasted animals treated with CS-917 showed pronounced hypoglycemia, a condition involving abnormally low blood glucose levels that can lead to coma or death. Hypoglycemia has been observed in one patient participating in a clinical trial that involved multi-day administration of the highest dose tested to date in patients (400 milligrams twice a day). This dose is above what is expected to be used in Phase III clinical trials if warranted. However,

we cannot yet rule out the possibility that CS-917 may increase a patient s susceptibility to hypoglycemia, including the potential for severe hypoglycemia, by inhibiting gluconeogenesis, especially in elderly patients who are already prone to develop this condition. Some rodent models of diabetes studied in pre-clinical trials of CS-917 demonstrated, at glucose lowering doses, increased levels of fat molecules known as triglycerides, which are associated with an increased risk of cardiovascular disease. Elevated triglyceride levels have not been observed in human clinical trials to date. Other side effects observed during early clinical trials of CS-917 included nausea and vomiting.

We apply our HepDirect technology to make liver-specific prodrugs of certain compounds. A prodrug is a drug to which a chemical modification has been made that renders it inactive until enzymes in the body convert it to its active form. When converted by the body to their active forms, HepDirect prodrugs produce a byproduct that is within a class of compounds that have the potential of causing toxicity, genetic mutations and cancer. We are unaware of any byproduct-related toxicities demonstrated to date in clinical trials of either pradefovir or MB07133. However, we cannot be certain that this byproduct will not cause adverse effects in current or future clinical trials of these product candidates or other HepDirect prodrugs we may develop. In addition, because our current product candidates are in early stages of development and have been tested in relatively small populations, additional side effects may be observed as their development progresses.

In addition, undesirable side effects seen in the clinical trials of our product candidates may have other significant adverse implications on our business, for example:

we may be unable to obtain additional financing on acceptable terms, if at all,

our stock price could decline,

our collaborators may ultimately terminate development of our partnered products, may further decide not to develop backup product candidates and may terminate our agreements,

if these agreements were terminated we may determine not to further develop the affected product candidates due to resource constraints and may not be able to establish additional collaborations for their further development on acceptable terms, if at all,

if we were to later continue the clinical trials of these product candidates and receive regulatory approval, earlier findings may significantly limit their marketability and thus significantly lower our potential future revenues from their sale,

we may be subject to product liability or stockholder litigation, and

we may be unable to attract and retain key employees.

In addition, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product:

regulatory authorities may withdraw their approval of the product, or we may decide to cease marketing and sale of the product voluntarily,

we may be required to change the way the product is administered, conduct additional clinical trials, change the labeling of the product, or change the product s manufacturing facilities, and

our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from generating significant revenues from the sale of the product.

We are dependent on our collaborations with Valeant and Daiichi Sankyo for development of pradefovir and CS-917, respectively, and events involving these collaborations, our collaborations with Merck, or any future collaborations could prevent us from developing and commercializing our product candidates and achieving or sustaining profitability.

We have entered into collaborations with Valeant and Daiichi Sankyo for the development and commercialization of pradefovir and CS-917, respectively. Valeant and Daiichi Sankyo have agreed to finance the clinical trials for pradefovir and CS-917, respectively, and, if they are approved, manufacture and market them. Accordingly, we are dependent on Valeant and Daiichi Sankyo to gain FDA and other foreign regulatory agency approval of, and to commercialize, pradefovir and CS-917. We have also entered into two collaborations with Merck. The first collaboration with Merck seeks to develop and

commercialize new products for the treatment of hepatitis C infection and the second seeks to develop and commercialize new products to treat several metabolic diseases including type 2 diabetes, hyperlipidemia and obesity. Although our collaborations with Merck have not yet yielded any product candidates, should a candidate ultimately be selected, we will be dependent on Merck for further development and commercialization of any resulting product candidates. In addition, since we do not currently possess the resources necessary to independently develop and commercialize all of the potential products that may be based upon our technologies, including MB07133, MB07803 and MB07811 we may need to enter into additional collaborative agreements to assist in the development and commercialization of some of these potential products. However, our discussions with potential collaborators may not lead to the establishment of new collaborations on acceptable terms, if at all, or it may take longer than expected to establish new collaborations, leading to development and commercialization delays.

We have limited control over the amount and timing of resources that Valeant, Daiichi Sankyo, Merck or any future collaborators devote to our programs or potential products. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Further, our collaborators may not develop products that arise out of our collaborative arrangements or devote sufficient resources to the development, manufacture, marketing or sale of these products. In the event that one of our collaborations is terminated, and we believe that the continued development or commercialization of a product candidate or drug compound covered by the collaboration is warranted, we would seek to obtain rights to develop and commercialize the product candidate or drug compound, if we did not already have those rights. We would then determine whether to continue the development or commercialization of the product candidate or drug compound independently or together with a new collaborator. However, in the event that we do not have sufficient resources to independently develop or commercialize the product candidate or drug compound, and we cannot establish a new collaboration on acceptable terms, we would be forced to discontinue its development or commercialization.

Our agreement with Daiichi Sankyo contains certain rights and restrictions regarding our access to and use of confidential data and information generated by Daiichi Sankyo. We have initiated Phase I clinical trials of MB07803, a second-generation gluconeogenesis inhibitor to which Daiichi Sankyo has no rights and that may be a direct competitor to CS-917. Because of this competitive situation and with our consent, the transfer to us of confidential information and data related to CS-917 from Daiichi Sankyo has already been reduced and we expect that further reductions in information flow will occur. This situation may limit our ability to (i) provide information regarding clinical results unless they are publicly released by Daiichi Sankyo, (ii) influence decisions made at Daiichi Sankyo regarding CS-917 and (iii) accurately track Daiichi Sankyo s diligence on the development program

We and our present and future collaborators may fail to develop or effectively commercialize products or drug compounds covered by our present and future collaborations if:

we do not achieve our objectives under our collaboration agreements,

we are unable to obtain patent protection for the product candidates or proprietary technologies we discover in our collaborations,

we are unable to manage multiple simultaneous product discovery and development collaborations,

our potential collaborators are less willing to expend their resources on our programs due to their focus on other programs or as a result of general market conditions,

our collaborators become competitors of ours or enter into agreements with our competitors,

we or our collaborators encounter regulatory hurdles that prevent commercialization of our product candidates,

we develop products and processes or enter into additional collaborations that conflict with the business objectives of our other collaborators,

consolidation in our target markets limits the number of potential collaborators, or

we are unable to negotiate additional collaboration agreements under terms satisfactory to us.

If we are unable to develop or commercialize our products as a result of the occurrence of any of these events, we may not be able to generate sufficient revenues to achieve or maintain profitability.

Because our collaborations with Merck may involve Merck s proprietary compounds, if Merck terminates development of product candidates we may not have the right to pursue development of these product candidates on our own.

The objective of our hepatitis C collaboration with Merck has been to discover product candidates for the treatment of this disease by applying our technology to certain compounds. The funded research phase of this collaboration has ended. Merck has evaluated and may continue to evaluate the drug compounds discovered under the research phase of the collaboration to determine if one or more will be recommended for clinical development. If Merck so designates a product candidate and then subsequently terminates this collaboration before a defined stage of development of that product candidate, which it may do without cause at any time upon 90 days advance written notice to us, we will not have any right to develop or commercialize that product candidate. In addition, if this collaboration with Merck terminates and Merck successfully develops products based on these proprietary compounds without applying our technology, we will not be entitled to milestone payments or royalties with respect to those products.

Our agreement with Merck to develop and commercialize new products to treat several metabolic diseases including type 2 diabetes, hyperlipidemia and obesity may include the development of compounds owned or controlled by Merck. Accordingly, if Merck terminates this collaboration it may prove difficult for us to continue development of such compounds.

Conflicts may arise between us and any of our collaborators that could delay or prevent the development or commercialization of our product candidates.

Conflicts may arise between our collaborators and us, such as conflicts concerning the interpretation of clinical data, the achievement of milestones or the ownership of intellectual property developed during the collaboration. If any conflicts arise with Valeant, Daiichi Sankyo, Merck or any future collaborators, they may act in their self-interest, which may be adverse to our best interests. Any such disagreement between us and a collaborator could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating sufficient revenues to achieve or maintain profitability:

unwillingness on the part of a collaborator to pay us research funding, milestone payments or royalties we believe are due to us under our collaboration agreement,

uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations, or disagreements with our collaborators regarding the protection of intellectual property rights,

unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities, or

slowing or cessation of a collaborator s development or commercialization efforts with respect to our product

candidates.

Our efforts to discover product candidates beyond our current product candidates may not succeed, and any product candidates we recommend for clinical development may not actually begin clinical trials.

We intend to use our proprietary technologies and our knowledge and expertise to develop and commercialize **novel drugs to address some of the world s most widespread and costly chronic diseases** involving pathways in the liver. Our goal is to expand our clinical development pipeline by continuing to recommend new drug compounds for clinical development. However, the process of researching and discovering drug compounds is expensive, time-consuming and unpredictable. Data from our current research programs may not support the clinical development of our lead compounds or other compounds from these programs, and we may not identify any additional drug compound suitable for recommendation for clinical development. Moreover, any drug compounds we recommend for clinical development may not demonstrate, through pre-clinical testing, indications of safety and potential efficacy, that such drug compounds warrant advancement into clinical trials. Such findings would potentially impede our ability to maintain or expand our clinical development pipeline. Our ability to identify new drug compounds and advance them into clinical development also depends upon our ability to fund our research and development operations, and we cannot be certain that additional funding will be available on acceptable terms, or at all.

Delays in the commencement or completion of clinical testing could result in increased costs to us and delay our ability to generate significant revenues.

Delays in the commencement or completion of clinical testing could significantly impact our product development costs. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. The commencement of clinical trials can be delayed for a variety of reasons, including delays in:

obtaining regulatory approval to commence a clinical trial,

reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites,

manufacturing sufficient quantities of a product candidate,

obtaining institutional review board approval to conduct a clinical trial at a prospective site, and

recruiting and enrolling patients to participate in a clinical trial.

In addition, once a clinical trial has begun, it may be suspended or terminated by us, our collaborators, the FDA or other regulatory authorities due to a number of factors, including:

failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols,

inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold,

unforeseen safety issues, or

lack of adequate funding to continue the clinical trial.

If we experience significant delays in the commencement or completion of clinical testing, our product development costs may increase, we may lose any competitive advantage associated with early market entry and our ability to generate significant revenues may be delayed. For example, events in early 2005 related to CS-917 have delayed our clinical timeline for CS-917 as well as our second-generation gluconeogenesis inhibitor, MB07803. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully meet their obligations under our agreements, we may not be able to obtain regulatory approval for or commercialize our product candidates.

Valeant and Daiichi Sankyo are responsible for conducting clinical trials of pradefovir and CS-917, respectively. Although our collaborations with Merck to discover product candidates for the treatment of hepatitis C and metabolic diseases including type 2 diabetes, hyperlipidemia and obesity have not yet yielded product candidates, should they be successful, we will be dependent on Merck to conduct clinical trials of any resulting product candidates. We intend to rely on other third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories, to conduct our clinical trials of MB07133, MB07803, MB07811 and any other product candidates that we may develop for which a collaborator is not responsible for clinical development. If Valeant, Daiichi Sankyo, Merck or these other third parties do not successfully meet their obligations under our agreements, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to clinical protocols or for other reasons, clinical trials may be extended, delayed or terminated, and these product candidates may not receive regulatory approval or be successfully commercialized.

Because our product candidates, research programs and collaborative efforts depend on our proprietary technologies, adverse events affecting our proprietary technologies may delay or prevent the commercialization of our product candidates.

We used our HepDirect technology to discover pradefovir, MB07133 and in certain other programs and our NuMimetic technology to identify CS-917 and MB07803. We intend to use these and future proprietary technologies to expand our product pipeline in the future. We also may leverage our HepDirect and other liver-targeting technology through strategic alliances and collaborations with other companies, such as our hepatitis C collaboration with Merck in which we applied our technology to certain Merck compounds. Our proprietary technologies are subject to many of the same risks as our product candidates, including risks related to:

obtaining and maintaining patent and trade secret protection for these technologies,

avoiding infringement of the proprietary rights of third parties,

the development of competing technologies by others, and

in HepDirect s case, the safety and effectiveness of this technology in humans.

Because certain of our product candidates and research programs are dependent on our proprietary technologies, adverse events affecting our proprietary technologies may in turn delay or prevent the development or commercialization of our product candidates, which could impede our ability to generate revenues and achieve or maintain profitability.

Our product candidates are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable governmental authorities in foreign markets. In the U.S., neither we, nor our collaborators, are permitted to market our product candidates until we or our collaborators receive approval of an NDA from the FDA or receive similar approvals abroad. The process of obtaining these approvals is expensive, often takes many years, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. Approval policies or regulations may change. In addition, as a company, we have not previously filed NDAs with the FDA or filed similar applications with other foreign regulatory agencies. This lack of experience may impede our ability to obtain FDA or other foreign regulatory agency approval in a timely manner, if at all, for our product candidates for which development and commercialization is our responsibility.

Despite the time and expense invested, regulatory approval is never guaranteed. The FDA or other foreign regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

a product candidate may not be safe and effective,

FDA or other foreign regulatory agency officials may not find the data from pre-clinical testing and clinical trials sufficient,

the FDA or other foreign regulatory agency may not approve of our third-party manufacturers processes or facilities, or

the FDA or other foreign regulatory agency may change its approval policies or adopt new regulations.

Any delay in obtaining, or inability to obtain, these approvals would prevent us from commercializing our product candidates.

Even if any of our product candidates receive regulatory approval, our product candidates may still face future development and regulatory difficulties.

If any of our product candidates receive regulatory approval, the FDA or other foreign regulatory agencies may still impose significant restrictions on the indicated uses or marketing of the product candidates or impose ongoing requirements for potentially costly post-approval studies. In addition, regulatory agencies subject a product, its manufacturer and the manufacturer s facilities to continual review and periodic inspections. If a regulatory agency discovers previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, our collaborators or us, including requiring withdrawal of the product from the market. Our product candidates will also be subject to ongoing FDA and other foreign regulatory agency requirements for the labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information on the drug. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters or other notices of possible violations,

impose civil or criminal penalties or seek disgorgement of revenue or profits,

suspend regulatory approval,

suspend any ongoing clinical trials,

refuse to approve pending applications or supplements to approved applications filed by us or our collaborators,

impose restrictions on operations, including costly new manufacturing requirements, or

seize or detain products or require a product recall.

In order to market any products outside of the U.S., we and our collaborators must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks regarding FDA approval in the U.S. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse impact regarding FDA approval in the U.S., including the risk that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and adversely impact potential royalties and product sales, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

If we and our collaborators fail to comply with applicable foreign regulatory requirements, we and our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

If our competitors have products that are approved faster, marketed more effectively or demonstrated to be more effective than ours, our commercial opportunity will be reduced or eliminated.

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Due to the high demand for treatments for liver and metabolic diseases, research is intense and new treatments are being sought out and developed by our competitors.

We are aware of many competitive products currently marketed or under development that are used to treat some of the diseases we have targeted. If CS-917 and/or MB07803 are ultimately determined safe and effective and approved for marketing, these products may compete for

market share with established therapies from a number of competitors, including large pharmaceutical companies such as GlaxoSmithKline, Bristol-Myers Squibb, Eli Lilly, sanofi-aventis Group, Novo Nordisk and Takeda Pharmaceuticals. Such marketed products include, but are not limited to the following classes:

metformin - members of the biguanide drug class, related to guanidine and the standard of care for type 2 diabetes,

sulfonylureas increase the secretion of insulin by the pancreas, thereby lowering the level of the sugar glucose in the blood,

insulins mimic the naturally occurring hormone insulin made by the pancreas to control blood glucose levels,

peroxisome proliferator-activated receptor agonists - improve insulin sensitivity by activating certain genes involved in fat synthesis and carbohydrate metabolism,

incretin mimetics mimic the naturally occurring hormone incretin . Incretin reduces blood glucose levels by increasing the secretion of insulin from the pancreas, slowing absorption of glucose from the gut, and reducing the action of glucagon (glucagon is a hormone that increases glucose production by the liver),

alpha-glucosidase inhibitors - decrease the absorption of carbohydrates from the intestine, resulting in a slower and lower rise in blood glucose throughout the day,

glinides - stimulate the pancreas beta-cells to produce insulin, and

metformin combination therapies combines metformin with members of the above-mentioned classes, particularly sulfonylureas and PPARs.

Of particular note, metformin is a drug that, like CS-917 and MB07803, inhibits liver glucose production, albeit through an unknown mechanism. Because it does not cause weight gain, metformin is often prescribed as a first line therapy to obese diabetics, who are reported to comprise more than 90% of newly diagnosed type 2 diabetics. Generic forms of metformin have recently become available. Accordingly, unless CS-917 and MB-7803 demonstrate significant benefits over metformin or demonstrate that they can be used in the patient population who do not tolerate and/or adequately respond to metformin treatment, the price required to effectively compete with the generic form of metformin may be so low that it becomes uneconomical for us or Sankyo to market CS-917 and/or for us to market MB07803. Moreover, if the combination of CS-917 with metformin is contraindicated for safety reasons the market potential of CS-917 could be reduced and/or selling expenses could be increased. Should CS-917 eventually be approved and combination with metformin remains an issue, the FDA may require additional measures be taken during marketing, such as prominent warning labels known as black-box warnings, physician education programs and/or other steps regarding concomitant use of CS-917 and metformin.

In addition, many companies are developing novel therapies that target diabetes. These companies may develop and introduce products competitive with or superior to CS-917 and/or MB7803.

If pradefovir is ultimately determined safe and effective and approved for marketing, it may compete for market share with established therapies from a number of competitors, including large pharmaceutical companies such as GlaxoSmithKline, Schering-Plough Corporation, Bristol-Myers Squibb, and Hoffman-La Roche. Such marketed products include, but are not limited to the following classes:

interferons - mimic the naturally occurring interferon . Interferon is an infection-fighting immune substance produced by the body,

nucleoside analogues - chemically engineered nucleoside compounds structurally similar to the building blocks of DNA and RNA that interferes with the replication of HBV, and

nucleotide analogues - chemically engineered nucleotide compounds structurally similar to the building blocks of DNA and RNA that interferes with the replication of HBV.

A competitor to pradefovir will be Hepsera (adefovir dipivoxil), which is a nucleotide analogue marketed in the U.S. by Gilead Sciences, Inc. Pradefovir and Hepsera are prodrugs of the same active drug, and therefore will directly compete. In order to effectively compete with Hepsera, pradefovir may have to be significantly more beneficial or less expensive than Hepsera. In addition, marketed products approved to treat HIV infections are being evaluated for their effectiveness in treating hepatitis B infections.

There are no currently approved drugs for primary liver cancer. However, a few companies are developing novel therapies specifically for primary liver cancer. In addition, companies are developing therapies for other solid tumors which may be efficacious in treating primary liver cancer. These companies may develop and introduce products competitive with or superior to MB7133.

If MB07811 is ultimately determined safe and effective and approved for marketing, it would compete with products marketed by several large pharmaceutical companies that currently comprise a large share of the hyperlipidemia market. Major classes of hyperlipidemia drugs include, but are not limited to:

statins - reduce serum cholesterol levels by inhibiting a key enzyme involved in the biosynthesis of cholesterol,

fibrates reduce the amount of cholesterol and triglycerides (fatty substances) in blood,

nicotinic acid derivatives (NADs) - **lower cholesterol and triglycerides. NADs decrease low density lipoproteins and increase high density lipoproteins,**

cholesterol absorption inhibitors - inhibit the absorption of dietary and biliary cholesterol,

bile acid sequestrants bind with cholesterol-containing bile acids in the intestines and remove them in bowel movements, and

statin combination therapies - combine statins with members of the above-mentioned classes, particularly CAIs.

These large pharmaceutical companies are also developing novel therapies that target hyperlipidemia. These companies may develop and introduce products competitive with or superior to MB07811. Lipitor (atorvastatin; a statin marketed by Pfizer) is currently the best selling prescription medicine. In addition, generic statins (cholesterol-reducers) have recently been approved in the major pharmaceutical markets, which would also compete with MB07811.

In addition, many other competitors are developing products for the treatment of the diseases we are targeting and if successful, these products could compete with our products. If we receive approval to market and sell any of our product candidates, we may compete with these companies and their products as well as others in varying stages of development.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, pre-clinical testing, clinical trials, regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our competitors may succeed in developing technologies and therapies that are more effective, better tolerated or less costly than any which we are developing, or that would render our product candidates obsolete and noncompetitive. Our competitors may succeed in obtaining approvals from the FDA and foreign regulatory authorities for their products sooner than we do for ours. We will also face competition from these third parties in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, and in acquiring and in-licensing technologies and products complementary to our programs or advantageous to our business.

We do not have internal manufacturing capabilities, and if we fail to develop and maintain supply relationships with collaborators or other third-party manufacturers, we may be unable to develop or commercialize our products.

Our ability to develop and commercialize our products depends in part on our ability to manufacture, or arrange for collaborators or other third parties to manufacture, our products at a competitive cost, in accordance with regulatory requirements and in sufficient quantities for clinical testing and eventual commercialization. Valeant and Daiichi Sankyo are responsible for all clinical and commercial manufacturing of pradefovir and CS-917, respectively. We have relied on a number of suppliers to manufacture sufficient quantities of MB07133 and MB07803 for use in our current clinical trials. Although none of our current product candidates has been manufactured on a commercial scale our historical suppliers have manufactured other companies products on a commercial scale. However, we have not yet determined if our suppliers are capable of manufacturing our products on a commercial scale. Similarly, we rely on outside manufacturing for MB07811. We, our collaborators and third-party manufacturers may encounter difficulties with the small- and large-scale formulation and manufacturing processes required to manufacture our product candidates, resulting in delays in our clinical trials and regulatory submissions, in the commercialization of our product candidates or, if any of our product candidates is approved, in the recall or withdrawal of the product from the market. Further, development of large-scale manufacturing processes may require additional validation studies, which the FDA and other foreign regulatory agencies must review and approve. Our inability to enter into or maintain agreements with collaborators or capable third-party manufacturers on acceptable terms could delay or prevent the commercialization of our products, which would adversely affect our ability to generate revenues and could prevent us from achieving or maintaining profitability.

We currently expect that in any future clinical trials of MB07133, MB07803 and MB07811, we will rely on our current suppliers to manufacture these compounds. However, we do not have long-term supply agreements with these third parties, and we may not be able to enter into new supply agreements with them in a timely manner or on acceptable terms, if at all. These third parties may also be subject to capacity constraints that would cause them to limit the amount of these compounds that we can purchase. While we believe alternative sources to manufacture these compounds are readily available, in the event we have to seek such alternative sources we will incur costs associated with identifying and qualifying one or more alternate suppliers. In addition, any resulting interruption or delay we experience in the supply of MB07133, MB07803 or MB07811 may impede the clinical development of these compounds.

In addition, we, our collaborators or other third-party manufacturers of our products must comply with CGMP requirements enforced by the FDA and other foreign regulatory agencies through their facilities inspection programs. These requirements include quality control, quality assurance and the maintenance of records and documentation. In addition, product manufacturing facilities in California are subject to licensing requirements of the California Department of Health Services and may be inspected by the California Department of Health Services, and other applicable regulatory authorities, at

any time. We, our collaborators or other third-party manufacturers of our products may be unable to comply with these CGMP requirements and with other FDA, state and foreign regulatory requirements. We have little control over third-party manufacturers compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may be unable to generate significant revenues.

We do not have a sales and marketing organization, and we have no experience as a company in the sales, marketing and distribution of pharmaceutical products. Valeant and Daiichi Sankyo are responsible for worldwide marketing and commercialization for pradefovir and CS-917, respectively, although we have an option to co-promote CS-917 in North America with Daiichi Sankyo. Although our hepatitis C and metabolic disease collaborations with Merck have not yet yielded product candidates, should they be successful, Merck will be responsible for worldwide marketing and commercialization of any resulting product candidates (subject to, in the case of our metabolic disease collaboration, our option to co-promote the product in the U.S. with certain financial assistance from Merck). In order to co-promote any of these products, or to commercialize MB07133, MB07803, MB07811 or any future product candidates, we must develop our sales, marketing and distribution capabilities, or make arrangements with a third party to perform these services. Even though we may receive financial assistance from Merck if we exercise our co-promotion option under the metabolic disease collaboration developing a sales force for any resulting product or any product resulting from any of our other product candidates is expensive, and time consuming and could delay any product launch. We may be unable to establish and manage an effective sales force in a timely or cost-effective manner, if at all, and any sales force we do establish may not be capable of generating sufficient demand for our product candidates. To the extent that we enter into arrangements with collaborators or other third parties to perform sales and marketing services, our product revenues are likely to be lower than if we directly marketed and sold our product candidates. If we are unable to establish adequate sales and marketing capabilities, independently or with others, we may not be able to generate significant revenues and may not become profitable.

The commercial success of our product candidates depends upon their market acceptance among physicians, patients, healthcare payors and the medical community.

Even if our product candidates obtain regulatory approval, our products, if any, may not gain market acceptance among physicians, patients, healthcare payors and the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

our ability to provide acceptable evidence of safety and efficacy,

relative convenience and ease of administration,

the prevalence and severity of any adverse side effects,

restrictions on use in combination with other products,

availability of alternative treatments,

pricing and cost effectiveness,

effectiveness of our or our partners sales and marketing strategy, and

our ability to obtain sufficient third-party coverage or reimbursement.

If approved, CS-917 may have to be administered several times daily. Additionally, it may result in variable drug levels in different patient populations, which could complicate its use and limit its marketability. Since CS-917 is eliminated from the body through the kidney, it may be of limited use in diabetics with kidney dysfunction. In addition, CS-917 and HepDirect prodrugs such as pradefovir and MB07133 may also exhibit interactions with other marketed drugs that could limit their combination with those drugs. Serious adverse events observed in early 2005 in a Phase I clinical trial of CS-917 in combination with metformin have raised questions about the safety of the potential use of CS-917 and metformin in combination. Therefore, even if CS-917 receives regulatory approval, its combination with metformin may be restricted which may reduce its market potential. In addition, various risk management strategies may be required to minimize inadvertent use with metformin including prominent warning labels known as black-box warnings, physician education programs and/or other steps designed to more tightly control the sale and use of CS-917. Such strategies and programs, if required, will likely

adversely impact the sales of CS-917 and may incur additional selling expenses thereby reducing profits. In addition, primarily because the number of treatable patients in the U.S. with primary liver cancer is relatively small, we expect to market MB07133, if approved, at a relatively high price in the U.S. in order to generate sufficient revenues to recoup our costs and provide a return on our investment. This could limit or prevent us from achieving the market acceptance of MB07133 in the U.S. The number of treatable patients outside of the U.S. is much larger than the number of treatable patients in the U.S. However, because third party reimbursement in many of these countries is uncertain, we may be unable to recoup our costs or generate sufficient returns on our investment in these countries. If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate sufficient revenue from this product candidate and we may not become or remain profitable.

We are subject to uncertainty relating to health care reform measures and reimbursement policies which, if not favorable to our product candidates, could hinder or prevent our product candidates commercial success.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of health care costs to contain or reduce costs of health care may adversely affect:

our ability to set a price we believe is fair for our products,

our ability to generate revenues and achieve or maintain profitability,

the future revenues and profitability of our potential customers, suppliers and collaborators, and

the availability of capital.

In certain foreign markets, the pricing of prescription drugs is subject to government control. In the U.S., given recent federal and state government initiatives directed at lowering the total cost of health care, Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription drugs and the reform of the Medicare and Medicaid systems. For example, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 was recently enacted. This legislation provides a new Medicare prescription drug benefit that began in 2006 and mandates other reforms. While we cannot predict the full outcome of the implementation of this legislation, it is possible that the new Medicare prescription drug benefit, which will be managed by private health insurers and other managed care organizations, will result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. It is also possible that other similar proposals will be adopted.

Our ability to commercialize our product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate coverage and reimbursement levels for the cost of our products and related treatments. Third-party payors including state governments are increasingly challenging the prices charged for medical products and services. Also, the trend toward managed health care in the U.S., which could significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may result in lower prices for our product candidates or exclusion of our product candidates from coverage and reimbursement programs. The cost containment measures that health care

payors and providers are instituting and the effect of any health care reform could significantly reduce our revenues from the sale of any approved product.

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

Since we became an independent company in 1999, we have increased the number of our full-time employees from 50 to 95 as of December 31, 2005. We may need to continue to expand our managerial, operational, financial and other resources in order to manage and fund our operations and clinical trials, continue our research and development and collaborative activities, and commercialize our product candidates. It is possible that our management and scientific personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we continue to improve our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and commercialization goals.

If we fail to attract and keep key management and scientific personnel, we may be unable to successfully develop or commercialize our product candidates.

Our success depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. The loss of the services of certain principal members of our management or scientific staff could delay or

prevent the commercialization of our product candidates. We employ these individuals on an at-will basis and their employment can be terminated by us or them at any time, for any reason and with or without notice, subject to the terms of their stock restriction agreements and severance agreements.

Competition for qualified personnel in the biotechnology field is intense. We will need to hire additional personnel as we establish and/or expand our sales, manufacturing, research and development activities in the future. We may not be able to attract and retain quality personnel on acceptable terms given the competition for such personnel among biotechnology, pharmaceutical and other companies.

We have established a scientific advisory board, the members of which assist us in formulating our research, development and clinical strategies. These scientific advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We have limited experience in identifying, completing and integrating acquisition targets, and if we do not successfully integrate any future acquisitions, we may incur unexpected costs and disruptions to our business.

An important part of our business strategy is to continue to develop a broad pipeline of product candidates. In addition to our internal drug development efforts, we may seek to expand our product pipeline, at the appropriate time and as resources allow, by acquiring products or businesses or in-licensing technologies that we believe are a strategic fit with our business and complement our existing product candidates and research programs. Future acquisitions, however, may entail numerous operational and financial risks including:

exposure to unknown liabilities,

disruption of our business and diversion of our management s time and attention to developing acquired products or technologies,

incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions,

higher than expected acquisition and integration costs,

increased amortization expenses,

difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel,

impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership, and

inability to retain key employees of any acquired businesses.

We have limited experience in identifying acquisition targets, successfully completing potential acquisitions and integrating any acquired products, businesses or technologies into our current infrastructure. Moreover, we may devote resources to potential acquisitions that are never completed or fail to realize the anticipated benefits of any acquisition.

Risks Related to our Finances and Capital Requirements

We have a history of net losses, which we expect to continue for the foreseeable future, and we are unable to predict the extent of future losses or when we will become profitable, if ever.

We have incurred net losses from our inception. As of December 31, 2005, we had an accumulated deficit of approximately $74.9 million. We expect to increase our operating expenses over the next several years as we continue and expand our research and development activities, including conducting clinical trials for our product candidates and further developing our product pipeline, acquiring or in-licensing products, technologies or businesses, and funding other working capital and general corporate purposes. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with our product development efforts, we are unable to predict the extent of any future losses or when we will become profitable, if ever.

We currently lack a significant continuing revenue source and may not become or remain profitable.

Our ability to become and remain profitable depends upon our ability to generate continuing revenues. To date, our product candidates and strategic collaborations have not generated any significant revenues, other than one-time or time-limited payments associated with our collaborations such as milestone payments and option fees. Our ability to generate significant continuing revenues depends on a number of factors, including:

successful completion of ongoing clinical trials for our product candidates,

achievement of regulatory approval for our product candidates,

successful completion of our current and future strategic collaborations, and

successful sales, manufacturing, distribution and marketing of our products.

We do not anticipate that we will generate significant continuing revenues for several years. If we are unable to eventually generate significant continuing revenues, we will not become or remain profitable, and we may be unable to continue our operations.

We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our research and development programs or commercialization efforts and affect our ability to continue as a going concern.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least the next twelve months. Because we do not anticipate that we will generate significant continuing revenues for several years, if at all, we will need to raise substantial additional capital to finance our operations in the future. Our additional funding requirements will depend on, and could increase significantly as a result of, many factors, including:

the rate of progress and cost of our clinical trials and other research and development activities,

the scope, prioritization and number of clinical development and research programs we pursue,

the costs of expanding our operations,

the terms and timing of any collaborative, licensing and other arrangements that we may establish,

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

the costs and timing of regulatory approvals,

the costs of establishing or contracting for sales and marketing capabilities,

the effect of competing technological and market developments, and

the extent to which we acquire or in-license new products, technologies or businesses.

Until we can generate significant continuing revenues, if ever, we expect to satisfy our future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements, as well as through interest income earned on cash balances. We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research and development programs or our commercialization efforts and we may be unable to continue as a going concern.

Raising additional funds by issuing securities or through collaboration and licensing arrangements will cause dilution to existing stockholders, restrict our operations or require us to relinquish proprietary rights.

We will raise additional funds through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. For example, we have an effective shelf registration statement on file with the SEC which allows us to issue shares of our common stock and warrants to purchase our common stock for an aggregate initial offering price of up to $75 million. We may sell any of these securities from time to time in one or more offerings in amounts, at prices and on terms that we will determine at the time of the offering. To the extent that we raise additional capital by issuing equity securities, pursuant to our effective shelf registration statement or otherwise, our existing stockholders ownership will be diluted.

Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing, specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. In addition, if we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us.

Our quarterly operating results and stock price may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. The revenues we generate, if any, and our operating results will be affected by numerous factors, including:

the development status of our product candidates, including results of our clinical trials,

our recommendation of additional drug compounds for clinical development,

our addition or termination of research programs or funding support,

variations in the level of expenses related to our product candidates or research programs, and

our execution of collaborative, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements.

Quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Risks Related to our Intellectual Property

Our success depends upon our ability to protect our intellectual property, including the proprietary technologies and compounds used in our business.

Our commercial success depends on obtaining and maintaining patent protection and/or trade secret protection of our product candidates, proprietary technologies and their uses, as well as successfully defending any patents that issue against third-party challenges. We may only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The filing, prosecution and defense of patents at pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the U.S. The biotechnology patent situation outside the U.S. is even more uncertain. We may be particularly affected by this because we expect that pradefovir and MB07133, if approved, will be marketed in foreign countries with high incidences of hepatitis B and primary liver cancer, respectively. Decisions or actions regarding patent filing and/or changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property.

Decisions or actions regarding patent filing are complex and we may not be successful in protecting our products from competition. Patent positions for products are highly uncertain and involve complex legal and factual questions which may ultimately be decided to the detriment of our products competitive positions in the U.S. and these other countries. We may not be

able to develop patentable products or processes in the U.S. and these other countries, and may not be able to obtain patents from pending applications. Even if patent claims are allowed in the U.S. and these other countries, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us. Any patents or patent rights that we obtain in the U.S. and other countries may be circumvented, challenged or invalidated by our competitors. In addition, we are dependent on outside patent firms for advice and action regarding our efforts to secure patents. Should these firms fail to take appropriate action to secure or enforce our patents in a timely manner, or should they provide us with incorrect or inappropriate advice it could be detrimental to our patent positions.

Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents in the U.S. and other countries.

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 might not have been the first to make the inventions covered by each of our pending patent applications and issued patents,

we might not have been the first to file patent applications for these inventions,

others may independently develop similar or alternative technologies or duplicate any of our technologies,

it is possible that none of our pending patent applications will result in issued patents,

our issued patents may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or may be challenged by third parties,

our issued patents may not be valid or enforceable,

we may not develop additional proprietary technologies that are patentable, or

the patents of others may have an adverse effect on our business.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into proprietary information and inventions agreements with our employees and consultants and entering into confidentiality agreements with other third parties to whom we disclose our proprietary information, third parties may still obtain this information without our knowledge and consent. Enforcing a claim that a third party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect this information. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe. We have not conducted a complete search of existing patents to identify existing patents that our product candidates or proprietary technologies may inadvertently infringe.

We may be exposed to future litigation by the companies holding these patents or other third parties based on claims that our product candidates and/or proprietary technologies infringe their intellectual property rights. If one of these patents was found to cover our product candidates, proprietary technologies or their uses, we or our collaborators could be required to pay damages and could be unable to commercialize our product candidates or use our proprietary technologies unless we or they obtained a license to the patent. In addition, while we are not currently subject to pending litigation nor are we aware of any threatened litigation, third parties may contact us or our collaborators in the ordinary course of business to bring certain patents to our

attention. We and our collaborators evaluate all such communications on a case-by-case basis to assess whether such patents cover our product candidates or proprietary technologies and if so, whether to seek a license from such third parties. A license may not be available to us or our collaborators on acceptable terms, if at all.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we or our collaborators infringe on its technology, we may face a number of issues, including:

infringement and other intellectual property claims which, with or without merit, may be expensive and time-consuming to litigate and may divert our management s attention from our core business,

substantial damages for infringement, including treble damages and attorneys fees, as well as damages for products developed using allegedly infringing drug discovery tools or methods, which we may have to pay if a court decides that the product or proprietary technology at issue infringes on or violates the third party s rights,

a court prohibiting us from selling or licensing the product or using the proprietary technology unless the third party licenses its technology to us, which it is not required to do,

if a license is available from the third party, we may have to pay substantial royalties, fees and/or grant cross licenses to our technology, and

redesigning our products or processes so they do not infringe, which may not be possible or may require substantial funds and time.

We have conducted searches of U.S. and foreign patents, but cannot guarantee that the searches were comprehensive and therefore whether any of our product candidates or the methods of using, making or identifying our product candidates infringe the patents searched, or that other patents do not exist that cover our product candidates or these methods. There may also be pending patent applications that are unknown to us and may prevent us from marketing our product candidates. Other product candidates that we may develop, either internally or in collaboration with others, could be subject to similar delays and uncertainties.

Existing patents and patent applications covering adefovir or prodrugs of adefovir in the U.S. and foreign countries may prevent the commercialization of pradefovir in the future.

Our product candidate pradefovir is a prodrug of adefovir. A third party, Gilead, has rights to another product called Hepsera that is a non-liver specific prodrug of adefovir. Adefovir is covered by U.S. and foreign patents that are scheduled to expire in April 2006. On their face, these

patents are assigned to Gilead. We currently anticipate that, if approved, pradefovir will not be commercialized until after April 2006, and therefore should not infringe upon these patents. However, in some cases, the terms of U.S. and foreign patents covering drug products approved for commercialization may be extended if the holder of the patents requests an extension within a specified period following the date of regulatory approval and the request for extension is approved by the appropriate agencies. We are not aware that the term of the U.S. patents covering adefovir was extended following regulatory approval of Hepsera in the U.S., and the period in which extensions may have been requested has ended. The extension of any patent covering adefovir may prevent the commercialization of pradefovir in the relevant country until the expiration of the extended patent term, unless we or Valeant obtained a license to this patent. We are not aware of any request for an extension of patents covering adefovir in Europe.

We are aware of third party patents and patent applications in the U.S. and in European and other foreign countries with claims to prodrugs of adefovir. These patents are scheduled to expire in September 2011 overseas and in 2014 in the U.S. Although we do not believe that any valid claim covers pradefovir, we cannot guarantee this. If it is determined that patent claims are valid and cover pradefovir, we may not be able to commercialize pradefovir in such countries, including those in Europe. Further, we are aware that a patent term extension of one of these prodrug patents has been granted in multiple European countries based on the regulatory approval of Hepsera thereby extending protection of Hepsera in those countries to September 2016. Additional third party patents covering Hepsera or adefovir may exist, and may expire later than our expected date of regulatory approval in the country where the patent is in force.

Risks Related to Other Legal Matters

We may incur significant costs complying with environmental laws and regulations.

We use hazardous materials, including chemicals, biological agents and radioactive isotopes and compounds that could be dangerous to human health and safety or the environment. As appropriate, we store these materials and wastes resulting from their use at our facility pending their ultimate use or disposal. We currently contract with a third party to dispose of these materials and wastes. We are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these materials and wastes. We may also incur significant costs complying with environmental laws and regulations adopted in the future.

We may incur substantial liabilities from any product liability claims if our insurance coverage for those claims is inadequate.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical

trials, and will face an even greater risk if we sell our product candidates commercially. For example, two cases of lactic acidosis were recently observed in a clinical trial combining CS-917 with metformin. As a result, unless further data changes the situation, the combination of CS-917 and metformin is contraindicated and the inadvertent combination of the drugs could put patients at risk for lactic acidosis. Therefore, even if CS-917 receives regulatory approval the FDA may require that additional measures be taken during marketing, such as prominent warning labels known as black-box warnings, physician education programs and/or other steps regarding concomitant use of metformin and CS-917. However, none of these programs can be assured of eliminating the possibility of the inadvertent use of CS-917 with metformin and the consequent risk of lactic acidosis. Therefore, these programs may not effectively protect us from a liability claim.

An individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for our product candidates,

injury to our reputation,

withdrawal of clinical trial participants,

costs of related litigation,

substantial monetary awards to patients or other claimants,

loss of revenues, and

the inability to commercialize our product candidates.

We have product liability insurance that covers our clinical trials, up to an annual aggregate limit of $10 million. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for any of our product candidates. However, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost and we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise.

If we use biological and hazardous materials in a manner that causes injury, we may be liable for damages.

Our research and development and manufacturing activities involve the use of biological and hazardous materials. Although we believe our safety procedures for handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot entirely eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of these materials. If one of our employees was accidentally injured from the use, storage, handling or disposal of these materials, the medical costs related to his or her treatment would be covered by our workers compensation insurance policy. However, we do not carry specific biological or hazardous waste insurance coverage and our property and casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste

exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources.

Risks Related to the Securities Markets and Investment in our Common Stock

Market volatility may affect our stock price and the value of your investment.

The market price for our common stock has been and is likely to continue to be volatile. In addition, the market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including:

changes in the regulatory status of our product candidates, including the status and results of our clinical trials,

events affecting Valeant, Daiichi Sankyo, Merck or any future collaborators,

announcements of new products or technologies, commercial relationships or other events by us or our competitors,

regulatory developments in the U.S. and foreign countries,

fluctuations in stock market prices and trading volumes of similar companies,

variations in our quarterly operating results,

changes in securities analysts estimates of our financial performance,

changes in accounting principles,

issuances of new equity securities by us, pursuant to our effective shelf registration statement or otherwise,

sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders,

additions or departures of key personnel, and

discussion of us or our stock price by the financial and scientific press and in online investor communities.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

We may incur increased costs as a result of changes in laws and regulations relating to corporate governance matters.

Changes in the laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002 and rules adopted or proposed by the Securities and Exchange Commission and by the Nasdaq Stock Market, will result in increased costs to us as we continue to evaluate the implications of these laws and regulations and respond to their requirements.

These laws and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. We are presently evaluating and monitoring developments with respect to these laws and regulations and cannot predict or estimate the amount or timing of additional costs we may incur to respond to their requirements.

Investor confidence and share value may be adversely impacted if our independent auditors are unable to provide us with the attestation of the adequacy of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act of 2002.

Beginning with our annual report on Form 10-K for the fiscal year ending December 31, 2006, we will be required pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 to include in our annual reports on Form 10-K an assessment by our management of the effectiveness of our internal controls over financial reporting. In addition, our independent auditors must attest to and report on our management s assessment. How companies are implementing these new requirements including internal control reforms, if any, and how independent auditors are applying these new requirements and testing internal controls, remain subject to some uncertainty. In addition, any control system, regardless of how well designed, operated and evaluated, can provide only reasonable, not absolute, assurance that its objectives will be met. If, during any year, our independent auditors are not satisfied with our internal controls over financial reporting or the level at which these controls are documented, designed, operated, tested or assessed, or if our independent auditors interpret the applicable requirements, rules or regulations differently than we do, then they may decline to attest to management s assessment or may issue a report that is qualified. This could result in an adverse reaction in the financial marketplace due to a loss of investor confidence in the reliability of our financial statements, which could negatively impact the market price of our common stock.

If our executive officers, directors and largest stockholders choose to act together, they may be able to control our operations and act in a manner that advances their best interests and not necessarily those of other stockholders.

Our executive officers, directors and holders of 5% or more of our outstanding common stock, beneficially owned approximately 71% of our common stock as of December 31, 2005. As a result, these stockholders, acting together, are able to control all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with our interests or the interests of other stockholders, and they may act in a manner that advances their best interests and not necessarily those of other stockholders.

Future sales of our common stock may cause our stock price to decline.

A large portion of our shares are held by a small number of persons and investment funds. In addition, these persons and funds hold warrants to purchase 3,797,176 shares of common stock that, if exercised, will result in these additional shares becoming available for sale. Moreover, several of our stockholders and warrant holders have rights, subject to some conditions, to require us to file registration statements covering the unregistered shares they currently hold or may acquire upon exercise of warrants, or to include these shares in registration statements that we may file for ourselves or other stockholders. For example, the Securities and Exchange Commission recently declared effective a registration statement we filed covering the resale of the shares of common stock we issued in our recent private placement and the shares of common stock issuable upon exercise of the warrants issued in the private placement. Sales by these stockholders or warrant holders of a substantial number of shares could significantly reduce the market price of our common stock.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We lease approximately 82,000 square feet of space in La Jolla, California. We perform all of our research, development, management, administrative and other activities in this facility. The initial term of the lease expires in 2015. We have options to extend the lease for two renewal periods of five years each.

We believe that our facilities are adequate for our current needs.

Item 3. Legal Proceedings

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

Item 4. Submission of Matters to a Vote of Security Holders

Not applicable.

PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been traded on the Nasdaq National Market since June 16, 2004 under the symbol MBRX. Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales prices for our common stock as reported on the Nasdaq National Market for the periods indicated.

	High	Low
Year Ended December 31, 2005		
Fourth Quarter	$ 8.43	$ 5.03
Third Quarter	$ 6.75	$ 3.10
Second Quarter	$ 3.68	$ 2.32
First Quarter	$ 8.09	$ 3.00

	High	Low
Year Ended December 31, 2004		
Fourth Quarter	$ 7.25	$ 5.11
Third Quarter	$ 6.95	$ 5.15
Second Quarter (beginning June 16, 2004)	$ 7.13	$ 5.75

As of March 1, 2006, there were approximately 127 holders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities and Use of Proceeds

Our initial public offering of our common stock, par value $0.001, was effected through a Registration Statement on Form S-1 (File No. 333-112437) that was declared effective by the Securities and Exchange Commission on June 15, 2004. The Registration

Statement covered the offer and sale of up to 5,750,000 shares of our common stock for an aggregate offering price of $40.3 million. Our initial public offering commenced on June 15, 2004. On June 21, 2004, 5,000,000 shares of our common stock were sold for an aggregate offering price of $35.0 million. On July 20, 2004, 75,000 shares of our common stock were sold for an aggregate offering price of $525,000 upon the partial exercise of the underwriters over-allotment option. Our initial public offering terminated following the sale of all of the securities registered on the registration statement and the expiration of the underwriters over-allotment option. Our initial public offering resulted in aggregate proceeds to us of approximately $31.1 million, net of underwriting discounts and commissions of approximately $2.5 million and offering expenses of approximately $1.9 million, through a syndicate of underwriters managed by SG Cowen & Co., LLC, Deutsche Bank Securities Inc., Thomas Weisel Partners LLC, and Legg Mason Wood Walker, Incorporated.

No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or person owning ten percent or more of any class of our equity securities or to any other affiliates. All offering expenses were paid directly to others.

As of December 31, 2005, we had used approximately $15.4 million of the initial public offering proceeds for investments in medium-term, interest-bearing obligations, investment-grade instruments, or guaranteed obligations of the U.S. government. As of December 31, 2005, we had used approximately $15.7 million of the initial public offering proceeds for operating expenses.

The foregoing payments were direct payments made to third parties who were not our directors or officers (or their associates), persons owning ten percent or more of any class of our equity securities or any other affiliate, except that the proceeds used for working capital included regular compensation for officers and directors. The use of proceeds does not represent a material change from the use of proceeds described in the prospectus we filed pursuant to Rule 424(b)(4) of the Securities Act of 1933, as amended, with the Securities and Exchange Commission on June 16, 2004.

In October 2005, we raised approximately $41.3 million in a private placement of common stock and the concurrent issuance of warrants for the purchase of common stock. Placement fees and other expenses were approximately $2.3 million. Under the terms of the financing, we sold 7.0 million shares of common stock at $5.86 per share, the closing bid price for our common stock immediately preceding the entering into of the binding agreement for the transaction. We also issued warrants to purchase approximately 2.5 million shares of our common stock at an exercise price of $6.74 per share. At the closing, investors in the financing paid an additional price equal to $0.125 per each share issuable upon exercise of the warrants. The common stock and warrants to purchase our common stock issued in the private placement were issued in reliance on the exemption from registration contained in Section 4(2) of the Securities Act of 1933, as amended, and/or Regulation D, Rule 506 promulgated under the Securities Act of 1933, as amended, in that the issuance did not involve a public offering. Each investor in the private placement represented that it was an accredited investor as defined in Regulation D and that it was acquiring the common stock and warrants for investment only and with a view to or for a sale in connection with any distribution thereof. On October 14, 2005, we filed a registration statement with the Securities and Exchange Commission covering the resale of the shares of common stock issued in the private placement and the shares of common stock issuable upon exercise of the warrants issued in the private placement. This registration statement was declared effective by the Securities and Exchange Commission on October 27, 2005.

Equity Compensation Plan Information

The information required to be disclosed by Item 201(d) of Regulation S-K, Securities Authorized for Issuance Under Equity Compensation Plans, is incorporated by reference to Item 12 of Part III of this Form 10-K.

Item 6. Selected Financial Data

The statement of operations data and balance sheet data presented below should be read in conjunction with Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations, and the financial statements and related notes appearing elsewhere in this Form 10-K.

	Years Ended December 31,				
	2005	2004	2003	2002	2001
	(In thousands, except per share amounts)				
Statements of Operations Data:					
Revenues	$ 3,771	$ 6,837	$ 9,124	$ 2,278	$ 7,664
Operating expenses:					
Research and development	21,460	16,675	15,048	12,609	9,464
General and administrative	5,283	3,804	2,955	2,531	2,131
Amortization of employee stock-based compensation(1)	1,695	1,633	504	23	
Total operating expenses	28,438	22,112	18,507	15,163	11,595
Loss from operations	(24,667)	(15,275)	(9,383)	(12,885)	(3,931)
Other income (expense), net	1,087	303	(46)	88	249
Net loss(2)	(23,580)	(14,972)	(9,429)	(12,797)	(3,682)
Preferred stock deemed dividend(3)			(24,900)		
Net loss applicable to common stockholders	$ (23,580)	$ (14,972)	$ (34,329)	$ (12,797)	$ (3,682)
Basic and diluted net loss per share:(2)					
Historical	$ (1.20)	$ (1.49)	$ (23.84)	$ (10.12)	$ (4.44)
Pro forma	$ (1.20)	$ (0.98)	$ (3.74)		
Shares used to compute basic and diluted net loss per share:					
Historical	19,706	10,034	1,440	1,265	830
Pro forma	19,706	15,254	9,187		

(1) The amortization of employee stock-based compensation is composed of $1,170,000 and $1,138,000 related to research and development activities and $525,000 and $495,000 related to general and administrative activities for the years ended December 31, 2005 and 2004, respectively.

(2) Please see Note 1 to our financial statements for an explanation of the method used to calculate the historical and pro forma net loss per share and the number of shares used in the computation of the per share amounts.

(3) As disclosed in Note 7 to our financial statements, we recorded a deemed dividend in connection with the issuance of our Series E preferred stock.

	As of December 31,				
	2005	2004	2003	2002	2001
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and securities available-for-sale	$ 66,893	$ 43,855	$ 25,257	$ 19,562	$ 25,572
Working capital	59,691	40,906	22,342	13,693	24,539
Total assets	73,878	47,860	29,110	21,733	28,438
Long-term obligations (including current portion)	3,168	2,226	1,820	2,854	3,907
Accumulated deficit	(74,945)	(51,365)	(36,393)	(26,964)	(14,167)
Total stockholders equity	59,582	41,864	23,437	8,756	21,475

Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis together with our audited financial statements and the notes to those statements included elsewhere in this annual report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. See Forward-Looking Statements in Part I, Item 1 of this annual report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel drugs to address some of the world s most widespread and costly chronic diseases involving pathways in the liver. These diseases include metabolic diseases such as diabetes, hyperlipidemia, a disease involving elevated levels of lipids such as cholesterol, and obesity, among others, and liver diseases such as hepatitis and primary liver cancer. We have established a broad and growing product pipeline targeting large markets with significant unmet medical needs. We have discovered all of our product candidates internally using our proprietary technologies.

We currently have four product candidates in clinical trials, pradefovir, CS-917, MB07133 and MB07803. Pradefovir and MB07133 are being developed for the treatment of hepatitis B and primary liver cancer, respectively. CS-917 and MB07803 both work by the same mechanism and both are being developed for the treatment of type 2 diabetes.

We have incurred annual net losses since inception. As of December 31, 2005, our accumulated deficit was approximately $74.9 million. We expect to incur substantial and increasing losses for the next several years as we:

- continue to develop current and future clinical development candidates,
- commercialize our product candidates, if any, that receive regulatory approval,
- continue and expand our research and development programs, and
- acquire or in-license products, technologies or businesses that are complementary to our own.

We have a limited history of operations and, to date, we have not generated any product revenues. In addition to our initial public offering in June 2004 and our private placement of common stock and warrants in October 2005, we have financed our operations and internal growth through private placements of preferred stock as well as direct payments of sponsored research funding, license fees, milestone payments and equity investments from our collaborative partners. We have received additional funding through equipment financing arrangements and Small

Business Innovation Research, or SBIR, grants.

Our agreements with collaborators may include joint marketing or promotion arrangements of our products or products licensed from our collaborators. For example, we have retained co-promotion rights for CS-917 in North America with Daiichi Sankyo. Alternatively, we may grant exclusive marketing rights to our collaborators in exchange for up-front fees, milestones and royalties on future sales, if any. We have licensed worldwide commercialization rights for pradefovir to Valeant. We have retained rights to MB07133, MB07803, MB07811 and all of the compounds generated from our current research programs, with the exception of product candidates covered by our collaborations with Merck. We intend to eventually market one or more of the product candidates for which we retain commercialization rights through our own sales force or with a co-promotion partner in the U.S. and through strategic collaborations abroad.

We will rely on our partners or third-party manufacturers to produce sufficient quantities of these products for pre-clinical and clinical studies and large-scale commercialization upon their approval.

Our business is subject to significant risks, including the risks inherent in our ongoing clinical trials and the regulatory review and approval process, the results of our research and development efforts, reliance on third parties for the development and commercialization of our product candidates, competition from other products and uncertainties associated with obtaining and enforcing patent rights.

Research and Development

Our research and development expenses consist primarily of compensation and other expenses for research and development personnel, costs associated with pre-clinical development and clinical trials of our product candidates, facility costs,

supplies and materials, costs for consultants and related contract research and depreciation. We charge all research and development expenses to operations as they are incurred.

Our research and development activities are primarily focused on the clinical development of MB07133, MB07803 and the potential further advanced pre-clinical development and potential clinical trials of MB07811. In addition, research and development activities include work on lead compounds in our other research programs. In February 2006, we began a Phase I clinical trial of MB07803. We plan to file an IND for MB07811 and to commence clinical trials of MB07811 in 2006 if the pre-clinical data is supportive and the proposed clinical trials are cleared by the FDA. We are responsible for all costs incurred in our research programs with the exception of the AMPK program partnered with Merck. Under the terms of our collaboration agreements with Merck, we had received approximately $4.4 million in research funding through December 31, 2005. Valeant and Daiichi Sankyo are responsible for the costs of clinical development of pradefovir and CS-917, respectively.

At this time, due to the risks inherent in the clinical trial process and given the early stage of development of our product candidates and lead compounds from our research programs, we are unable to estimate with any certainty the costs we will incur in the continued development of our product candidates for commercialization. Due to these same factors, we are unable to determine the anticipated completion dates for our current research and development projects. However, we expect our research and development costs to be substantial and to increase as we continue the development of our current product candidates, as well as continue and expand our research programs.

Generally, Phase I clinical trials can be expected to last from 6 to 18 months, Phase II clinical trials can be expected to last from 12 to 24 months and Phase III clinical trials can be expected to last from 18 to 36 months. However, clinical development timelines vary widely, as do the likelihood of success and total costs of clinical trials. Although we are currently focused primarily on advancing MB07133 and MB07803 through clinical development and MB07811 into clinical development, we anticipate that we will make determinations as to which research and development projects to pursue and how much funding to direct to each project on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as an ongoing assessment of its market potential.

The lengthy process of seeking regulatory approvals for our product candidates, and the compliance with applicable regulations, require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could cause our research and development expenditures to increase and, in turn, have a material unfavorable effect on our results of operations. We cannot be certain when or if any net cash inflow due to sales of any of our current product candidates will commence.

General and Administrative

General and administrative expenses consist primarily of salaries and other related costs for personnel in executive, finance, accounting, business development, investor relations and human resource functions. Other costs include facility costs not otherwise included in research and development expenses and professional fees for legal and accounting services.

We anticipate continued increases in general and administrative expenses for investor relations and other activities associated with operating as a publicly-traded company. These increases will also likely include the hiring of additional personnel.

Other Income, Net

Other income, net includes interest earned on our cash, cash equivalents and securities available-for-sale, net of interest expense.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations are based on our audited financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. We review our estimates on an on-going basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and

liabilities. Actual results may differ from these estimates under different assumptions or conditions. We believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition. Our revenue recognition policies are in accordance with Securities and Exchange Commission Staff Accounting Bulletin, or SAB 104, *Revenue Recognition*, and Emerging Issues Task Force, or EITF, Issue 00-21, *Revenue Arrangements with Multiple Deliverables*. Our agreements generally contain multiple elements, including downstream milestones and royalties. All fees are nonrefundable. Revenue from milestones is recognized when earned, provided that:

the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, and

collaborator funding, if any, of our performance obligations after the milestone achievement will continue at a level comparable to before the milestone achievement.

If both of these criteria are not met, the milestone payment is recognized over the remaining minimum period of our performance obligations under the agreement. Upfront, nonrefundable fees under our collaborations are recognized over the period the related services are provided. Nonrefundable upfront fees not associated with our future performance are recognized when received. Amounts received for research funding are recognized as revenues as the services are performed. Amounts received for research funding for a specific number of full-time researchers are recognized as revenue as the services are provided, as long as the amounts received are not refundable regardless of the results of the research project.

Clinical Trial Expenses. Our clinical trials are often conducted under contracts with multiple research institutions and clinical research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Generally, these agreements set forth the scope of work to be performed at a fixed fee or unit price. Payments under the contracts depend on factors such as the successful enrollment of patients or the completion of clinical trial milestones. Expenses related to clinical trials generally are accrued based on contracted amounts applied to the actual level of patient enrollment and activity according to the protocol. Other incidental costs related to patient enrollment are accrued when known. If contracted amounts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our accruals accordingly on a prospective basis.

Recently Issued Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board (FASB) issued SFAS No. 123R, *Share Based Payment*. This statement is a revision to SFAS No. 123 and supersedes APB 25 and amends FASB Statement No. 95, *Statement of Cash Flows*. This statement requires a public entity to expense the cost of employee services received in exchange for an award of equity instruments. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements of these equity arrangements. This statement is effective for

us in the first quarter of 2006.

SFAS No. 123R permits public companies to choose between the following two adoption methods:

1. A modified prospective method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date, or

2. A modified retrospective method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

As permitted by SFAS No. 123, we currently account for share-based payments to employees using APB 25 s intrinsic value method and, as such, we generally recognize no compensation cost for employee stock options. The impact of the adoption of SFAS No. 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, valuation of employee stock options under SFAS No. 123R is similar to SFAS No. 123, with minor exceptions. The impact on our results of operations and earnings per share had we adopted SFAS No. 123 is described in Note 1 to our audited financial statements accompanying this Annual Report on Form 10-K. Accordingly, the adoption of SFAS No. 123R s fair value method will have a significant impact on our results of operations, although it will have no impact on our overall financial

position. SFAS No. 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under current literature. This requirement will reduce net operating cash flows and increase net financing cash flows in periods after adoption.

In March 2004, the EITF reached a final consensus on Issue No. 03-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. EITF Issue No. 03-1 requires that when the fair value of an investment security is less than its carrying value, an impairment exists for which the determination must be made as to whether the impairment is other-than-temporary. The EITF Issue No. 03-1 impairment model applies to all investment securities accounted for under SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities* and to investment securities accounted for under the cost method to the extent an impairment indicator exists. Under the guidance, the determination of whether an impairment is other-than-temporary and therefore would result in a recognized loss depends on market conditions and management s intent and ability to hold the securities with unrealized losses. In September 2004, the FASB approved FASB Staff Position (FSP) EITF 03-1-1, which defers the effective date for recognition and measurement guidance contained in EITF Issue No. 03-1 until certain issues are resolved. In November 2005, the FASB issued FSP FAS 115-1. FSP FAS 115-1 replaces the impairment evaluation guidance of EITF Issue No. 03-1 with references to the existing other-than-temporary impairment guidance. EITF 03-1 s disclosure requirements remain in effect. The FSP also supersedes EITF Topic No. D-44, *Recognition of Other-Than-Temporary Impairment upon the Planned Sale of a Security Whose Cost Exceeds Fair Value*, and clarifies that an investor should recognize an impairment loss no later than when the impairment is deemed other-than-temporary, even if a decision to sell an impaired security has not been made. The guidance in this FSP will be applied in the first quarter of 2006. We not expect the adoption of EITF Issue No. 03-1 or FSP FAS 115-1 to have a material effect on our liquidity, results of operations and financial condition.

Results of Operations

Comparison of the Years Ended December 31, 2005 and 2004

Revenues. Revenues were $3.8 million for the year ended December 31, 2005, compared with $6.8 million for the year ended December 31, 2004. The $3.0 million decrease was mainly due to a decline in milestone revenue of approximately $4.5 million which was attributable primarily to a $3.5 million payment earned in the prior year period under our collaboration agreement with Daiichi Sankyo. This decrease was partially offset by an additional collaboration agreement entered into with Merck in June 2005 which included sponsored research revenue of $1.1 million and payments earned under license revenue of $0.4 million.

Research and Development Expenses. Research and development expenses were $21.5 million for the year ended December 31, 2005, compared with $16.7 million for the year ended December 31, 2004. The $4.8 million increase was mainly due to increased spending of $1.3 million in payroll and related benefits as a result of a higher average number of employees in 2005, a $1.1 million increase in pre-clinical development expense for MB07803, increased research and development services expense of $1.1 million, increased occupancy costs related to our new facility of $0.7 million and increased travel, supplies and insurance expense of $0.6 million.

General and Administrative Expenses. General and administrative expenses were $5.3 million for the year ended December 31, 2005, compared with $3.8 million for the year ended December 31, 2004. The $1.5 million increase reflected mainly an increase in professional services expense of $0.4 million, higher payroll and related benefits costs

of $0.5 million as a result of a higher average number of employees in 2005, an increase in corporate promotion expense of $0.3 million, and increased travel, occupancy and public company costs of $0.3 million.

Amortization of Employee Stock-based Compensation. In connection with the grant of stock options to employees and directors, we recorded amortization of deferred stock-based compensation of approximately $1.7 and $1.6 million for the years ended December 31, 2005 and 2004, respectively. As of December 31, 2005, we had approximately $2.9 million of deferred stock-based compensation. Prior to the adoption of SFAS 123(R) in 2006, deferred compensation is presented as a separate component of stockholders equity.

In 2003, our board of directors authorized a transaction, effective June 30, 2003, calling for three of our executive officers to agree to tender 487,702 shares of their previously vested common stock and subject them to a new monthly vesting schedule over a four-year period commencing on June 30, 2003. This transaction was entered into as repayment for outstanding principal and accrued interest on loans we made to those executive officers in connection with their purchase of our common

stock in June 1999. We recorded $711,000 of deferred compensation at June 30, 2003, to be amortized over the four-year vesting period of the underlying common stock. We recorded amortization of deferred compensation of approximately $178,000 and $178,000 for the years ended December 31, 2005 and 2004, respectively. Prior to the adoption of SFAS 123(R) in 2006, deferred compensation is presented as a separate component of stockholders equity.

Other Income, Net. Net interest income was $1.1 million for the year ended December 31, 2005, compared to net interest income of $0.3 million for the year ended December 31, 2004. The $0.8 million net increase was mainly due to higher levels of invested cash in 2005 resulting from the proceeds of our private placement in October 2005 as well as higher investment yields.

Comparison of the Years Ended December 31, 2004 and 2003

Revenues were $6.8 million for the year ended December 31, 2004, compared with $9.1 million for the year ended December 31, 2003. The $2.3 million decrease was mainly due to a decline in license fee revenue of approximately $7.2 million which was attributable to a one-time payment associated with an exclusive option agreement with Daiichi Sankyo that expired in 2003. This decrease was partially offset by higher milestone revenue in 2004, which included $3.5 million earned under our collaboration agreement with Daiichi Sankyo. Additionally, we realized a $1.4 million increase in sponsored research resulting from the initiation in 2004 of the research portion of our collaboration agreement with Merck.

Research and Development Expenses. Research and development expenses were $16.7 million for the year ended December 31, 2004, compared with $15.0 million for the year ended December 31, 2003. The $1.7 million increase was mainly due to increased spending of $0.7 in payroll and related benefits as a result of a higher average number of employees in 2004, a $0.6 million increase in pre-clinical development expense for MB07803 and a $0.4 million increase in clinical trials expenses related to MB07133.

General and Administrative Expenses. General and administrative expenses were $3.8 million for the year ended December 31, 2004, compared with $3.0 million for the year ended December 31, 2003. The $0.8 million increase reflected mainly an increase in professional services expense of $0.4 million and higher payroll and related benefits costs of $0.4 million as a result of a higher average number of employees in 2004.

Amortization of Employee Stock-based Compensation. In connection with the grant of stock options to employees and directors, we recorded amortization of deferred stock-based compensation of approximately $1.6 million and $0.5 million for the years ended December 31, 2004 and 2003, respectively. As of December 31, 2004, we had approximately $4.9 million of deferred stock-based compensation.

Other Income, Net. Net interest income was $303,000 for the year ended December 31, 2004, compared to net interest expense of $46,000 for the year ended December 31, 2003. The $349,000 net increase was mainly due to higher

invested cash resulting from the proceeds of our initial public offering in June 2004.

Liquidity and Capital Resources

In October 2005, we raised approximately $41.3 million in a private placement of common stock and the concurrent issuance of warrants for the purchase of common stock. Placement agent fees and other offering expenses were approximately $2.3 million. Under the terms of the financing, we sold 7.0 million shares of common stock at $5.86 per share, the closing bid price for our common stock immediately preceding the entering into of the binding agreement for the transaction. We also issued warrants to purchase approximately 2.5 million shares of our common stock at an exercise price of $6.74 per share. At the closing, investors in the financing paid an additional purchase price equal to $0.125 per each share issuable upon exercise of the warrants.

On June 21, 2004, we completed an initial closing of our initial public offering in which we sold 5.0 million shares of common stock for proceeds of $30.6 million, net of underwriting discounts and commissions and offering expenses. In addition, on July 20, 2004, we completed an additional closing of our initial public offering in which we sold an additional 75,000 shares of common stock pursuant to the exercise by the underwriters of an over-allotment option which resulted in proceeds of $0.5 million, net of underwriting discounts and commissions.

As of December 31, 2005, we have financed through leases and loans the purchase of equipment and leasehold improvements totaling approximately $4.7 million, of which $3.2 million was outstanding at that date. The loans are collateralized with the purchased equipment, bear interest at rates ranging from approximately 8.0% to 12.85%, and are due in monthly installments through October 2015. Additionally, we have received cumulative SBIR grant funding of approximately $1.4 million through December 31, 2005.

As of December 31, 2005, we had $66.9 million in cash and cash equivalents and securities available-for-sale as compared to $43.9 million as of December 31, 2004, an increase of $23.0 million. The increase mainly reflected net proceeds of $39.0 million raised from our private placement in October 2005 and a $5.0 million non-refundable license payment under our AMPK collaboration with Merck which was offset by net cash used in operations of $14.0 million and net cash used in investing activities of $4.6 million for the year ended December 31, 2005 resulting from net purchases of investments of $1.4 million and $3.2 million of equipment purchases.

The following summarizes our long-term contractual obligations as of December 31, 2005 (in thousands):

		Payments Due by Period			
Contractual Obligations	**Total**	**Less than 1 Year**	**1 to 3 Years**	**4 to 5 Years**	**After 5 Years**
Operating leases	$ 27,759	$ 1,554	$ 4,065	$ 5,868	$ 16,272
Capital leases	91	25	50	16	
Equipment financing	3,652	1,285	1,717	439	211
Total	$ 31,502	$ 2,864	$ 5,832	$ 6,323	$ 16,483

We also enter into agreements with clinical sites and contract research organizations for the conduct of our clinical trials. We will make payments to these sites and organizations based upon the number of patients enrolled and the length of their participation in the clinical trials. At this time, due to the variability associated with these agreements, we are unable to estimate with certainty the future patient enrollment costs we will incur.

Our future capital uses and requirements depend on numerous forward-looking factors. These factors may include but are not limited to the following:

- the rate of progress and cost of our clinical trials and other research and development activities,
- the scope, prioritization and number of clinical development and research programs we pursue,
- the costs of expanding our operations,
- the terms and timing of any collaborative, licensing and other arrangements that we may establish,

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

the costs and timing of regulatory approvals,

the costs of establishing or contracting for manufacturing, sales and marketing capabilities,

the effect of competing technological and market developments, and

the extent to which we acquire or in-license new products, technologies or businesses.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to meet our projected operating requirements through at least the next twelve months.

Until we can generate significant continuing revenues, we expect to continue to satisfy our future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements, as well as through government grants and interest earned on cash balances. For example, we have an effective shelf registration statement on file with the SEC which allows us to issue shares of our common stock and warrants to purchase our common stock for an

aggregate initial offering price of up to $75 million. We may sell any of these securities from time to time in one or more offerings in amounts, at prices and on terms that we will determine at the time of the offering.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders ownership will be diluted. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing, specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. In addition, if we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us.

We cannot be sure that our existing cash, cash equivalents and short-term investment resources will be adequate or that additional financing will be available when needed or that, if available, financing will be obtained on terms favorable to us or our stockholders. Having insufficient funds may require us to delay, scale back or eliminate some or all of our research or development programs or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Failure to obtain adequate financing also may adversely affect our ability to operate as a going concern.

Off-Balance Sheet Arrangements

As of December 31, 2005, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. In addition, we do not engage in trading activities involving non-exchange traded contracts. As such, we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

Related Party Transactions

For a description of our related party transactions, see Item 13 of Part III of this Form 10-K, Certain Relationships and Related Transactions.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because the majority of our investments are in short-term marketable securities. Due to the nature of our short-term investments, we believe that we are not subject to any material market risk exposure. We do not have any foreign currency or other derivative financial instruments.

Our long-term capital lease obligations bears interest at fixed rates and therefore we do not have significant market risk exposure with respect to these obligations.

Item 8. Financial Statements and Supplementary Data

The information required to be disclosed herein is incorporated by reference to Item 15 of Part III of this Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosures

Not applicable.

Item 9A. Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission s rules and forms and that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control

objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Securities and Exchange Commission Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this report. Based on the foregoing, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

There was no change in our internal control over financial reporting during the fourth fiscal quarter of the period covered by this report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On March 19, 2006, the compensation committee of our board of directors approved increases in base salary and the grant of additional stock options for certain of our executive officers. The following table sets forth the 2006 base salary and the number of shares of common stock underlying the stock option grants for these executive officers:

Name	2006 Base Salary	Stock Options
Paul K. Laikind, Ph.D.	$ 361,000	125,000
Mark D. Erion , Ph.D.	$ 305,000	75,000
John W. Beck, C.P.A.	$ 243,000	50,000
Edgardo Baracchini, Ph.D., M.B.A.	$ 251,000	37,300

The stock options described above (i) were granted pursuant to our Amended and Restated 2001 Equity Incentive Plan, (ii) terminate ten years after March 19, 2006, the date of grant, or earlier in the event the optionholder s service to us is terminated and (iii) have an exercise price per share of $9.03, or the closing price of our common stock as reported on the Nasdaq National Market for Friday, March 17, 2006. Subject to the optionholder s continued service to us, 25% of the shares of common stock subject to such stock options vest on the first anniversary of the date of grant, and the remaining shares vest monthly over the following three years.

Also on March 19, 2006, the compensation committee reviewed our achievement of the corporate and individual goals set for 2005 and based on that review, the compensation committee approved 2005 incentive cash bonuses to certain of our executive officers as follows:

Name	2005 Bonus
Paul K. Laikind, Ph.D.	$ 99,015
Mark D. Erion , Ph.D.	$ 71,885
John W. Beck, C.P.A.	$ 57,658
Edgardo Baracchini, Ph.D., M.B.A.	$ 58,284

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PART III

Item 10. Directors and Executive Officers of the Registrant

The information required by this item will be set forth in the sections entitled Election of Directors , Code of Business Conduct and Ethics , Executive Officers and Section 16(a) Beneficial Ownership Reporting Compliance in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with the Annual Meeting of our Stockholders (the Proxy Statement), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2005, and is incorporated in this report by reference.

Item 11. Executive Compensation

The information required by this item will be set forth in the section entitled Compensation of Executive Officers in the Proxy Statement and is incorporated in this report by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in the sections entitled Security Ownership of Certain Beneficial Owners and Management and Equity Compensation Plan Information in the Proxy Statement and is incorporated in this report by reference.

Item 13. Certain Relationships and Related Transactions

The information required by this item will be set forth in the section entitled Certain Relationships and Related Transactions in the Proxy Statement and is incorporated in this report by reference.

Item 14. Principal Accountant Fees and Services

The information required by this item will be set forth in the section entitled Ratification of Selection of Independent Registered Public Accounting Firm in the Proxy Statement and is incorporated in this report by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this report:

1) The following financial statements of Metabasis Therapeutics, Inc. are included in this report beginning on page F-1 hereto:

Report of Independent Registered Public Accounting Firm

Balance sheets as of December 31, 2005 and 2004

Statements of operations for the years ended December 31, 2005, 2004 and 2003

Statements of stockholders equity for the years ended December 31, 2005, 2004 and 2003

Statements of cash flows for the years ended December 31, 2005, 2004 and 2003

Notes to financial statements

2) List of financial statement schedules. All financial statement schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3) List of exhibits required by Item 601 of Regulation S-K. See part (b) below.

(b) Exhibits. The following exhibits are filed as a part of this report:

Exhibit Number		Description
2.1(1)		Asset and Liability Transfer Agreement dated December 17, 1997 between the Company and Gensia Sicor Inc.
2.2(1)		Master Agreement dated June 30, 1999 among the Company, Sicor Inc., Paul K. Laikind, Mark D. Erion and John W. Beck.

3.1(1)		Amended and Restated Certificate of Incorporation of the Company.
3.2(1)		Amended and Restated Bylaws of the Company.
4.1(1)		Form of Common Stock Certificate.
4.2(1)		Stock Purchase Warrant dated February 6, 2001 issued to GATX Ventures, Inc.
4.3(1)		Warrant to Purchase 26,000 Shares of Series C Preferred Stock dated February 6, 2001 issued to GATX Ventures, Inc., as amended July 26, 2001.
4.4(1)		Warrant to Purchase 19,000 Shares of Series C Preferred Stock dated July 26, 2001, issued to GATX Ventures, Inc.
4.5(1)		Warrant to Purchase 30,666 Shares of Series D Preferred Stock dated April 8, 2002, issued to GATX Ventures, Inc.
4.6(1)		Form of Stock Purchase Warrant issued to participants in the Company s Series C Preferred Stock financing dated July 18, 2000.
4.7(1)		Form of Stock Purchase Warrant issued to participants in the Company s Series D Preferred Stock financing dated October 18, 2001.
4.8(1)		Form of letter agreement entered into between the Company and its warrantholders.
4.9(1)		Letter agreement dated October 18, 2001 entered into between the Company and Sprout Capital IX, L.P. and its affiliates.
4.10(1)		Series E Preferred Stock Purchase Agreement dated October 28, 2003 between the Company and certain of its stockholders.
4.11(1)		Amended and Restated Investors Rights Agreement dated October 28, 2003 between the Company and certain of its stockholders.

Exhibit Number		Description
4.12(6)		Securities Purchase Agreement dated September 30, 2005, by and among the Company. and the individuals and entities identified on Exhibit A thereto (the ***Securities Purchase Agreement***).
4.13(6)		Form of Warrant issued pursuant to the Securities Purchase Agreement.
10.1(1)+		Form of Indemnity Agreement.
10.2(1)+		Amended and Restated 2001 Equity Incentive Plan and Form of Stock Option Agreement thereunder.
10.3(1)+		2004 Non-Employee Directors Stock Option Plan and Form of Stock Option Agreement thereunder.
10.4(1)+		2004 Employee Stock Purchase Plan and Form of Offering Document thereunder.
10.5(1)+		Employment offer letter dated March 17, 1998 between the Company and John W. Beck.
10.6(1)+		Employment offer letter dated March 31, 2002 between the Company and Edgardo Baracchini.
10.8(1)+		Stock Restriction Agreement dated June 30, 2003 between the Company and Paul K. Laikind.
10.9(1)+		Stock Restriction Agreement dated June 30, 2003 between the Company and Mark D. Erion.
10.10(1)+		Stock Restriction Agreement dated June 30, 2003 between the Company and John W. Beck.
10.11(1)+		Severance Agreement dated April 3, 2002 between the Company and Edgardo Baracchini.
10.12(1)+		Severance Agreement dated June 30, 2003 between the Company and Paul K. Laikind.
10.13(1)+		Severance Agreement dated June 30, 2003 between the Company and Mark D. Erion.
10.14(1)+		Severance Agreement dated June 30, 2003 between the Company and John W. Beck.
10.15(1)		License Agreement dated June 30, 1999 between the Company and Sicor Inc.
10.17(1)*		Amended and Restated Collaborative Research and Development and License Agreement dated June 30, 1999 between the Company and Daiichi Sankyo Company, Ltd., as amended February 9, 2000 and March 22, 2001.
10.18(1)*		Exclusive Option Agreement dated October 21, 2002 between the Company and Daiichi Sankyo Company, Ltd.
10.19(2)		Development and License Agreement dated October 1, 2001 between the Company and Valeant Pharmaceuticals International.
10.20(1)		Letter agreement dated March 8, 2002 among the Company, Valeant Pharmaceuticals International and Ribapharm Inc.
10.21(1)		Equipment Loan and Security Agreement dated February 6, 2001 between the Company and GATX Ventures, Inc., as amended July 26, 2001 and April 8, 2002.
10.22(1)		Master Security Agreement dated August 27, 2003 between the Company and Oxford Finance Corporation.
10.23(1)*		

		Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.26(3)		Lease Agreement dated December 21, 2004 between the Company and CarrAmerica Realty, L.P.
10.27(4)*		Amendment dated January 21, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.28(5)*		License and Collaboration Agreement dated June 22, 2005 between the Company and Merck & Co., Inc.
10.29 ^		Amendment dated August 29, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.30 ^		Amendment dated November 2, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
21.1(1)		Subsidiaries of the Company.
23.1		Consent of Independent Registered Public Accounting Firm.
31.1		Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

Exhibit Number		Description
31.2		Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32		Certifications of Chief Executive Officer and Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

+ Indicates management contract or compensatory plan.

* Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

^ Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

(1) Incorporated by reference to the exhibit of the same number to the Company s Registration Statement on Form S-1 (No. 333-112437), originally filed on February 3, 2004.

(2) Incorporated by reference to Exhibit 10.18 to the Registration Statement on Form S-1 (No. 333-39350), originally filed on June 15, 2000 by Ribapharm Inc., now a wholly-owned subsidiary of Valeant Pharmaceuticals International.

(3) Incorporated by reference to Exhibit 99.1 to the Company s Current Report on Form 8-K filed on December 23, 2004.

(4) Incorporated by reference to Exhibit 10.27 to the Company s Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2005.

(5) Incorporated by reference to Exhibit 10.28 to the Company s Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2005.

(6) Incorporated by reference to the exhibit of the same number to the Company s Current Report on Form 8-K

filed on October 5, 2005.

SIGNATURES

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

METABASIS THERAPEUTICS, INC.

Dated: March 23, 2006

By: /s/ Paul K. Laikind
Paul K. Laikind, Ph.D.
Chief Executive Officer and President

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.

Signature	Title	Date
/s/ Paul K. Laikind	Chairman of the Board, Chief Executive Officer,	March 23, 2006
Paul K. Laikind, Ph.D.	President and Secretary (Principal Executive	
	Officer)	
/s/ John W. Beck	Senior Vice President of Finance, Chief Financial	March 23, 2006
John W. Beck, C.P.A.	Officer and Treasurer (Principal Financial and	
	Accounting Officer)	
/s/ Daniel D. Burgess	Director	March 23, 2006
Daniel D. Burgess, M.B.A.		
/s/ Mark D. Erion	Executive Vice President of Research and	March 23, 2006
Mark D. Erion, Ph.D.	Development, Chief Scientific Officer and	
	Director	
/s/ Luke B. Evnin	Director	March 23, 2006
Luke B. Evnin, Ph.D.		
/s/ David F. Hale	Director	March 23, 2006
David F. Hale		
/s/ Arnold L. Oronsky	Director	March 23, 2006
Arnold L. Oronsky, Ph.D.		
/s/ William R. Rohn	Director	March 23, 2006
William R. Rohn		

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METABASIS THERAPEUTICS, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of

Metabasis Therapeutics, Inc.

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

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. 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 Metabasis Therapeutics, Inc. at December 31, 2005 and 2004 and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

San Diego, California
February 16, 2006

METABASIS THERAPEUTICS, INC.

BALANCE SHEETS

(in thousands, except par value data)

	December 31,	
	2005	**2004**
Assets		
Current assets:		
Cash and cash equivalents	$ 32,597	$ 10,921
Securities available-for-sale	34,296	32,934
Accounts receivable	928	525
Other current assets	1,241	1,126
Total current assets	69,062	45,506
Property and equipment, net	4,664	2,354
Other assets	152	
Total assets	$ 73,878	$ 47,860
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 1,745	$ 864
Accrued liabilities	4,392	2,835
Deferred rent		67
Deferred revenue, current portion	2,192	
Current portion of capital lease obligations, net of discount	1,042	834
Total current liabilities	9,371	4,600
Deferred revenue, net of current portion	2,463	
Deferred rent	330	
Other long-term liabilities	6	4
Capital lease obligations, net of current portion and discount	2,126	1,392
Stockholders equity:		
Preferred stock, $0.001 par value; 5,000 shares authorized at December 31, 2005 and December 31, 2004, no shares issued or outstanding		
Common stock, $.001 par value; 100,000 shares authorized at December 31, 2005 and December 31, 2004; 25,313 and 18,169 shares issued and outstanding at December 31, 2005 and December 31, 2004, respectively	25	18
Additional paid-in capital	137,822	98,602
Deferred compensation	(3,266)	(5,337)
Accumulated deficit	(74,945)	(51,365)
Accumulated other comprehensive loss	(54)	(54)
Total stockholders equity	59,582	41,864
Total liabilities and stockholders equity	$ 73,878	$ 47,860

See accompanying notes.

METABASIS THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS

(in thousands, except per share data)

	Years Ended December 31,		
	2005	2004	2003
Revenues:			
Sponsored research	$ 2,493	$ 1,375	$
Milestones		4,500	1,000
License fees	871	458	7,631
Other revenue	407	504	493
Total revenues	3,771	6,837	9,124
Operating expenses:			
Research and development	21,460	16,675	15,048
General and administrative	5,283	3,804	2,955
Amortization of employee stock-based compensation	1,695	1,633	504
Total operating expenses	28,438	22,112	18,507
Loss from operations	(24,667)	(15,275)	(9,383)
Other income (expense):			
Interest income	1,297	531	177
Interest expense	(210)	(228)	(226)
Other, net			3
Total other income (expense)	1,087	303	(46)
Net loss	(23,580)	(14,972)	(9,429)
Deemed dividend-beneficial conversion feature for Series E preferred stock			(24,900)
Net loss applicable to common stockholders	$ (23,580)	$ (14,972)	$ (34,329)
Basic and diluted net loss per share (1)	$ (1.20)	$ (1.49)	$ (23.84)
Shares used to compute basic and diluted net loss per share (1)	19,706	10,034	1,440
The composition of employee stock-based compensation is as follows:			
Research and development	$ 1,170	$ 1,138	$ 358
General and administrative	525	495	146
	$ 1,695	$ 1,633	$ 504

(1) As a result of the conversion of our preferred stock into 11.0 million shares of our common stock upon completion of our initial public offering on June 21, 2004, there is a lack of comparability in the basic and diluted net loss per share amounts between the year ended December 31, 2003 and the subsequent periods presented above. Please reference Note 1 for an unaudited pro forma basic and diluted net loss per share calculation for the periods presented.

See accompanying notes.

METABASIS THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS EQUITY

(in thousands)

	Convertible Preferred Stock		Common Stock		Additional Paid-In	Deferred	Notes Receivable From	Accumulated	Accumulated Other Comprehensive	Total Stockholders
	Shares	Amount	Shares	Amount	Capital	Compensation	Stockholders	Deficit	Income (Loss)	Equity
Balance at December 31, 2002	39,600	40	1,706	2	36,340	(238)	(425)	(26,964)	1	8,756
Net loss								(9,429)		(9,429)
Unrealized loss on short-term investments									(7)	(7)
Net comprehensive loss										(9,436)
Issuance of common stock for option exercises			67		45					45
Issuance of Series E preferred stock, net of offering costs of approximately $1,137	24,032	24			23,739					23,763
Beneficial conversion feature for Series E preferred stock					24,900					24,900
Deemed dividend for Series E convertible preferred stock					(24,900)					(24,900)
Deferred employee stock-based compensation					5,209	(5,209)				
Adjustment to deferred compensation for cancellation of options					(80)	80				
Amortization of deferred employee stock-based compensation						504				504
Shares tendered in exchange for notes receivable from stockholders							425			425
Issuance of stock options for services					2					2
Deferred compensation from tendered shares subject to vesting						(711)				(711)
Amortization of deferred compensation from tendered shares subject to vesting						89				89

Balance at December 31, 2003	63,632	64	1,773	2	65,255	(5,485)		(36,393)	(6)	23,437
Net loss								(14,972)		(14,972)
Unrealized loss on short-term investments									(48)	(48)
Net comprehensive loss										(15,020)
Issuance of common stock in initial public offering and follow-on offering, net of offering costs of $1,894			5,075	5	31,139					31,144
Conversion of convertible preferred stock into common stock	(63,632)	(64)	11,036	11	53					
Issuance of common stock for option exercises			255		314					314
Issuance of common stock pursuant to the Employee Stock Purchase Plan			30		178					178
Deferred employee stock-based compensation					1,705	(1,705)				
Adjustment to deferred compensation for cancellation of options					(42)	42				
Amortization of deferred employee stock-based compensation						1,633				1,633
Amortization of deferred compensation from tendered shares subject to vesting						178				178
Balance at December 31, 2004			18,169	18	98,602	(5,337)		(51,365)	(54)	41,864
Net loss								(23,580)		(23,580)
Unrealized loss on short-term investments										
Net comprehensive loss										(23,580)
Issuance of common stock in private placement offering net of offering costs of $2,280			7,000	7	39,039					39,046
Issuance of common stock for option exercises			40		54					54
Issuance of stock options for services					65					65
Issuance of common stock pursuant to the Employee Stock Purchase Plan			104		280					280
Repurchase unvested common stock					(20)					(20)

Adjustment to deferred compensation for cancellation of options					(198)	198				
Amortization of deferred employee stock-based compensation						1,695				1,695
Amortization of deferred compensation from tendered shares subject to vesting						178				178
Balance at December 31, 2005		$	25,313	$ 25	$ 137,822	$ (3,266)	$	$ (74,945)	$ (54)	$ 59,582

See accompanying notes.

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METABASIS THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS

(in thousands)

	Years ended December 31,		
	2005	**2004**	**2003**
Operating activities			
Net loss	$ (23,580)	$ (14,972)	$ (9,429)
Adjustments to reconcile net loss to net cash used in operating activities:			
Amortization of deferred employee stock-based compensation	1,695	1,633	504
Amortization of deferred compensation on tendered shares	178	178	89
Deferred rent	263	(55)	(10)
Depreciation and amortization	910	699	564
Amortization of discount on equipment loan	5	15	15
Stock options issued for services	65		2
Change in operating assets and liabilities:			
Accounts receivable	(403)	432	(778)
Other current assets	(115)	(660)	(205)
Other assets	(152)	199	50
Deferred revenue	4,655	(458)	(7,175)
Accounts payable	881	97	6
Accrued liabilities and other long-term liabilities	1,559	333	638
Net cash flows used in operating activities	(14,039)	(12,559)	(15,729)
Investing activities			
Purchases of securities available-for-sale	(36,795)	(40,327)	(15,215)
Sales/maturities of securities available-for-sale	35,433	21,585	8,450
Purchases of property and equipment	(3,220)	(1,326)	(898)
Net cash flows used in investing activities	(4,582)	(20,068)	(7,663)
Financing activities			
Issuance of preferred stock, net			23,763
Issuance of common stock, net	39,380	32,140	45
Payments under capital lease obligations	(870)	(788)	(413)
Repurchase unvested common stock	(20)		
Payments on notes payable			(1,500)
Proceeds from capital lease obligations	1,807	1,179	864
Prepaid offering costs			(430)
Net cash flows provided by financing activities	40,297	32,531	22,329
Increase (decrease) in cash and cash equivalents	21,676	(96)	(1,063)
Cash and cash equivalents at beginning of year	10,921	11,017	12,080
Cash and cash equivalents at end of period	$ 32,597	$ 10,921	$ 11,017
Supplemental disclosure of cash flow information:			
Interest paid	$ 205	$ 214	$ 232
Supplemental schedule of noncash investing and financing activities:			
Shares tendered from stockholders for repayment of the principal and accrued interest of stockholder loans	$	$	$ 514
Conversion of convertible preferred stock to common stock upon initial public offering	$	$ 64	$
Deemed beneficial conversion feature for Series E preferred stock	$	$	$ 24,900

See accompanying notes.

METABASIS THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

Organization and Business

Metabasis Therapeutics, Inc. (Metabasis or the Company) is a biopharmaceutical company focused on the discovery, development and commercialization of novel drugs to address some of the world s most widespread and costly chronic diseases involving pathways in the liver.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements. Estimates also affect the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and highly liquid instruments with original maturities of three months or less when purchased.

Securities Available-For-Sale

Short-term investments are classified as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders equity. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income. The cost of securities sold is based on the specific-identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

Fair Value of Financial Instruments

The carrying amount of cash and cash equivalents, securities available-for-sale, accounts receivable, accounts payable and accrued liabilities are considered to be representative of their respective fair values because of the short-term nature of those instruments. Based on the borrowing rates currently available to the Company for loans with similar terms, management believes the fair value of the long-term obligations approximate their carrying value.

Concentration of Credit Risks and Major Partners

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist primarily of cash and cash equivalents and securities available-for-sale. The Company invests its excess cash in U.S. government securities, asset backed securities and debt instruments of financial institutions and corporations with strong credit ratings. The Company has established guidelines relative to diversification of its cash investments and their maturities that are intended to secure safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates and changes in the Company s operations and financial position. To date, the Company has not experienced any impairment losses on its cash equivalents or securities available-for-sale.

One collaborative partner individually accounted for 90% of total revenues during the year ended December 31, 2005, and a different collaborative partner individually accounted for 51% and 83% of total revenues during the years ended December 31, 2004 and 2003 (see Note 5).

Property and Equipment

Property and equipment is carried at cost less accumulated depreciation. Depreciation is computed on the straight-line method and depending on asset classification, over a period of three to five years. Leasehold improvements are amortized over the estimated useful life of the asset or the lease term, whichever is shorter.

Impairment of Long-Lived Assets

The Company assesses potential impairments to its long-lived and intangible assets in accordance with Statement of Financial Accounting Standards (SFAS) No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. There have been no indicators of impairment through December 31, 2005.

Revenue Recognition

The Company s revenue recognition policies are in accordance with the Securities and Exchange Commission Staff Accounting Bulletin (SAB) 104, *Revenue Recognition,* and Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables*. Many of the Company s revenues are primarily related to collaborations with pharmaceutical companies. The Company s agreements generally contain multiple elements, including sponsored research funding, future milestone payments and royalties. All fees are nonrefundable.

Upfront, nonrefundable fees under the Company s collaborations and advance payments for sponsored research, which are in excess of amounts earned are classified as deferred revenue and are recognized as income over the period the related services are provided. Nonrefundable upfront fees, which do not require the Company s continuing involvement, or which do not contain future performance obligations, are recognized when received.

Amounts received for sponsored research funding are recognized as revenues as the services are performed. These agreements are on a best-efforts basis and do not require scientific achievement as a performance obligation and provide for payment to be made when costs are incurred or the services are performed.

Revenue from milestones is recognized 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) collaborator funding (if any) of the Company s performance obligations after the milestone achievement will continue at a level comparable to before the milestone achievement. If both of these criteria are not met, the milestone payment is recognized as revenue over the remaining minimum period of the Company s performance obligations under the agreement.

Research and Development

All costs of research and development, including those incurred in relation to the Company s collaborative agreements, are expensed in the period incurred. Research and development costs primarily consist of salaries and related expenses for personnel, outside service providers, fees paid to consultants and materials used in clinical trials and research and development. The Company reviews and accrues clinical trials expenses based on work performed, which relies on estimates of total costs incurred based on completion of patient studies and other events. The Company follows this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical development costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

Comprehensive Loss

SFAS No. 130, *Reporting Comprehensive Income*, requires that all components of comprehensive loss, including net loss, be reported in the financial statements in the period in which they are recognized. Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from nonowner sources. The Company s other comprehensive loss for December 31, 2005, 2004 and 2003 consisted of unrealized gains and losses on available-for-sale securities and is reported in stockholders equity.

Stock-Based Compensation

The Company has elected to follow Accounting Principles Board Opinion No. 25 (APB 25), *Accounting for Stock Issued to Employees*, and related interpretations in accounting for its employee and director stock options. Under APB 25, if the exercise price of the Company s employee and director stock options equals or exceeds the estimated fair value of the underlying stock on the date of grant, no compensation expense is recognized. In conjunction with the Company s initial public offering completed in June 2004, the Company reviewed its historical exercise prices through June 15, 2004 and, as a result, revised the estimate of fair value for the stock underlying all stock options granted subsequent to June 30, 2002. The weighted average exercise price for the 930,000 options granted to the Company s employees and directors during July 2002 through June 15, 2004 was $1.46. With respect to employee and director options granted, the Company has deferred stock compensation balances of $2.9 million and $4.9 million at December 31, 2005 and 2004, respectively, for the difference between the original exercise price per share determined by the Board of Directors and the revised estimate of fair value per share at the respective grant dates. Deferred stock compensation is recognized and amortized on a straight-line basis over the vesting period of the related options, generally four years. Compensation expense related to stock options granted to the Company s employees and directors was approximately $1.7 million, $1.6 million, and $0.5 million for the twelve months ended December 31, 2005, 2004 and 2003, respectively. SFAS No. 123R is discussed in *Recent Accounting Pronouncements*.

Options or stock awards issued to nonemployees have been valued in accordance with SFAS No. 123, *Accounting for Stock-Based Compensation*, and EITF Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other than Employees for Acquiring, or in Conjunction with Selling Goods or Services*, and expensed over the period the services are provided. Deferred charges for options granted to non-employees are periodically remeasured as the options vest. The Company granted stock options and stock awards to non-employees as follows: 72,832, 987 and 0 for the years ended December 31, 2005, 2004 and 2003, respectively. Compensation expense related to non-employee stock option grants and stock awards was $65,000, $0 and $0 million for the years ended December 31, 2005, 2004 and 2003, respectively. The options and stock awards were valued using the Black-Scholes option pricing model with the following weighted-average assumptions for the year ended December 31, 2005: (a) risk free interest rate of 3.8%; (b) dividend yield of 0%; (c) expected volatility of 70%; and (d) expected life of five years.

As required under SFAS No. 123, the pro forma effects of stock-based compensation on net loss were estimated at the date of grant using the minimum-value method for all grants made through June 16, 2004, the effective date of the Company s registration statement for its initial public offering, and the Black-Scholes method thereafter. The Company completed its initial public offering on June 21, 2004, and accordingly began using the Black-Scholes valuation model in accordance with SFAS No. 123. The minimum-value method and the Black-Scholes valuation model were developed for use in estimating the fair value of publicly traded options that have no vesting restrictions and are fully transferable. Because the Company s employee and director stock options have characteristics significantly different from those of publicly traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management s opinion, these existing models do not necessarily provide a reliable single measure of the fair value of the Company s employee and director stock options. The fair value of options issued to employees were estimated at the date of grant using the Black-Scholes option valuation model or the minimum-value method, as described above, with the following weighted average assumptions for the years ended December 31, 2005, 2004 and 2003: (a) risk-free interest rates of 4.2%, 3.5% and 3.1%; (b) expected dividend yield of 0% for all periods; (c) volatility factor of 70% for all periods; and (d) five-year estimated life of the options for all periods. The estimated weighted average fair value of stock options granted during 2005 and 2004 was $2.38, $6.32 and $9.34 respectively.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the vesting period of such stock options. The Company s pro forma information is as follows:

	Years Ended December 31,		
	2005	2004	2003
	(in thousands, except per share amounts)		
Net loss applicable to common stockholders as reported	$ (23,580)	$ (14,972)	$ (34,329)
Add: Stock-based employee compensation expense included in reported net loss	1,695	1,633	504
Deduct: Stock-based employee compensation expense determined under fair value method	(2,459)	(1,802)	(537)
Pro forma net loss applicable to common stockholders	$ (24,344)	$ (15,141)	$ (34,362)
Basic and diluted net loss per share as reported	$ (1.20)	$ (1.49)	$ (23.84)
Pro forma basic and diluted net loss per share	$ (1.24)	$ (1.51)	$ (23.86)

Net Loss Per Share

The Company calculated net loss per share in accordance with SFAS No. 128, *Earnings Per Share*. Basic earnings per share (EPS) is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted EPS is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, common stock subject to repurchase by the Company, options, and warrants are considered to be common stock equivalents and are only included in the calculation of diluted earnings per share when their effect is dilutive.

The actual net loss per share amounts for the years ended December 31, 2005 and 2004 were computed based on the shares of common stock outstanding during these years. The number of common shares outstanding for the year ended December 31, 2004 includes 11.0 million shares of the Company s common stock issued upon conversion of the Company s preferred stock in conjunction with the initial public offering. As a result of the conversion, there is a lack of comparability in the basic and diluted net loss per share amounts between the year ended December 31, 2003 and subsequent periods presented. In order to provide a more relevant measure of operating results, the following unaudited pro forma net loss per share calculation has been included. The shares used to compute unaudited pro forma basic and diluted net loss per share represent the weighted average common shares outstanding for the period, reduced by the weighted average unvested common shares subject to repurchase, and including the assumed conversion of all outstanding shares of preferred stock into shares of common stock using the as-if converted method as of the beginning of each year presented or the date of issuance, if later.

	Years Ended December 31,		
	2005	2004	2003
	(in thousands, except per share amounts)		
Actual:			
Numerator:			
Net loss	$ (23,580)	$ (14,972)	$ (9,429)
Deemed dividend-beneficial conversion feature for Series E preferred stock			(24,900)
Net loss applicable to common stockholders	$ (23,580)	$ (14,972)	$ (34,329)
Denominator:			
Weighted average common shares	19,981	10,452	1,731
Weighted average unvested common shares subject to repurchase	(275)	(418)	(291)
Denominator for basic and diluted net loss per share	19,706	10,034	1,440
Basic and diluted net loss per share	$ (1.20)	$ (1.49)	$ (23.84)
Pro forma:			
Numerator:			
Pro forma net loss	$ (23,580)	$ (14,972)	$ (34,329)
Denominator:			
Shares used above	19,706	10,034	1,440
Pro forma adjustments to reflect assumed weighted average effect of conversion of preferred stock		5,220	7,747
Pro forma shares used to compute basic net loss per share	19,706	15,254	9,187
Pro forma basic and diluted net loss per share	$ (1.20)	$ (0.98)	$ (3.74)
Historical outstanding antidilutive securities not included in diluted net loss per share calculation*:			
Preferred stock			63,632
Common stock subject to repurchase	207	459	437
Options to purchase common stock	1,406	1,108	951
Warrants	3,797	1,347	8,016
	5,410	2,914	73,036

* Represents the historical amount of the securities and not the common stock equivalent number of shares.

Recent Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board (FASB) issued SFAS No. 123R, *Share Based Payment*. This statement is a revision to SFAS No. 123 and supersedes APB 25 and amends FASB Statement No. 95, *Statement of Cash Flows*. This statement requires a public entity to expense the cost of employee services received in exchange for an award of equity instruments. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements of these equity arrangements. This statement is effective for the Company in the first quarter of 2006.

SFAS No. 123R permits public companies to choose between the following two adoption methods:

1. A modified prospective method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date, or

2. A modified retrospective method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

As permitted by SFAS No. 123, the Company currently accounts for share-based payments to employees using APB 25 s intrinsic value method and, as such, the Company generally recognizes no compensation cost for employee stock options.

The impact of the adoption of SFAS No. 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, valuation of employee stock options under SFAS No. 123R is similar to SFAS No. 123, with minor exceptions. The impact on the results of operations and earnings per share had the Company adopted SFAS No. 123, is described in stock based compensation section of Note 1 above. Accordingly, the adoption of SFAS No. 123R s fair value method will have a significant impact on the Company s results of operations, although it will have no impact on the Company s overall financial position. SFAS No. 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under current literature. This requirement will reduce net operating cash flows and increase net financing cash flows in periods after adoption.

In March 2004, the EITF reached a final consensus on Issue 03-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. EITF Issue No. 03-1 requires that when the fair value of an investment security is less than its carrying value, an impairment exists for which the determination must be made as to whether the impairment is other-than-temporary. The EITF Issue No. 03-1 impairment model applies to all investment securities accounted for under SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities* and to investment securities accounted for under the cost method to the extent an impairment indicator exists. Under the guidance, the determination of whether an impairment is other-than-temporary and therefore would result in a recognized loss depends on market conditions and management s intent and ability to hold the securities with unrealized losses. In September 2004, the FASB approved FASB Staff Position (FSP) EITF 03-1-1, which defers the effective date for recognition and measurement guidance contained in EITF Issue No. 03-1 until certain issues are resolved. In November 2005, the FASB issued FSP FAS 115-1. FSP FAS 115-1 replaces the impairment evaluation guidance of EITF Issue No. 03-1 with references to the existing other-than-temporary impairment guidance. EITF 03-1 s disclosure requirements remain in effect. The FSP also supersedes EITF Topic No. D-44, *Recognition of Other-Than-Temporary Impairment upon the Planned Sale of a Security Whose Cost Exceeds Fair Value*, and clarifies that an investor should recognize an impairment loss no later than when the impairment is deemed other-than-temporary, even if a decision to sell an impaired security has not been made. The guidance in this FSP will be applied in the Company s first quarter of 2006. The Company does not expect the adoption of EITF Issue No. 03-1 or FSP FAS 115-1 to have a material effect on its liquidity, results of operations and financial condition.

2. Securities Available-For-Sale

Securities available-for-sale consists of the following (in thousands):

	December 31, 2005			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate debt securities	$ 27,845	$	$ (49)	$ 27,796
Asset-backed securities	6,505		(5)	6,500
Total	$ 34,350	$	$ (54)	$ 34,296

	December 31, 2004			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate debt securities	$ 32,988	$	$ (54)	$ 32,934
Total	$ 32,988	$	$ (54)	$ 32,934

Gross realized gains and losses on available-for-sale securities were immaterial during the years ended December 31, 2005 and 2004. All of the available-for-sale securities have a contractual maturity at December 31, 2005 of one year or less.

3. Property and Equipment

Property and equipment consisted of the following (in thousands):

	December 31,	
	2005	2004
Laboratory equipment	$ 7,561	$ 6,420
Computers and electronics	2,322	2,200
Office furniture and fixtures	987	643
Leasehold improvements	943	145
Construction in progress	456	66
	12,269	9,474
Less: accumulated depreciation and amortization	(7,605)	(7,120)
	$ 4,664	$ 2,354

Depreciation and amortization expenses, which include assets held under capital leases, were $910,000, $699,000 and $564,000 for the years ended December 31, 2005, 2004 and 2003, respectively. Assets held under capital leases totaled approximately $4.5 million and $4.0 million at December 31, 2005 and 2004, respectively. The related accumulated amortization was approximately $2.4 million and $2.0 million at December 31, 2005 and 2004, respectively.

4. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2005	2004
Accrued employee benefits	$ 1,207	$ 1,077
Bonus accrual	700	654
Accrued development expenses	1,008	610
Accrued legal and patent fees	613	286
Other accrued liabilities	864	208
	$ 4,392	$ 2,835

5. Collaborative Research and Development Agreements

Valeant

In October 2001, the Company entered into a development and license agreement with Valeant Pharmaceuticals International (Valeant) for the development and commercialization of pradefovir for the treatment of hepatitis type B. Under the agreement, Valeant was granted exclusive

worldwide rights to develop and commercialize pradefovir. Valeant is solely responsible for conducting and funding all development work. The Company will continue to receive certain payments upon Valeant s achievement of specified development, regulatory and commercial milestones and to receive royalties on any product sales that result from the collaboration. As of December 31, 2005, the Company had achieved developmental milestones triggering a total of $2.0 million in payments from Valeant. The first milestone was earned in April 2003 and the second milestone was earned in July 2004. If all development, regulatory and commercial milestones are achieved, and including the $2.0 million license fee received to date under the agreement, the Company may be entitled to payments which total up to $20.0 million, plus royalties.

Daiichi Sankyo

The Company has a research, development and commercialization agreement with Daiichi Sankyo Company, Ltd., (Daiichi Sankyo) to develop novel FBPase inhibitors for the treatment of diabetes. The research period ended in April 2002. Daiichi Sankyo is responsible for funding any clinical development compounds or compounds selected for development under the agreement. The Company will receive certain payments upon the achievement of specified milestones under the development portion of the collaboration. As of December 31, 2005, the Company had achieved three developmental milestones triggering a total of $6.5 million in payments, including $3.5 million received in 2004 from Daiichi

Sankyo. In 2003, the Company recognized $7.6 million related to an option fee as license revenue as Daiichi Sankyo chose not to exercise an option with the Company to negotiate a new agreement for next generation compounds to treat diabetes and therefore, because there were no future performance obligations of the Company, the Company recognized the remaining unamortized option fee. Under the Daiichi Sankyo collaboration agreement, the Company has recognized $0, $3.5 million and $7.6 million in revenues for the years ended December 31, 2005, 2004 and 2003, respectively. If all clinical and regulatory milestones are achieved, and including the $36.0 million in license fees, sponsored research payments and an equity investment received to date under the agreement, the Company may be entitled to payments which total up to $54.5 million.

Assuming a compound is successfully developed and commercialized, the Company would receive royalties on net sales. Daiichi Sankyo will have exclusive, worldwide commercialization rights to those products selected for development and subsequently licensed. The Company would also have co-promotion rights in North America to any commercialized product, on terms to be negotiated.

Merck

In December 2003, the Company entered into a collaboration agreement with Merck to discover new treatments for hepatitis C. Under this collaboration, the Company is creating liver-targeting prodrugs of certain compounds that Merck is supplying to us. These compounds target the hepatitis C virus residing in the liver. The research term of the collaboration was initially for one year and in January 2005, was extended for an additional year through December 2005. At the same time, the scope of the technology that the Company applies to the Merck compounds was expanded. As part of this collaboration, Merck paid an upfront fee of $500,000 which was recognized as revenue over the initial one-year term of the agreement and paid research support total of $2.7 million during 2004 and 2005. Revenue recognized under the agreement was $1.4 million, $1.8 million and $0 for the years ended December 31, 2005, December 31, 2004 and December 31, 2003, respectively. Merck is also obligated to pay pre-clinical and clinical milestone payments if specified development and regulatory events occur and royalties on sales of products resulting from the collaboration. If all pre-clinical and clinical milestones are achieved, and including the $500,000 upfront fee, the $2.7 million in research support and an additional exclusive option, the Company may be entitled to payments which total up to $93.3 million, plus royalties. Merck is solely responsible for conducting and funding all development work for compounds resulting from the collaboration and for commercializing any resulting products.

In June 2005, the Company entered into a second collaboration agreement with Merck to research, develop and commercialize novel small molecule therapeutics with the potential to treat several metabolic diseases including type 2 diabetes, hyperlipidemia and obesity by activating an enzyme in the liver called AMP-activated Protein Kinase. As part of this collaboration, Merck paid an initial non-refundable license fee of $5.0 million in July 2005 and will provide research support funding of a minimum of $2.1 million each year during the three year research term. The three year research term is subject to renewal for one additional year by mutual agreement of the Company and Merck. The Company s level of research activities, and the minimum research support funding, may be increased during the term upon mutual agreement of both parties. Merck is also obligated to pay milestone payments if specified pre-clinical and clinical development and regulatory events occur and to pay royalties on sales of any product resulting from this collaboration. As of December 31, 2005, the Company has not achieved any developmental milestones and thus, no payments have been received for milestones from Merck. The Company would also have the option to co-promote any such product in the United States. If all pre-clinical and clinical milestones are achieved on multiple indications, and including the $5.0 million initial, non-refundable license fee and the minimum $6.3 million in research support funding, the Company may be entitled to payments which total up to $74.3 million, plus royalties. Merck is solely responsible for conducting and funding all development work for compounds resulting from this collaboration. Under the agreement, the Company recognized revenue of $1.9 million for the year ended December 31, 2005. The Company has deferred revenue of $ 4.7 million under the agreement as of December 31, 2005.

6. Commitments

The Company leases its office and research facilities and certain laboratory and electronic equipment under operating and capital lease agreements. In December 2004, the Company entered into an operating lease agreement pursuant to which the Company leased approximately 82,000 square feet of real estate space in La Jolla, California consisting of laboratory and office space. The lease commenced in October 2005 and has an initial term of 10 years unless extended or sooner terminated. The Company has options to extend the lease for two renewal periods of five years each. The Company s aggregate lease payments through 2015 will be $27.8 million. The facility lease provides for various forms of rent abatement during the first 48 months of the lease and annual rent increases of 3.0%. The difference between the straight-line expense over the term of the lease and actual

amounts paid are recorded as deferred rent. Prior to October 2005, the Company leased its office and research facilities under a different operating lease.

Rent expense was approximately $1.4 million, $1.3 million and $1.3 million for each of the years ended December 31, 2005, 2004 and 2003.

In connection with the facility lease which commenced in October 2005, the Company agreed to a $300,000 loan for tenant improvements. The term of the loan corresponds to the initial 10 year term of the lease. The interest rate is 8.0% per annum.

In 2001, the Company entered into a $650,000 equipment loan agreement with a financing company. This agreement was subsequently amended two times to increase the loan amount to approximately $2.1 million. The proceeds were used to finance laboratory equipment, computer and electronic equipment, tenant improvements and furniture. The Company made drawdowns of approximately $1.7 million before the amended equipment loan agreement ended on December 31, 2002. The equipment loan was collateralized by the related equipment acquired with the loan. Each drawdown had a payment term of 48 months with the interest rate being fixed at the funding date of each drawdown (9.58% to 12.05%).

In conjunction with the initial equipment loan and first amendment, warrants to purchase up to 53,938 shares of Series C Convertible Preferred Stock (Series C Preferred) at $1.25 per share were issued, of which 45,000 shares are exercisable at any time through June 16, 2007. The remaining warrant to purchase 8,938 shares of Series C Preferred is exercisable at any time through December 31, 2007. The cash exercise of these warrants would result in the issuance of 8,877 shares of the Company s common stock.

In conjunction with the second amendment to the initial equipment loan, the Company issued warrants to purchase 30,666 shares of Series D Convertible Preferred Stock (Series D Preferred). The warrants have an exercise price of $1.50 per share and are exercisable at any time through June 16, 2007. The cash exercise of these warrants would result in the issuance of 5,290 shares of the Company s common stock.

The warrants issued by the Company in connection with the equipment loan and related amendments were accounted for under APB 14, *Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants* and EITF Issue No. 96-18, which requires the warrants to be recorded at their fair value. The fair value of the warrants was accounted for under SFAS No. 123 using the Black Scholes Valuation Model. The warrants were valued at $59,000 using the following assumptions: risk-free interest rates of 4.59% to 4.97%, respectively; dividend yield of 0%; expected volatility of 70%; and a term of 1.7 to 5 years. The fair market value was recorded as a discount on the equipment loan and is being amortized to interest expense over the term of the equipment loan. The unamortized discount was $1,000 and $9,000 at December 31, 2005 and 2004, respectively.

In August 2003, the Company entered into an additional $1.4 million equipment loan agreement with a different financing company. This agreement was subsequently amended to increase the amount to $5.8 million. The proceeds are used to finance lab equipment, computer and electronic equipment and furniture. The loan is collateralized by the related equipment acquired with the loan. As of December 31, 2005, the Company had drawn down approximately $3.5 million under the equipment loan agreement. Each drawdown had a payment term of 48 months with the interest rate being fixed at the funding date of each drawdown (8.62% to 10.40%). No warrants were issued in connection with the equipment loan agreement.

Future minimum rental payments under capital and operating leases as of December 31, 2005, are as follows (in thousands):

	Capital Leases	Operating Leases
2006	$ 1,310	$ 1,554
2007	1,054	1,760
2008	713	2,305
2009	406	2,781
2010	49	3,087
Thereafter	211	16,272
Total minimum lease payments, excluding discount	3,743	$ 27,759
Less amount representing interest	(575)	
Present value of net minimum payments	3,168	
Less current portion, excluding discount of $1	(1,042)	
Long-term obligation under capital leases, excluding discount of $1	$ 2,126	

7. Stockholders Equity

Common Stock

In October 2005, the Company raised approximately $41.3 million in a private placement of common stock and the concurrent issuance of warrants for the purchase of common stock. Placement fees and other expenses were approximately $2.3 million. Under the terms of the financing, the Company sold 7.0 million shares of common stock at $5.86 per share, the closing bid price for the Company s common stock immediately preceding the entering into of the binding agreement for the transaction.

On June 21, 2004, the Company completed an initial closing of its initial public offering in which it sold 5.0 million shares of common stock for proceeds of $30.6 million, net of underwriting discounts and commissions and offering expenses. In addition, on July 20, 2004, the Company completed an additional closing of its initial public offering in which it sold an additional 75,000 shares of common stock pursuant to the exercise by the underwriters of an over-allotment option which resulted in proceeds of $0.5 million, net of underwriting discounts and commissions.

Convertible Preferred Stock

Effective immediately prior to the initial closing of the Company s initial public offering, shares of outstanding subordinated and Series A, C, D and E convertible preferred stock then outstanding were automatically converted into 11.0 million shares of common stock.

Series E Preferred Stock Deemed Dividend

The Series E Preferred financing, which closed in October 2003, involved the sale of preferred stock at a price per share below the initial public offering price contemplated in the Company s 2004 initial public filing. Accordingly, pursuant to EITF 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, the Company in 2003 recorded a deemed dividend on the Series E Preferred of $24.9 million, which was the difference between the gross proceeds from the Series E Preferred offering and the underlying value of the conversion shares (adjusted for a conversion price adjustment feature and limited to the proceeds allocated to the convertible instrument). The $24.9 million deemed dividend was entirely recognized as an adjustment to net loss applicable to common stockholders since the preferred stock was convertible, at any time, at the option of the holder. In accordance with EITF 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments*, the Company calculated the deemed dividend of $24.9 million using the most favorable conversion price of $3.12 per conversion share.

Warrants

In conjunction with the October 2005 private placement offering, the Company issued warrants to purchase approximately 2.5 million shares of its common stock at an exercise price of $6.74 per share. At the closing of the private placement offering, investors in the financing paid an additional price equal to $0.125 per each share issuable upon exercise

of the warrants which can be exercised until September 30, 2010.

In conjunction with the Series C Preferred offering, the Company sold warrants to the Series C investors to purchase 4.5 million shares of Series C Preferred at a purchase price of $0.01 per warrant resulting in proceeds of approximately $45,000. The stock purchase warrants have an exercise price of $1.00 per share and shall terminate December 31, 2007. The cash exercise of these warrants would result in the issuance of 735,670 shares of the Company s common stock

In conjunction with the Series D Preferred offering, the Company sold warrants to the Series D investors to purchase 3.5 million shares of Series D Preferred at a purchase price of $0.01 per warrant resulting in proceeds of approximately $35,000. The stock purchase warrants have an exercise price of $1.50 per share and can be exercised until the earlier of October 18, 2008, or after the Company s common stock trades on a securities exchange or the Nasdaq National Market and the average closing price of such common stock over any consecutive 20-trading day period equals or exceeds $27.34 (adjusted to reflect subsequent stock dividends, stock splits or recapitalizations). The cash exercise of these warrants would result in the issuance of 597,339 shares of the Company s common stock.

Additional warrants were issued in connection with the issuance of the equipment loans (see Note 6).

None of the above issued warrants had been exercised through December 31, 2005.

Equity Incentive Plan

On June 21, 2004, the Company authorized 2,213,995 shares of its common stock for issuance upon exercise of options or restricted stock granted under the 2001 Equity Incentive Plan (the Plan). On January 1, 2005, approximately 619,000 shares were added to the plan pursuant to an evergreen provision contained in the Plan. The Plan provides for the grant of stock options and restricted stock to officers, directors, and employees of, and consultants and advisors to, the Company. Options under the Plan may be designated as incentive stock options or nonstatutory stock options, generally vest over four years and expire ten years from the date of grant. In addition, incentive stock options may not be granted at prices less than 100% of the fair value on the date of grant. The number of vested options available for exercise as of December 31, 2005 and 2004 were approximately 580,000 and 374,000, respectively.

Directors Stock Option Plan

On June 21, 2004, the Company authorized 300,000 shares of its common stock for issuance upon exercise of options or restricted stock granted under the 2004 Non-Employee Directors Stock Option Plan (the Directors Plan). On January 1, 2005, 100,000 shares were added to the plan pursuant to an evergreen provision contained in the Directors Plan. The Directors Plan provides for the grant of stock options and restricted stock to directors of the Company. Options under the Directors Plan are designated as nonstatutory stock options, generally vest from one to two years, and expire ten years from the date of grant. In addition, options granted under the Directors Plan may not be granted at prices less than 100% of the fair value on the date of grant. The number of vested options available for exercise as of December 31, 2005 and 2004 were approximately 109,000 and 23,000, respectively.

The weighted-average remaining contractual life of the options outstanding under both plans at December 31, 2005 was approximately 8.1. The estimated weighted average fair value of stock options granted during 2005, 2004 and 2003 was $2.38, $6.32 and $9.84, respectively.

At December 31, 2005, a total of approximately 1,407,000 shares of common stock remained available for issuance under both plans.

The following is a further breakdown of the options outstanding as of December 31, 2005 (in thousands, except per share data):

	Options Outstanding			Options Vested and Exercisable	
Ranges of Exercise Prices	Number of Options	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price
$0.00 to $0.91	30	4.0	$ 0.30	30	$ 0.30
$0.91 to $1.82	702	7.5	1.44	452	1.43
$1.82 to $2.73	146	9.4	2.65	61	2.65
$2.73 to $3.64	80	6.8	3.01	29	3.04
$3.64 to $4.56	11	9.6	4.00		
$5.46 to $6.38	206	9.2	5.63	36	5.57
$6.38 to $7.29	159	8.7	6.70	81	6.59
$7.29 to $8.20	71	10.0	7.65		
Total	1,405	8.1	$ 3.17	689	$ 2.38

The following table summarizes stock option activity as follows (in thousands, except per share amounts):

	Shares	Weighted-average exercise price
Outstanding at December 31, 2002	505	$ 1.22
Granted	540	$ 1.46
Exercised	(66)	$ 0.67
Canceled	(28)	$ 1.50
Outstanding at December 31, 2003	951	$ 1.39
Granted	445	$ 4.19
Exercised	(255)	$ 1.24
Canceled	(34)	$ 1.45
Outstanding at December 31, 2004	1,107	$ 2.54
Granted	509	$ 4.39
Exercised	(40)	$ 1.35
Canceled	(171)	$ 3.12
Outstanding at December 31, 2005	1,405	$ 3.18

As of December 31, 2005 and 2004, respectively, there were approximately 24,000 and 56,000 shares of common stock outstanding pursuant to option exercises that were subject to repurchase by the Company.

Employee Stock Purchase Plan

On June 21, 2004, the Company authorized 500,000 shares of its common stock for issuance under the 2004 Employee Stock Purchase Plan (ESPP). On January 1, 2005, approximately 206,000 shares were added to the plan pursuant to an evergreen provision contained in the ESPP. The ESPP provides for all eligible employees to purchase shares of common stock at 85% of the lower of the fair market value on the first day of each two year offering period or any purchase date during such offering period (generally held every six months during such period). Employees may authorize the Company to withhold up to 15% of their total compensation during each six-month purchase period, subject to

certain limitations to pay for the ESPP shares. During the year ended December 31, 2004, approximately 30,000 shares were issued under the plan at a purchase price of $5.95 per share. During the year ended December 31, 2005, approximately 104,000 shares were issued under the plan at a purchase price of $2.67 per share, and approximately 572,000 shares were reserved for future issuance.

Shares Reserved For Future Issuance

The following shares of common stock were reserved for future issuance at December 31, 2005 (in thousands):

Warrants to purchase shares in conjunction with Series C Preferred	745
Warrants to purchase shares in conjunction with Series D Preferred	603
Warrants to purchase shares in conjunction with private placement	2,450
Common stock options:	
Granted and outstanding	1,405
Reserved for future issuance	1,407
Employee stock purchase plan	572
	7,182

8. Income Taxes

Significant components of the Company s deferred tax assets as of December 31, 2005 and 2004 are shown below (in thousands). A valuation allowance of $32.9 million and $22.9 million has been established at December 31, 2005 and 2004, respectively, to offset the net deferred tax assets as realization is uncertain.

	December 31, 2005	2004
Deferred tax assets:		
Net operating loss carryforwards	$ 27,874	$ 19,087
Research and development credits	4,601	3,523
Deferred revenue		
Other, net	557	422
Total deferred tax assets	33,032	23,032
Deferred tax liabilities:		
Deferred compensation	(97)	(174)
Total deferred tax liabilities	(97)	(174)
Valuation allowance for deferred tax assets	(32,935)	(22,858)
Net deferred assets	$	$

At December 31, 2005, the Company had federal and California net operating loss carryforwards of $68.4 million and $68.7 million, respectively, which will begin to expire in 2020 and 2008, respectively, unless previously utilized. The Company also had federal and state research and development tax credit carryforwards of approximately $2.8 million and $2.6 million respectively. The federal research and development tax credit carryforwards will begin expiring in 2020 unless previously utilized and the state credits do not expire.

Pursuant to Section 382 of the Internal Revenue Code, use of the Company s net operating loss and credit carryforwards may be limited since cumulative changes in ownership of more than 50% have occurred.

9. Related Party

In June 1999, the Company entered into an agreement with Sicor called the Master Agreement under which, among other things, the Company agreed to pay Sicor a 2% royalty on sales of products that would infringe on one of the Company s patents, patent applications, discoveries or inventions in existence as of the Company s restructuring, and 10% on any royalties the Company receives from licenses of these patents, patent applications, discoveries or inventions. The Company also agreed to pay Sicor a 1% royalty on sales of products that use, contain or are based on the Company s trade secrets, know-how and other proprietary rights in existence as of the Company s restructuring that are not covered by the 2% royalty, and 5% of any royalties the Company receives from licenses of these trade secrets, know-how and other proprietary rights that are not covered by the 10% royalty. Some or all of the Company s current product candidates and drug compounds from our research programs may be subject to these royalty provisions.

In June 1999, the Company extended approximately $425,000 in full recourse promissory notes (the Notes) to John Beck, Mark Erion, and Paul Laikind (the Founders) the Founders related to the purchase of an aggregate of 1,646,248 shares of

the Company s common stock (the Shares). The Notes accrued interest at a rate of 5.22% per annum. The entire principal balance of the Notes, together with all accrued and unpaid interest, was due on June 30, 2003.

In 2003, the Board of Directors authorized a transaction, effective June 30, 2003, calling for the Founders to agree to tender 487,702 shares of their previously vested common stock and subject them to a new monthly vesting schedule over a four-year period commencing on June 30, 2003. This transaction was entered into as repayment for outstanding principal and accrued interest on the Notes of approximately $514,000 and related taxes paid on their behalf by the Company. The amount of shares tendered was based upon the then fair value for the common stock as determined by the Board of Directors. The Company recorded approximately $711,000 of deferred compensation at June 30, 2003, to be amortized over the four-year vesting period of the underlying common stock. The Company has deferred compensation balances associated with this transaction of approximately $267,000 and $444,000 at December 31, 2005 and 2004, respectively. The Company recorded amortization of deferred compensation of approximately $178,000, $178,000 and $89,000 for the years ended December 31, 2005, 2004 and 2003, respectively. As of December 31, 2005, the unvested balance of shares subject to repurchase by the Company was 28,112, 74,414 and 80,368 held by Mr. Beck and Drs. Erion and Laikind, respectively.

10. Employee Benefit Plan

The Company established a defined contribution employee retirement plan (the 401(k) Plan) effective January 1, 1999, conforming to Section 401(k) of the Internal Revenue Code (IRC). All full-time employees (as defined in the 401(k) Plan) may elect to have a portion of their salary deducted and contributed to the 401(k) Plan up to the maximum allowable limitations of the IRC, which may be matched by the Company in an amount determined by the Board of Directors. No such Company matching contributions have been approved or made since the inception of the 401(k) Plan.

11. Subsequent Event

On February 3, 2006, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission covering the sale of the Company s common stock and/or warrants to purchase shares of the Company s common stock in one or more offerings with a total offering price of up to $75 million from time to time in amounts, at prices and on terms to be determined at the time of the applicable offering.

12. Summary of Quarterly Financial Data (Unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2005 and 2004 (in thousands, except for net loss per share data):

	Quarters Ended				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Year Ended Dec 31 (1)
2005					
Revenues	$ 397	$ 617	$ 1,395	$ 1,362	$ 3,771
Total operating expenses	6,837	6,549	6,710	8,342	28,438

Net loss applicable to common stockholders	(6,235)	(5,734)	(5,107)	(6,504)	(23,580)
Basic and diluted net loss per share:	(0.35)	(0.32)	(0.28)	(0.26)	(1.20)
2004					
Revenues	$ 4,170	$ 1,771	$ 470	$ 426	$ 6,837
Total operating expenses	4,691	5,414	5,638	6,369	22,112
Net loss applicable to common stockholders	(512)	(3,633)	(5,052)	(5,775)	(14,972)
Basic and diluted net loss per share:	(0.37)	(1.17)	(0.29)	(0.32)	(1.49)

(1) The sum of the four quarters may not necessarily agree to the year total due to rounding within a quarter.