

METABASIS THERAPEUTICS INC
Form 10-K
March 13, 2007

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)

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

For the fiscal year ended December 31, 2006

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
(State or other jurisdiction
of incorporation or organization)
11119 North Torrey Pines Road, La Jolla, CA
(Address of principal executive offices)

33-0753322
(I.R.S. Employer Identification No.)

92037
(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
Common Stock, par value \$0.001 per share

Name of Each Exchange on Which Registered
The Nasdaq Stock Market

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

None

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

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

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

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

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

Large accelerated filer Accelerated filer Non-accelerated filer

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

As of June 30, 2006, 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 \$ 84.1 million, based on the closing price of the registrant's common stock on the Nasdaq Stock Market on June 30, 2006 of \$7.63 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, 2007 was 30,505,043.

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, 2006 are incorporated by reference into Part III of this report.

METABASIS THERAPEUTICS, INC.

FORM 10-K ANNUAL REPORT

FOR THE YEAR ENDED DECEMBER 31, 2006

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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 by applying our proprietary technology, scientific expertise and unique capabilities for targeting the liver and liver pathways. These diseases include metabolic diseases such as diabetes, obesity and hyperlipidemia, among others, and liver diseases such as hepatitis and primary liver cancer. We have established a broad and growing product pipeline of product candidates and advanced research programs targeting large markets with significant unmet medical needs. We have discovered all of our product candidates internally using our proprietary technologies.

We currently have five product candidates in clinical trials. These five product candidates, by category, and in order from the most advanced in clinical trials within each category, are as follows:

Metabolic Diseases

- *CS-917, a product candidate for the treatment of type 2 diabetes that is currently in a Phase 2b clinical trial.* CS-917, which was discovered using our NuMimetic technology, is being developed in collaboration with Daiichi Sankyo Co., Ltd. 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. CS-917 has successfully completed a number of Phase 1 and Phase 2 clinical studies. Daiichi Sankyo is currently conducting a Phase 2b clinical trial of CS-917 which is fully enrolled and is designed to evaluate the safety and tolerability of CS-917 as well as its effect on blood levels of the molecule hemoglobin A1c, an important measure of long-term glucose control in patients with type 2 diabetes, after twice daily administration of CS-917 over three months. If successful, the trial should support selection of a dose for pivotal Phase 3 clinical trials which we believe Daiichi Sankyo could initiate in the second half of 2007 or early 2008.
- *MB07803, a product candidate for the treatment of type 2 diabetes that is expected to enter Phase 2 clinical trials in the first half of 2007.* MB07803 is a second-generation gluconeogenesis inhibitor for

the treatment of type 2 diabetes that was also discovered using our NuMimetic technology. MB07803 has completed four Phase 1 clinical trials in healthy volunteers, the most advanced of which was a 14-day rising multiple dose clinical trial, and is expected to enter Phase 2 clinical trials in the second quarter of 2007. We are currently independently developing this product candidate.

- *MB07811, a product candidate for the management of hyperlipidemia, including reduction of elevated cholesterol levels and triglycerides, or TGs, that is currently in a Phase 1 clinical trial.* MB07811 uses our HepDirect® prodrug technology and other structural characteristics to target a beta-subtype-selective thyroid hormone receptor, or TRβ, agonist to the liver to reduce cholesterol and TGs. Preclinical data suggest that MB07811 could be as effective at lowering cholesterol as the drug class known as statins, and have an additive effect in reducing cholesterol when used with statins. MB07811 has successfully completed a rising single dose Phase 1 clinical trial in healthy volunteers. We expect to initiate a rising multiple dose Phase 1 clinical trial designed to evaluate the safety and tolerability of MB07811 in healthy volunteers with elevated cholesterol after submitting the results of the first Phase 1 clinical trial and additional preclinical studies to the U.S. Food and Drug Administration, or FDA and after obtaining the FDA's agreement to proceed. We are currently independently developing this product candidate.

Liver Diseases

- *Pradefovir, a product candidate for the treatment of hepatitis B that has completed Phase 2 clinical trials.* Prior to January 2007 pradefovir had been developed in collaboration with Valeant Pharmaceuticals International. In April 2006 Valeant announced plans to out-license pradefovir as part of an overall restructuring of its operations. As a result of this restructuring plan Valeant, with our consent, assigned its development and commercial rights to pradefovir in January 2007 to Schering Corporation, a subsidiary of Schering-Plough Corporation, and we entered into an amended and restated license agreement for pradefovir with Schering-Plough. Pradefovir uses our HepDirect technology to target the active form of Hepsera, a marketed anti-viral drug indicated for the treatment of hepatitis B, specifically to the liver. Because pradefovir targets adefovir to the liver while limiting the amount that reaches other organs, we believe that higher liver levels of active drug may be achieved with pradefovir without causing kidney toxicity, thereby providing greater efficacy. Pradefovir has successfully completed a number of Phase 1 and Phase 2 clinical trials in healthy volunteers and patients which were designed to evaluate safety and efficacy, as applicable. Based on the results of the Phase 2b clinical trial and an end of Phase 2 meeting with the FDA, we believe that pradefovir is ready to commence Phase 3 clinical trials. However, the ultimate decision to proceed with Phase 3 clinical trials is the responsibility of Schering-Plough.

- *MB07133, a product candidate for the treatment of primary liver cancer that has completed a Phase 1/2 clinical trial and is expected to enter a Phase 2 clinical trial in 2007.* Few treatment options exist, and no drug has been approved, for treatment of primary liver cancer. Cytarabine, or araC, is a marketed anti-cancer drug used to treat leukemia. AraC has shown only limited success in solid tumors such as primary liver cancer because the liver lacks a particular protein, or kinase, necessary for converting it to an important intermediate form known as araCMP. MB07133 uses our HepDirect technology to deliver this intermediate form of araC to the liver where it is then readily converted by a different liver kinase into its anti-cancer form, known as araCTP. This approach bypasses the need for the first kinase which the liver lacks. In addition, araC, when systemically delivered is readily converted to araCTP in tissues such as the bone marrow where it can cause toxicity. MB07133 appears to avoid this potential toxicity because the HepDirect prodrug version of araCMP is not converted to araCTP in tissues outside the liver. We believe the unique ability of MB07133 to deliver araCMP selectively to the liver where it can be readily converted into its anti-cancer form will enhance efficacy while minimizing the toxicities associated with systemic araC

therapy. MB07133 has completed a Phase 1/2 clinical trial in 28 patients with primary liver cancer in which it was well tolerated and showed evidence of anti-tumor activity. MB07133 is expected to enter Phase 2 clinical trials in 2007. We are currently independently developing this product candidate.

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, processes referred to as drug uptake, metabolism and excretion, respectively. With this knowledge, we developed proprietary technologies, including two named 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 may also use it in certain of our internal research programs. In addition to our internal programs that may be using 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 or NASH, by inhibiting cholesterol and lipid production in the liver by activating a type of liver enzyme known as a protein kinase that is called AMPK.

We use our HepDirect technology to target drugs 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 other 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 with which we collaborate that have compounds that would benefit from this approach. Pradefovir, MB07133 and MB07811 use our HepDirect technology, as do some of our internal research programs. In addition to our internal programs, we have collaborations with Merck and Idenix Pharmaceuticals, Inc. to discover new treatments for hepatitis C by applying our HepDirect technology and other liver-targeting technology to compounds that they have supplied to us.

Our research programs focus on metabolic diseases such as type 2 diabetes and hyperlipidemia as well as liver diseases such as hepatitis C. Our goal is to expand our clinical development pipeline by continuing to develop and move additional new drug compounds into 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 a drug compound is recommended for clinical development it undergoes preclinical development including scale up, toxicology and formulations development. Successful compounds would then enter human clinical testing.

We have several internal and collaborative advanced research programs that we believe have the potential to yield additional clinical development candidates. These advanced research programs include:

- a second generation TR β agonist to reduce cholesterol and TGs for the management of hyperlipidemia,

- a program using our HepDirect and other liver-targeting technology in a collaboration with Merck to identify drug candidates to treat hepatitis C infection,
- a program using our HepDirect technology in a collaboration with Idenix to identify drug candidates to treat hepatitis C infection, and
- a metabolic disease program to identify drug candidates to treat type 2 diabetes via a mechanism other than those used in our other type 2 diabetes programs.

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 collaborations, and
- becoming a fully-integrated pharmaceutical company.

Disease Backgrounds

Metabolic Diseases

Metabolic diseases such as type 2 diabetes, hyperlipidemia, obesity and NASH 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 in the liver, such as the pathways responsible for the production and/or metabolism of glucose, cholesterol and fat molecules. Many drugs are currently 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 are also poorly treated with few drugs on the market showing suitable efficacy and safety for these patients and there currently are no approved treatments for NASH. As a result, we believe more effective drugs are needed to treat these diseases.

Liver Diseases

Liver diseases such as hepatitis B, hepatitis C and primary liver cancer represent some of the most widespread and serious diseases in the world. 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 the majority of patients. Some existing anti-viral and anti-cancer drugs, while effective outside of the liver, 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.

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.

Our Pipeline-Metabolic Diseases

The following table summarizes our metabolic disease product candidates currently in clinical development and advanced research programs, in order from the most advanced in clinical development:

| Product Candidates/Programs(1) | Disease/Condition | Partner | Our Commercial Rights | Status |
|--------------------------------|-------------------|----------------|---|-----------|
| CS-917 | Diabetes | Daiichi Sankyo | Royalties, North America Co-promotion Option | Phase 2b |
| MB07803 | Diabetes | None | Worldwide | Phase 1 |
| MB07811 | Hyperlipidemia | None | Worldwide | Phase 1 |
| Unnamed | Hyperlipidemia | None | Worldwide | Discovery |
| Unnamed | Diabetes | None | Worldwide | Discovery |

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

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 preclinical studies and two completed Phase 2a clinical trials, CS-917 has shown a statistically significant reduction in elevated glucose levels compared to placebo-treated patients. 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 (non-insulin dependent; adult onset diabetes). Approximately 90% of diabetes patients have type 2 diabetes. Elevated blood glucose levels in patients with type 2 diabetes are the result of 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 seen in patients with type 2 diabetes 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 and over 18 million people in the U.S.

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 patients with type 2 diabetes. However, other than insulin, at the present time 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, the primary mechanism of which is to 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 the maximum allowed dose. Metformin does not directly block the gluconeogenesis pathway as data generated to date indicate that CS-917 does. Therefore, a more effective hepatic glucose output inhibitor, such as CS-917, which directly inhibits the gluconeogenesis pathway, may provide improved efficacy compared to metformin. Metformin therapy is associated with an increased risk of lactic acidosis in certain patient populations, including patients with kidney dysfunction. In addition, metformin therapy commonly leads to transient gastrointestinal disturbances such as nausea, diarrhea and vomiting, which may 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 impact glucose control, 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 patients with type 2 diabetes. In the United Kingdom Prospective Diabetes Study, obese patients treated with maximum doses of metformin or an insulin secretion enhancer ultimately 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, patients with diabetes typically are treated with one or more additional oral drugs. It is estimated that more than 75% of patients with type 2 diabetes will require multiple oral drug therapies to attain adequate glucose control and just over 30% of patients with type 2 diabetes 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.

Markets

The U.S., Japan, France, Germany, Italy, Spain and the United Kingdom comprise the seven major pharmaceutical markets. Combined sales of oral products used to treat type 2 diabetes in these markets were \$12.5 billion in 2006, with the U.S. accounting for \$8.4 billion of that total. By 2020, combined sales of oral products used to treat type 2 diabetes in the seven major pharmaceutical markets are expected to increase to \$15.7 billion, and sales in the U.S. are expected to increase to \$9.7 billion.

If CS-917 is approved by regulatory authorities and its safety and/or efficacy profile is determined by physicians to be better than, or equal to, metformin based on data from clinical trials, then CS-917 may be used as first line therapy in a broad population of patients with type 2 diabetes and will likely be prescribed by physicians based on the difference between each respective drug's safety and/or efficacy profile as well as how individual patients respond to each drug. In addition to this broad population, CS-917 may also be prescribed to those patients who are intolerant to, or contraindicated for, metformin use and to those

patients who are not on metformin as well as those who are not achieving their glucose lowering targets while taking other oral therapies, or combinations of other oral therapies. Market research indicates that by 2017 these patient populations together are projected to comprise approximately 60% of patients with type 2 diabetes.

If CS-917 is approved by regulatory authorities, and it is ultimately determined in further clinical trials that the use of CS-917 cannot be safely combined with metformin, then CS-917 will be targeted to those patients who are intolerant to, or contraindicated for, metformin use and to those patients who are not on metformin as well as those who are not achieving their glucose lowering targets while taking other oral therapies, or combinations of other oral therapies. These patient populations, as indicated above, together are projected to represent approximately 60% of patients with type 2 diabetes in 2017.

Based on these data we believe there is a considerable market opportunity for CS-917 regardless of whether CS-917 is determined by physicians to have a superior or equivalent safety and/or efficacy profile compared to metformin or if it is ultimately determined in further clinical trials that the use of CS-917 cannot be safely combined with metformin.

CS-917

Studies show that the elevated blood glucose levels that characterize patients with type 2 diabetes are correlated with the overproduction of glucose by the liver, which arises from an increased rate of flow, or flux, 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 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 patients with type 2 diabetes. Pharmaceutical companies have tried to find inhibitors of FBPase, but have, to our knowledge, 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 patients with type 2 diabetes 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 patients with type 2 diabetes. 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 patients with advanced type 2 diabetes, 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 patients with prediabetes in which CS-917 may be effective in preventing or delaying the onset of diabetes.

We expect that the initial development and marketing focus for CS-917 will be on patients that are unable to tolerate the current first line therapy, metformin. The current alternative for these patients, which constitute as much as 15% of the total patient population with type 2 diabetes, is treatment with drugs such as insulin secretion enhancers, insulin sensitizers or more recently, a new class of diabetes drugs known as incretin mimetics which include dipeptidyl peptidase IV or DPP-IV inhibitors, and BYETTA® (exenatide) injection. However, these drugs are less efficacious than metformin and in the case of insulin secretion enhancers and sensitizers, they cause weight gain. Based on early data we believe that CS-917 has the potential to be more effective than these current second line agents and be the first

alternative therapy for this important and underserved patient population. Moreover, as physicians and patients gain more experience with CS-917, we believe it could be used as a first line therapy in newly diagnosed type 2 patients, in combination with additional oral therapies other than metformin and as an alternative for patients who have failed on other oral therapies prior to switching to insulin or in combination with insulin in these patients. In fact, many diabetic patients will eventually fail on oral therapies.

Clinical Trials

To date, our partner Daiichi Sankyo has completed a number of Phase 1 clinical trials of CS-917 in healthy volunteers as well as Phase 1 and Phase 2a clinical trials of CS-917 in patients with type 2 diabetes.

Results from two Phase 2a clinical trials, the first of which was completed in 2003, provide evidence that CS-917 is capable of significantly lowering blood glucose levels in humans. The first Phase 2a clinical trial completed involved treatment of 39 patients with type 2 diabetes 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 2a clinical trial, completed in 2004, 146 patients with type 2 diabetes 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.

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 1 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 the time were stopped while one Phase 1 clinical trial which did not combine CS-917 with metformin continued and was completed. After extensive analysis Daiichi Sankyo concluded that the lactic acidosis observed in the two patients was likely due to significantly increased blood levels of metformin. The reason for the increase in metformin blood levels observed in these two patients has not been determined to date. At high blood levels, metformin is believed to cause a form of cellular toxicity known as mitochondrial toxicity which can cause lactic acidosis. Subsequently, Daiichi Sankyo, in consultation with the FDA, decided that clinical trials of CS-917 could safely resume as a mono-therapy or in combination with other anti-diabetes agents other than metformin.

In January 2006 Daiichi Sankyo initiated a multi-center, randomized, double-blind, placebo-controlled Phase 2b clinical trial designed to evaluate safety and tolerability after three months dosing of CS-917, as well as its effect on blood levels of hemoglobin A1c. In February 2007 we announced that full enrollment of a total of 392 patients at approximately 100 sites had been achieved. Patients were evenly distributed among four groups consisting of two active dose groups of CS-917, an active comparator and placebo. If successful, this Phase 2b clinical trial could support selection of a dose for Phase 3 clinical trials which we believe Daiichi Sankyo could initiate in the second half of 2007 or early 2008.

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 proven.

Preclinical Studies

Results from clinical trials of CS-917 are consistent with the glucose-lowering effect observed in preclinical 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. Moreover, CS-917 lowered glucose both in the fed state (at meal time) as well as in the fasted state (between meals). 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.

Preclinical studies in diabetes animal models have also 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. In addition, preclinical studies may support the use of CS-917 in patients with advanced diabetes. 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 preclinical 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.

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

MB07803 is an oral product candidate for the treatment of type 2 diabetes that, like CS-917, was discovered using our NuMimetic technology and is designed to inhibit gluconeogenesis. While MB07803 is structurally different from CS-917 and may offer certain pharmacological advantages, both product candidates are designed to inhibit gluconeogenesis by targeting the same binding site on the FBPase enzyme. MB07803 is targeting the same market as CS-917 and is expected to have advantages over current therapies that are similar to those expected for CS-917. The preliminary efficacy results demonstrated by CS-917 in the Phase 2 clinical trials improve our confidence in the potential for MB07803 as an approach for treating diabetes. We are currently independently developing this product candidate.

Markets

Combined sales of oral products used to treat type 2 diabetes in the seven major pharmaceutical markets were \$12.5 billion in 2006, with the U.S. accounting for \$8.4 billion of that total. By 2020,

combined sales of oral products used to treat type 2 diabetes in the seven major pharmaceutical markets are expected to increase to \$15.7 billion, and sales in the U.S. are expected to increase to \$9.7 billion.

If MB07803 is approved by regulatory authorities and its safety and/or efficacy profile is determined by physicians to be better than, or equal to, metformin based on data from clinical trials, then MB07803 may be used as first line therapy in a broad population of patients with type 2 diabetes and will likely be prescribed by physicians based on the difference between each respective drug's safety and/or efficacy profile as well as how individual patients respond to each drug. In addition to this broad population, MB07803 may also be prescribed to those patients who are intolerant to, or contraindicated for, metformin use and to those patients who are not on metformin as well as those who are not achieving their glucose lowering targets while taking other oral therapies, or combinations of other oral therapies. Market research indicates that by 2017 these patient populations together are projected to comprise approximately 60% of patients with type 2 diabetes.

If MB07803 is approved by regulatory authorities, and it is ultimately determined in further clinical trials that the use of MB07803 cannot be safely combined with metformin, then MB07803 will be targeted to those patients who are intolerant to, or contraindicated for, metformin use and to those patients who are not on metformin as well as those who are not achieving their glucose lowering targets while taking other oral therapies, or combinations of other oral therapies. These patient populations, as indicated above, together are projected to represent approximately 60% of patients with type 2 diabetes in 2017.

Based on these data we believe there is a considerable market opportunity for MB07803 regardless of whether MB07803 is determined by physicians to have a superior or equivalent safety and/or efficacy profile compared to metformin or if it is ultimately determined in further clinical trials that the use of MB07803 cannot be safely combined with metformin.

Clinical Trials

We have completed four Phase 1 clinical trials in healthy volunteers, the most advanced of which was a 14-day, rising multiple dose clinical trial. The results from these completed clinical trials indicated that MB07803 was safe and well tolerated and support the advancement of MB07803 into Phase 2 clinical trials. We expect MB07803 to commence Phase 2 clinical trials in the second quarter of 2007.

MB07811: A liver-targeted thyroid receptor agonist for the management of hyperlipidemia, including elevated cholesterol and low-density lipoprotein cholesterol, or cholesterol, and TGs

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 uses our proprietary HepDirect prodrug technology and other structural characteristics to target a TR β agonist to the liver to lower cholesterol and TGs. We are currently independently developing this product candidate.

Hyperlipidemia

Hyperlipidemia is a disease characterized by an elevation of lipids, such as cholesterol or triglycerides, in the bloodstream. Elevation of cholesterol and/or triglycerides in the bloodstream can speed up a process called atherosclerosis, or hardening of the arteries through the formation of plaque deposits on the artery walls. As more plaque builds up, the arteries can narrow and stiffen. Eventually, enough plaque may build up to reduce blood flow through the arteries leading to a greater risk of cardiovascular disease and heart attack or stroke. Cardiovascular disease is the leading cause of death worldwide, and in the U.S. alone claims more lives than cancer, chronic respiratory diseases, accidents and diabetes combined.

Current Treatments

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 lower cholesterol, triglycerides and low density lipoproteins and increase high density lipoproteins,
- cholesterol absorption inhibitors or CAIs 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.

Lipitor® (atorvastatin; a statin marketed by Pfizer Inc.) is currently the best selling prescription medicine for the treatment of hyperlipidemia. Several large pharmaceutical companies are also developing novel therapies that target hyperlipidemia.

While many drug classes are currently available for treating hyperlipidemia either alone or in combination with other drugs, many patients are not achieving optimal cholesterol lowering and are not meeting their cholesterol lowering targets with current therapies. We believe that because of the limitations of currently marketed drugs, the hyperlipidemia market is receptive to new drugs, and new therapeutic approaches have the potential to experience rapid clinical acceptance. For example, the results from the Lipid Treatment Assessment Project or L-TAP, a large, multi-center study, showed that of the 4,888 patients with evaluable data, only 38% achieved their cholesterol target goals as defined by National Cholesterol Education Program guidelines on lipid-lowering drugs. One reason patients with hyperlipidemia fail to reach their cholesterol lowering goals may be inadequate titration, or gradual escalation, of the dose of statins that they are prescribed due to the increased potential of adverse events at higher doses and because doubling of the statin dose only provides a small incremental (6%) reduction in cholesterol. For patients with high cholesterol who do not respond well to statins, their options are limited to changing to another statin and/or using a statin in combination therapy with a non-statin, lipid-lowering agent. If MB07811 is ultimately determined to be safe and effective and approved for marketing, it may be capable of reducing cholesterol in combination with statins to a level that exceeds the cholesterol lowering potential of statins alone. In addition, while statins are generally considered to be first line agents for the majority of patients with hyperlipidemia, approximately 5% of patients with hyperlipidemia, or approximately 5.5 million patients in the U.S., are intolerant to statins. For these statin-intolerant patients, MB07811 may be considered as an alternative first line therapy.

Markets

Combined sales of products used to treat hyperlipidemia in the seven major pharmaceutical markets were \$24.6 billion in 2004, with the U.S. accounting for \$17.1 billion of that total. By 2014 combined sales in the seven major pharmaceutical markets are expected to increase to \$25.1 billion and sales in the U.S. are expected to decline to \$15.1 billion. The relatively modest growth in sales in the combined seven major markets, and the decline in U.S. sales over this period, are mainly due to the projected impact of the loss of exclusivity of the major statins, including the market leader Lipitor (atorvastatin), during this period. However, the number of patients diagnosed with hyperlipidemia is expected to increase from 301 million worldwide in 2004 to 327 million in 2014. In the U.S., the number of patients diagnosed with

hyperlipidemia is expected to increase from 109 million in 2004 to 124 million in 2014. In addition, MB07811, if approved, will likely constitute the first in an entirely new class of anti-hyperlipidemic agents which may help patients better reach targeted cholesterol levels either as first line therapy or in combination with statins. Therefore MB07811, if approved, may not be subject to competitive pressure from the introduction of generic statins during this period.

MB07811, if approved by regulatory authorities, will likely be initially targeted to patients who are either intolerant to statins, or for use in combination with statins for the significant portion of patients who fail to meet their targeted cholesterol reduction goals with statins. Both of these categories represent significant populations of patients with hyperlipidemia and therefore we believe there is a considerable market opportunity for MB07811.

MB07811

MB07811 uses our HepDirect prodrug technology and other structural characteristics to target a TR β agonist to the liver to reduce cholesterol and TGs. Thyroid hormone receptor agonists are known to reduce cholesterol in animal models, but typically at doses similar to those associated with potential safety concerns, including cardiac and other non-hepatic toxicities. MB07811 is an internally discovered HepDirect prodrug of a novel TR β receptor agonist that is designed to deliver the agonist to the site where cholesterol is produced and metabolized, i.e. the liver, while reducing the exposure of the agonist to other tissues. We believe that liver-targeting may avoid the safety concerns previously seen with non-liver targeted TR β agonists and thus unlock the therapeutic potential of this approach. Preclinical data suggest that MB07811 could be as effective at lowering cholesterol as statins and have an additive effect in reducing cholesterol when used with statins.

Clinical Trials

MB07811 has successfully completed a rising single dose Phase 1 clinical trial in healthy volunteers. We expect to initiate a rising multiple dose Phase 1 clinical trial designed to evaluate the safety and tolerability of MB07811 in healthy volunteers with elevated cholesterol after submitting the results of the first Phase 1 clinical trial and additional preclinical studies to the FDA and after obtaining the FDA's agreement to proceed.

Preclinical Studies

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 the toxicities which have been 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 with an acceptable therapeutic index. 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 (labeled AT in Chart B below).

Chart A

Chart B

Advanced Research Programs Metabolic Diseases

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 develop and move additional new drug compounds into clinical development. We believe our advanced research programs have the potential to yield additional clinical development candidates.

Our metabolic disease related advanced research programs are:

A second generation TR β agonist program to identify drug candidates to reduce cholesterol and TGs for the management of hyperlipidemia.

We have an advanced research program to identify second-generation TR β agonists to reduce cholesterol and TGs for the management of hyperlipidemia. This program may yield additional development candidates that lower cholesterol and TGs by the same mechanism as MB07811 but with potential improvements.

A metabolic disease program to identify drug candidates to treat type 2 diabetes via a mechanism other than those used in our other type 2 diabetes programs

We have an advanced research program to identify drug candidates to treat type 2 diabetes via a mechanism other than those used in our other type 2 diabetes programs. This program may yield additional development candidates to further expand our product pipeline.

Our Pipeline Liver Diseases

The following table summarizes our product candidates for the treatment of liver diseases that are currently in clinical development and our advanced research programs for the treatment of liver diseases, in order from the most advanced in clinical development:

| Product Candidates/Programs(1) | Disease/Condition | Partner | Our Commercial Rights | Status |
|---------------------------------------|--------------------------|-----------------|------------------------------|---------------------|
| Pradefovir | Hepatitis B | Schering-Plough | Royalties | Phase 2b completed |
| MB07133 | Primary Liver Cancer | None | Worldwide | Phase 1/2 completed |
| Unnamed(2) | Hepatitis C | Merck | Royalties | Discovery |
| Unnamed(3) | Hepatitis C | Idenix | Royalties | Discovery |

- (1) None of our product candidates have received regulatory approval in the U.S. or in foreign countries.
- (2) We are collaborating with Merck to apply our HepDirect and other liver-targeting technologies to certain compounds for the treatment of hepatitis C infection.
- (3) We are collaborating with Idenix to apply our HepDirect technology 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 2 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 preclinical 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. Prior to January 2007 pradefovir had been developed in collaboration with Valeant. In April 2006 Valeant announced plans to out-license pradefovir as part of an overall restructuring of its operations. As a result of this restructuring plan Valeant, with our consent, assigned its development and commercial rights to pradefovir in January 2007 to Schering Plough, and we entered into an amended and restated license agreement for pradefovir with Schering-Plough. Based on the results of the Phase 2b clinical trial and an end of Phase 2 meeting with the FDA, we believe that pradefovir is ready to commence Phase 3 clinical trials. However, the ultimate decision to proceed with Phase 3 clinical trials is the responsibility of Schering-Plough.

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 may 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.

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., there are five approved treatments for chronic hepatitis B: Intron A, Epivir-HBV, also referred to as Zeffix (lamivudine), Hepsera, Baraclude (entecavir) and TYZEKA (telbivudine). Each of these therapies has limitations in the treatment of patients with hepatitis B. For example, Intron A 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. To date, for the relatively short time that it has been on the market, 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. TYZEKA has not been on the market long enough for a clear profile to emerge. However, based on clinical data it appears to have the potential for inducing significant viral resistance over time.

Hepsera, lamivudine, Baraclude and TYZEKA all decrease virus levels, as measured by hepatitis B DNA in the blood serum. Nevertheless, further decreases are desirable since these reductions are not 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 of Hepsera led to a more than ten-fold greater reduction in hepatitis B DNA in the blood serum 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 that the approved dose of Hepsera (10 mg.) may be suboptimal for the reduction of virus levels in patients with hepatitis B.

Markets

In the seven major pharmaceutical markets combined sales of oral hepatitis B anti-viral products were \$486 million in 2005, with the U.S. accounting for \$197 million of that total. By 2015, combined sales in the seven major pharmaceutical markets are expected to increase to \$1.7 billion and sales in the U.S. are expected to increase to \$415 million. In addition to the seven major pharmaceutical markets, considerable potential exists in the growing Chinese pharmaceutical market, as there are more patients with hepatitis B in China than all other markets combined. Based on the results of clinical trials to date we believe that pradeфовir has the potential to become a best-in-class product that is used as first-line treatment in the majority of patients. Pradeфовir, if approved by regulatory authorities, may also be targeted as a second

line therapy in patients for whom treatment with other approved agents has failed. Therefore, we believe that there is a considerable worldwide market opportunity for pradefovir.

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 2 clinical trial, which is further discussed in the clinical trials section below.

Clinical Trials

Prior to assigning its rights to Schering-Plough, Valeant completed two single-dose Phase 1 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 1 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 1 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 1 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 preclinical studies.

Based on these initial results, in July 2004 Valeant commenced a 12-month dose-ranging Phase 2 clinical trial of pradefovir the purpose of which was to select appropriate doses for Phase 3 clinical trials. The Phase 2 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 2 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 2 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)

| | Dose | Number of Patients | Baseline Mean HBV DNA (Log (10) copies/mL) | Week 48 Mean Decline in HBV DNA | p-Value Compared to 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 percentages 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.

In January 2007, Valeant with our consent assigned its development and commercial rights to pradefovir to Schering-Plough and we entered into an amended and restated license agreement for pradefovir with Schering-Plough. Based on the results of the Phase 2b clinical trial and an end of Phase 2 meeting with the FDA, we believe that pradefovir is ready to commence Phase 3 clinical trials. However, the ultimate decision to proceed with Phase 3 clinical trials is the responsibility of Schering-Plough.

Preclinical Studies

Together with Valeant, we conducted preclinical 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.

The improvement in liver to kidney distribution resulting from treatment with pradefovir in comparison to Hepsera was also demonstrated in a study in rats using whole body autoradiography, a process in which a radioactive marker was included with the drugs when administered and the radioactivity of the rats was later analyzed to determine the distribution of adefovir and related metabolites in their bodies. At various times after dosing, rats treated with pradefovir exhibited high levels of adefovir and related metabolites in the liver relative to the kidney, whereas rats dosed with a similar amount of Hepsera showed high levels of adefovir and related metabolites in the kidney relative to the liver.

We believe that pradefovir achieves higher liver levels of adefovir and related metabolites relative to Hepsara because pradefovir more readily distributes into the liver where it is specifically converted to adefovir which is then converted to adefovir diphosphate. Moreover, unlike Hepsara, pradefovir is not readily converted to adefovir in the blood, intestine and kidney. Since kidney exposure to adefovir is implicated in kidney toxicity, decreased kidney exposure may result in a safer drug. This expectation was supported by six and nine-month toxicology studies in rats and monkeys, which showed pradefovir to have a significantly better safety profile than Hepsara, based on findings showing that pradefovir's highest non-toxic dose was approximately 15 -fold higher than the non-toxic dose for Hepsara in each species.

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

MB07133 is a product candidate that is expected to be administered intravenously and continuously over a multiple-day period on an out-patient basis. MB07133 has completed a Phase 1/2 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. Cytarabine, or araC, is a marketed anti-cancer drug used to treat leukemia. AraC has shown only limited success in solid tumors such as primary liver cancer because the liver lacks a particular protein, or kinase, necessary for converting it to an important intermediate form known as araCMP.

MB07133 uses our HepDirect technology to deliver this intermediate form of araC to the liver where it is then readily converted by a different liver kinase into its anti-cancer form, known as araCTP. This approach bypasses the need for the first kinase which the liver lacks. In addition, araC, when systemically delivered is readily converted to araCTP in tissues such as the bone marrow where it can cause toxicity. MB07133 appears to avoid this potential toxicity because the HepDirect prodrug version of araCMP is not converted to araCTP in tissues outside the liver. We believe the unique ability of MB07133 to deliver araCMP selectively to the liver where it can be readily converted into its anti-cancer form will enhance efficacy while minimizing the toxicities associated with systemic araC therapy. We are currently independently developing this product candidate.

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 19,000 new cases of primary liver cancer will be diagnosed in the U.S in 2007. 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 with unapproved agents that have shown limited efficacy. Nexavar® (sorafenib), a chemotherapy approved for the treatment of kidney cancer, is being evaluated for the treatment of primary liver cancer. The drug's developer, Bayer Healthcare Pharmaceuticals, recently announced that an ongoing Phase 3 clinical trial of Nexavar for the treatment of primary liver cancer was stopped early because the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar tablets versus those patients receiving placebo. Therefore it is likely that Nexavar will be approved for the treatment of patients with primary liver cancer and it is expected that it will experience significant off-label use prior to its approval. Still, even with the availability of Nexavar we believe the disease will remain poorly treated and that an agent with a different mechanism of action like MB07133, if approved, could find wide usage.

Markets

There are currently no approved drugs for the treatment of primary liver cancer. In the seven major pharmaceutical markets approximately 112,000 patients were afflicted with primary liver cancer in 2004. By 2014, the prevalence rate in the seven major global pharmaceutical markets is expected to increase to approximately 185,000 patients. The prevalence rate in the U.S. includes approximately 19,000 patients expected to be diagnosed in 2007, a number that is expected to grow to approximately 40,000 patients by 2010. In addition, China, which is not one of the seven major pharmaceutical markets, has an incidence rate of primary liver cancer of approximately 1.2 million patients as of 2004. This is greater than rest of the world combined. This incidence rate is expected to rise to 1.9 million by 2014.

MB07133, if approved by regulatory authorities, potentially could be targeted as a first line chemotherapeutic treatment for patients with inoperable primary liver cancer. Given the current and projected primary liver cancer prevalence rates, and the cost of similar cancer therapies, we believe that MB07133, if approved by regulatory authorities, could present a substantial worldwide commercial opportunity.

MB07133

Cytarabine, or araC, is a marketed anti-cancer drug used to treat leukemia. AraC has shown only limited success in solid tumors such as primary liver cancer because the liver lacks a particular protein, or kinase, necessary for converting it to an important intermediate form known as araCMP. MB07133 uses our HepDirect technology to deliver this intermediate form of araC to the liver where it is then readily converted by a different liver kinase into its anti-cancer form, known as araCTP. This approach bypasses the need for the first kinase which the liver lacks. In addition, araC, when systemically delivered is readily converted to araCTP in tissues such as the bone marrow where it can cause toxicity. MB07133 appears to

avoid this potential toxicity because the HepDirect prodrug version of araCMP is not converted to araCTP in tissues outside the liver. We believe the unique ability of MB07133 to deliver araCMP selectively to the liver where it can be readily converted into its anti-cancer form will enhance efficacy while minimizing the toxicities associated with systemic araC therapy.

Clinical Trials

In September 2003 we initiated a Phase 1/2 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. and Hong Kong. This clinical trial was an open label, dose escalation Phase 1/2 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 were eligible to receive up to a total of six infusions of MB07133 per the clinical trial protocol with additional infusions possible by request of each patient's attending physician. This Phase 1/2 clinical trial was designed to assess preliminary safety and tolerability, to identify the maximum tolerated dose and to evaluate indicators of potential efficacy. The results indicated that MB07133 was well tolerated and no drug-related adverse events were noted that limited dosing. A pharmacokinetic analysis was conducted, and the results were consistent with MB07133's expected liver-targeting mechanism. Although this Phase 1/2 clinical trial was not designed to evaluate efficacy, MB07133 showed evidence of anti-tumor activity with some patients showing evidence of tumor shrinkage and disease stabilization at three months. We believe these results indicate that MB07133 may offer an important new treatment for patients with this usually fatal type of cancer for which there are no currently approved drug treatments. The following computer assisted tomography scan image depicts evidence of tumor shrinkage with an observed overall decrease in tumor volume of 30% in one patient (patient number 1008) in the Phase 1/2 clinical trial after that patient had received 8 cycles of treatment with MB07133 over 8 months:

Preclinical 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. 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 araC. 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. The opposite was observed in bone marrow, where araCTP levels were high in the rats treated with araC 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 result in significant improvement in animal toxicology. Mice treated for five days with araC 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 show that relative to araC, MB07133 will deliver therapeutically active levels of araCTP to human primary liver cancer tumors with less toxicity.

Advanced Research Programs Liver Diseases

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 develop and move additional new drug compounds into clinical development. We believe our advanced research programs have the potential to yield additional clinical development candidates.

Our liver disease related advanced research programs are:

A viral enzyme inhibitor program 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 which 2.7 million are chronically infected. Since the discovery of the hepatitis C virus in 1989, many antiviral targets have been identified, and many novel approaches to hepatitis C infection are currently being evaluated. Protease and polymerase enzymes, which are proteins contained within the hepatitis C virus, have been targeted by several successful therapeutic approaches in treating human immunodeficiency virus or HIV, and are becoming the focus of the multiple agents entering clinical development for the treatment of hepatitis C. The polymerase and protease inhibitors have shown to be excellent targets for selective hepatitis C therapy. Clinical studies with a limited number of hepatitis C protease and polymerase inhibitors have demonstrated encouraging early results. However, and not unexpectedly, preclinical and clinical evidence suggests that the hepatitis C virus may become rapidly resistant to protease inhibitors. Consequently, combination therapies of drugs targeting both enzymes may be required.

We have entered into a non-exclusive collaboration with Merck to create liver-targeted prodrugs of certain compounds that Merck is supplying to us. These compounds target the polymerase enzyme structure within the hepatitis C virus residing in the liver. All of our activities under the collaboration were funded by Merck and the two-year, funded research phase of this collaboration has been completed. Merck is currently evaluating certain candidate 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. If a product is successfully developed, Metabasis will receive substantial milestone payments as well as receive a portion of the revenue from sales of the drug in the form of a royalty on net sales.

A second viral enzyme inhibitor program for the treatment of hepatitis C

We have entered into a non-exclusive collaboration with Idenix to create liver-targeted prodrugs of certain compounds that Idenix is supplying to us. All of our activities under the collaboration are being funded by Idenix during the two year, funded research phase of this collaboration. Idenix is solely responsible for conducting and funding all development work for compounds resulting from this collaboration and for commercializing any resulting products. If a product is successfully developed, Metabasis will receive substantial milestone payments as well as receive a portion of the revenue from sales of the drug in the form of a royalty on net sales.

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, MB07133 and MB07811 and will continue to use it in programs focused on the discovery of drugs for liver diseases such as hepatitis C as well as metabolic diseases.

NuMimetic Technology

The liver plays a central role in many metabolic diseases. Metabolic pathways 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 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 now becoming 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 enzyme activity and therefore the rate of flow 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 effectiveness 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.

HepDirect Technology

Developing drugs to treat diseases of the liver and metabolic diseases that involve 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 often 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. In addition, prior approaches to developing therapeutics for metabolic diseases were unable to selectively target pathways in the liver that were believed to play important roles in these diseases. We believe that our liver targeting technologies may be useful in developing therapeutics that selectively target these pathways in the liver and thus reduce the risk of peripheral toxicity due to exposure to tissues outside the liver.

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. We refer to the modified drug as a HepDirect prodrug. The following diagram shows 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-hyperlipidemic 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 collaborations with Merck and Idenix in which we are creating prodrugs of certain compounds to target the hepatitis C virus residing in the liver.

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 five product candidates in clinical development. These product candidates, in order from the most advanced in clinical trials, are pradefovir, CS-917, MB07803, MB07133 and MB07811 indicated for the treatment of hepatitis B, type 2 diabetes, primary liver cancer and hyperlipidemia, respectively. Daiichi Sankyo and Schering-Plough are primarily responsible for further clinical development of CS-917 and pradefovir, respectively. We participate on a joint development team with Schering-Plough. A joint development team with Daiichi Sankyo is in place, though the level of our participation on this team is currently limited. We are currently independently developing MB07803, MB07133 and MB07811.
- *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 develop and move additional new drug compounds into clinical development. We have advanced research programs to develop second-generation TR β agonists to reduce cholesterol and TGs for the management of hyperlipidemia, two programs to develop treatments for hepatitis C infection that we are working on in collaboration with Merck and Idenix, respectively, an advanced research program developing treatments for type 2 diabetes via a mechanism other than those used in our other type 2 diabetes programs and several research programs, one of which is focused on developing drugs that activate AMPK for the treatment for hyperlipidemia and NASH that is being conducted in collaboration with Merck. Using our internal drug discovery capabilities and our proprietary NuMimetic and HepDirect technologies, we intend to discover and develop new drug compounds for the treatment of metabolic diseases and liver diseases. 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 NuMimetic, HepDirect 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. 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 MB07803, MB07133 and MB07811, we are solely responsible for development of these product candidates. 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. MB07803, MB07133 and MB07811 all target markets which are highly sought after by potential pharmaceutical partners. In addition, due to a number of factors, there currently exists a climate of intense competition among large pharmaceutical companies for promising, in-licensable, clinical stage product candidates that target these markets. Therefore, we believe that MB07803, MB07133 and MB07811 will be highly sought after should we seek to further develop these product candidates in collaboration with pharmaceutical partners. Further, our goal for future collaborations is to establish them after we have demonstrated high value for each product candidate, a strategy which we believe will allow us to retain greater control over development and participation in 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, we have entered into non-exclusive collaborations with Merck and Idenix to discover new treatments for hepatitis C by applying our HepDirect technology to compounds that they have supplied to us. We may enter into additional, similar partnerships leveraging our HepDirect technology for this, as well as other, disease indications.
- *Becoming a fully-integrated pharmaceutical company.* We plan to become a fully-integrated pharmaceutical company. In time and as resources allow, we will 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, CS-917 and pradeфовir. In contrast, we have managed the early clinical development of MB07803, MB07133 and MB07811 entirely on our own. We are expanding our internal infrastructure and intend to continue to do so over time as the value of our pipeline grows, and as we further develop products internally.

Strategic Alliances

We use, or plan to use, strategic alliances and collaborative partnerships with pharmaceutical or 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 our current 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.

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 has 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 will have exclusive, worldwide commercialization rights to products developed under the agreement. Daiichi Sankyo selected CS-917 as a clinical candidate in 1999 and initiated Phase 1 clinical trials of CS-917 in July 2001. A joint development team composed of members from both Daiichi Sankyo and Metabasis is in place, though the level of our participation on this team is currently limited. 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 \$20.25 million over the five-year discovery research portion of the collaboration and made an investment of \$7.25 million in our Series A preferred stock. To date, Daiichi Sankyo has 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 \$20.25 million in license fees and sponsored research, the \$7.25 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 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. As a result, we believe that we retain all 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. However, it is possible that Daiichi Sankyo could challenge our rights to independently develop second generation gluconeogenesis inhibitors, including MB07803, a second-generation product candidate currently being independently developed by us. Such a challenge could delay

or prevent the development, partnering and/or commercialization of such product candidates. In addition, because MB07803 may be directly competitive with CS-917 should they both be developed, 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 Daiichi Sankyo does not diligently develop and market CS-917 in a particular country.

Schering-Plough

In October 2001, we entered into a development and license agreement with Valeant for the development and commercialization of pradefovir. In January 2007, Valeant with our consent assigned its rights, interests and obligations under the development and license agreement to Schering-Plough and further granted Schering-Plough a license to its intellectual property related to pradefovir. Concurrently, we and Schering-Plough entered into an amended and restated development and license agreement for the continued future development and commercialization of pradefovir. Under the amended and restated development and license agreement and pursuant to Valeant's assignment, Schering-Plough was granted exclusive worldwide rights to develop and commercialize pradefovir during the term of the agreement. Valeant paid us a license fee of \$2 million and made milestone payments of \$2 million under the original agreement. Schering-Plough paid us a non-refundable license fee of \$1.8 million in January 2007 and will be obligated to make future milestone payments to us upon the occurrence of specified development, regulatory and commercial milestones as well as royalties on sales of products resulting from the collaboration. If all development, regulatory and commercial milestones are achieved, and including the \$1.8 million non-refundable license fee, we may be entitled to payments which total up to \$25 million, plus royalties under the agreement with Schering-Plough. In addition, Schering-Plough is solely responsible for conducting and funding all development work. We participate on a joint development team with Schering-Plough.

The term of the development and license agreement will continue until all of Schering-Plough'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 for material breach of the other party which remains uncured. Schering-Plough has the sole right to terminate the agreement in its entirety or in certain countries by providing at least 180 days written notice to us.

Merck

In December 2003, we entered into a collaboration agreement with Merck to discover new treatments for hepatitis C. Under this collaboration, we created liver-targeting prodrugs of certain compounds that Merck supplied to us. These compounds target the polymerase enzyme structure within 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 of \$1.4 million per year during the two year research term. Merck is also obligated to pay preclinical and clinical milestone payments if specified development and regulatory events occur and royalties on sales of products resulting from the collaboration. If all preclinical 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 \$25.3 million, plus royalties. Merck is currently evaluating certain candidate 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 the collaboration and for commercializing any resulting products.

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 NASH 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 preclinical 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.

Idenix

In October 2006, we entered into a collaboration agreement with Idenix to apply our HepDirect technology to certain Idenix lead compounds with the goal of improving the safety and efficacy of these compounds for the treatment of hepatitis C. The research term will be for two years and may be extended beyond two years by mutual agreement of the parties. In addition, Idenix will have the option to terminate the research term upon the first anniversary of the effective date of the agreement or upon the achievement of certain preclinical and clinical development milestones during the research term. As part of this collaboration, Idenix paid us an initial, non-refundable license fee of \$2.0 million in November 2006 and agreed to provide us research funding of up to \$1.7 million per year during the research term. Idenix will also pay us milestones if specified preclinical and clinical development and regulatory events occur and royalties on product sales that result from the collaboration. If all milestones are achieved, and including the \$2.0 million license fee and the up to \$1.7 million per year in research funding over the term, we may be entitled to payments which total up to \$68.8 million, plus royalties. Idenix 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 Idenix'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. Idenix also has the right to terminate the agreement without cause after the expiration or early termination of the research term upon 60 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 are covered by a claim of an issued, valid and unexpired patent or a patent application, that was in existence or based on any 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 of our current product candidates and drug compounds from our research programs may be subject to these royalty provisions. The determination of any potential obligations will be assessed at the time such products are commercially available.

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 22, 2007 we owned a total of 36 issued U.S. patents, 3 allowed U.S. applications and 27 pending U.S. applications. In foreign countries, as of the same date, we owned a total of 148 issued patents and 232 pending applications. As of the above date, we co-owned 2 pending U.S. applications and 4 foreign granted applications. As of the same date, we held rights to a total of 4 in-licensed U.S. patents.

We believe we have a strong intellectual property position, including 16 issued U.S. patents, 3 allowed U.S. applications, 25 pending U.S. applications, 107 foreign issued patents and 227 foreign pending applications that relate to proprietary technologies and compounds used in our current business. Patents and patent applications, if they issue as patents, in the U.S. that cover our compounds currently in clinical development will expire as follows: CS-917, December 2020; MB07803, August 2025; pradeфовir, May 2023; MB07133, October 2023; and, MB07811, November 2024. The preceding patent term expirations do not include possible patent term extensions.

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, as well as consultants and advisors when appropriate, 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 Schering-Plough worldwide marketing and commercialization rights for CS-917 and pradeфовir, respectively. However, we have retained a co-promotion option to directly market CS-917 in North America. In addition, at this point we have not entered into collaborative partnerships for MB07803, MB07133 and MB07811 and are currently independently developing these product candidates.

We may either independently market, or collaborate with third parties to further develop and market some or all of these product candidates in the future. We currently retain all rights to compounds from our research programs, with the exception of hepatitis C and metabolic disease product candidates that are covered by our hepatitis C and AMPK collaborations with Merck and hepatitis C product candidates that are covered by our collaboration with Idenix.

We intend to make decisions regarding independent 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 independent marketing of any product candidates, we anticipate building a sales force designed to call on specialists that would be expected to prescribe a significant portion of the 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 inhibits liver glucose production like CS-917 and MB07803, but does so through an unknown mechanism other than inhibition of gluconeogenesis. Because it does not cause weight gain, metformin is often prescribed as a first-line therapy to obese type 2 diabetes patients, who are reported to comprise more than 90% of newly diagnosed type 2 subjects. In addition, inexpensive generic forms of metformin are available.

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 insulin, the naturally occurring hormone made by the pancreas to control blood glucose levels,
- **peroxisome proliferator-activated receptor agonists, or PPARs** improve insulin sensitivity by activating certain genes involved in fat synthesis and carbohydrate metabolism,
- **incretin mimetics** lower glucose levels by increasing the levels of certain naturally occurring hormones from the pancreas, including glucagon-like peptide-1 or GLP-1, a peptide that facilitates the response of the pancreas and liver to fluctuations in glucose levels by its action on pancreatic beta and alpha cells. Compounds in this class include dipeptidyl peptidase IV or DPP-IV inhibitors, and BYETTA[®] (exenatide) injection. DPP-IV is an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-IV thus increases the half-life of endogenous GLP-1 by preventing cleavage and inactivation of GLP-1. BYETTA is an injectable medication that exhibits many of the same glucose regulating actions of GLP-1. The overall effect of these compounds is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion,
- **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
- **combination therapies** combine metformin with members of several of the above-mentioned classes, particularly sulfonylureas and PPARs.

In addition, many companies are developing novel therapies that target diabetes.

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

- **interferons** mimic interferon, the naturally occurring 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 may 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 may directly compete. 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. Nexavar (sorafenib), a chemotherapy approved for the treatment of kidney cancer, is being evaluated for the treatment of primary liver cancer. The drug's developer, Bayer Healthcare Pharmaceuticals, recently announced that an ongoing Phase 3 clinical trial of Nexavar for the treatment of primary liver cancer was stopped early because the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar tablets versus those patients receiving placebo. Therefore it is likely that Nexavar will be approved for the treatment of patients with primary liver cancer and it is expected that it will experience significant off-label use prior to its approval. Still, even with the availability of Nexavar we believe the disease will remain poorly treated and that an agent with a different mechanism of action like MB07133, if approved, could find wide usage.

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 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 lower cholesterol and triglycerides, decrease low density lipoproteins and increase high density lipoproteins,
- CAIs 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 and 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.

Manufacturing

Daiichi Sankyo and Schering-Plough are responsible for all clinical and commercial manufacturing of CS-917 and pradefovir, respectively. We rely on several suppliers to produce sufficient quantities of MB07803, MB07133 and MB07811 for use in clinical trials. We currently intend to continue this practice for any future clinical trials and the possible large-scale commercialization of MB07803, MB07133 and MB07811 and for any other potential products that we independently develop and commercialize. 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

Our metabolic disease product candidates, CS-917, MB07803 and MB07811; our liver disease product candidates, pradefovir and MB07133; and any other product candidates that we or our collaborators develop will require regulatory approval during clinical development and before they can be commercialized. Daiichi Sankyo and Schering-Plough are responsible for clinical development and regulatory approval of CS-917 and pradefovir, respectively. We actively participate on a joint development team with Schering-Plough. While a joint development team with Daiichi Sankyo is in place, our participation on this team is currently limited. Although our collaborations with Merck and Idenix have not yet yielded product candidates, should they be successful, we will be dependent on Merck and/or Idenix, as applicable, for clinical development and regulatory approval of any resulting product candidates. We are solely responsible for clinical development and regulatory approval of MB07803, MB07133 and MB07811.

Product Regulation

Governmental authorities in the U.S. and foreign countries regulate, among other things, the preclinical 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 preclinical 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 preclinical laboratory tests and preclinical 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 preclinical 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.

Preclinical 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 preclinical safety tests must be conducted in compliance with FDA's GLP and similar international regulations. The results of the preclinical 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 1, 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 2 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 2b study. Phase 3 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. Some clinical trials that combine elements of two Phases may be referred to as a Phase 1/2 or a Phase 2/3 clinical trial. Phase 1, Phase 2 or Phase 3 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 preclinical 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 affect 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 preclinical 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 preclinical 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 ANDA 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 ANDAs 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 March 1, 2007, we employed 127 full-time employees, consisting of 95 employees in research, development and regulatory affairs and 32 in management, administration, finance, receiving and facilities. As of the same date, 41 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 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 metabolic disease product candidates, CS-917, MB07803 and MB07811, and our liver disease product candidates, pradefovir and MB07133. Clinical trials conducted to date in patients treated with CS-917 and 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 trials designed to provide clinical and statistically significant 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 preclinical 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 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 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, 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 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, 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 our metabolic disease product candidates CS-917, MB07803 and MB07811, our liver disease product candidates pradefovir and MB07133, 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 3 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 preclinical 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 CS-917 have been, and will continue to be, primarily established by Daiichi Sankyo. The targeted endpoints for clinical trials of pradefovir have been primarily established by Valeant and, in the future, will be primarily established by Schering-Plough. We are solely responsible for establishing the targeted endpoints for clinical trials of MB07803, MB07133 and MB07811. 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, preclinical 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 preclinical 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 2 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 product candidates 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 1 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 the time were stopped while one Phase 1 clinical trial which did not combine CS-917 with metformin continued and was completed. After extensive analysis Daiichi Sankyo concluded that the lactic acidosis observed in the two patients was likely due to significantly increased blood levels of metformin. The reason for the increase in metformin blood levels observed in these two patients has not been determined. At high blood levels, metformin is believed to cause a form of cellular toxicity known as mitochondrial toxicity which can cause lactic acidosis. Subsequently, Daiichi Sankyo decided that clinical trials of CS-917 could safely resume.

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 use of CS-917 in combination with 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 the use of CS-917 in 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 1 clinical trials of our second-generation product candidate for type 2 diabetes, MB07803, which works by the same mechanism as CS-917 and thus may be subject to some or all of the same risks described previously for CS-917.

It is also possible that CS-917 and MB07803 may cause other side effects. In certain preclinical 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 of CS-917 tested to date in patients (400 milligrams twice a day). This dose is above what is expected to be used in Phase 3 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 preclinical 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 any of prafefovir, MB07133 or MB07811. 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.

MB07811 is a HepDirect prodrug of a potent TRB agonist discovered by us. Thyroid hormone and thyroid hormone mimetics are known to exhibit a wide array of physiological actions involving a variety of organs that can be assessed in preclinical animal studies. Both beneficial and undesirable effects can be inferred from studies of humans with hyperthyroidism (elevated thyroid hormone). The development of liver-selective thyroid receptor modulators for the treatment of hyperlipidemia is a novel approach seeking to exploit the beneficial hepatic effects while avoiding toxicities related to systemic exposure of thyromimetic agents. Successful development of MB07811 will require finding a dose range in humans that provides adequate benefit and an acceptable safety profile.

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

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We have entered into collaborations with Daiichi Sankyo and Schering-Plough for the development and commercialization of CS-917 and pradefovir, respectively. Daiichi Sankyo and Schering-Plough have

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agreed to finance the clinical trials for CS-917 and pradeфовir, respectively, and, if they are approved, manufacture and market them. Accordingly, we are currently dependent on Daiichi Sankyo and Schering-Plough to gain FDA and other foreign regulatory agency approval of, and to commercialize, CS-917 and pradeфовir. We have also entered into two collaborations with Merck and a collaboration with Idenix. 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 NASH. Our collaboration with Idenix seeks to develop and commercialize new products for the treatment of hepatitis C infection. Although our collaborations with Merck and Idenix have not yet yielded any product candidates, should they ultimately be successful, we will be dependent on Merck and/or Idenix, as applicable, 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 MB07803, MB07133 and MB07811, we may need to enter into additional collaborative agreements to assist in the development and commercialization of some or all of these product candidates. 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 Daiichi Sankyo, Schering-Plough, Merck, Idenix 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 may 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 clinical trials of MB07803, a second-generation gluconeogenesis inhibitor 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. In addition, the past and/or any future transfer to us of confidential information and data related to CS-917 may increase the risk of claims based on our access to this information and data. It is possible that Daiichi Sankyo could challenge our rights to independently develop second generation gluconeogenesis inhibitors, including MB07803, which may delay or prevent the development, partnering and/or commercialization of such product candidates.

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 provided by Merck. 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 NASH 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. Similarly, our agreement with Idenix to develop and commercialize new products to treat hepatitis C infection may include the development of compounds owned or controlled by Idenix. Accordingly, if Idenix 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 Daiichi Sankyo, Schering-Plough, Merck, Idenix 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 independently pursuing the development and/or commercialization of product candidates, 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. Our goal is to expand our clinical development pipeline by continuing to develop and move additional new drug compounds into 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 compounds suitable for recommendation for clinical development. Moreover, any drug compounds we recommend for clinical development may not demonstrate, through preclinical 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 trials could result in increased costs to us and delay our ability to generate significant revenues.

Delays in the commencement or completion of clinical trials 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 related to:

- 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 or other materials necessary to conduct the clinical trial,
- obtaining institutional review board approval to conduct a clinical trial at a prospective site,
- recruiting and enrolling patients to participate in a clinical trial, and
- the failure of our collaborators to adequately resource our product candidates due to their focus on other programs or as a result of general market conditions.

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. 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.

Daiichi Sankyo and Schering-Plough are currently responsible for conducting clinical trials of CS-917 and pradefovir, respectively. Although our collaborations with Merck and Idenix have not yet yielded product candidates, should they be successful, we will be dependent on Merck and/or Idenix, as applicable, 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 MB07803, MB07133, MB07811 and any other product candidates that we may develop for which a collaborator is not responsible for clinical development. If Daiichi Sankyo, Schering-Plough, Merck, Idenix 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 NuMimetic technology to identify CS-917 and MB07803. We used our HepDirect technology to discover pradefovir, MB07133, MB07811 and have applied it in certain other programs as well. 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 collaborations with Merck and

Idenix in which we are applying our technology to certain Merck and Idenix 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 preclinical 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 marketed products include, but are not limited to the following classes:

- metformin a member of the biguanide drug class, related to guanidine and currently is the most widely prescribed first line therapy 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 insulin, the naturally occurring hormone made by the pancreas to control blood glucose levels,
- PPARs improve insulin sensitivity by activating certain genes involved in fat synthesis and carbohydrate metabolism,
- incretin mimetics lower glucose levels by increasing the levels of certain naturally occurring hormones from the pancreas, including glucagon-like peptide-1 or GLP-1, a peptide that facilitates the response of the pancreas and liver to fluctuations in glucose levels by its action on pancreatic beta and alpha cells. Compounds in this class include dipeptidyl peptidase IV or DPP-IV inhibitors, and BYETTA[®] (exenatide) injection. DPP-IV is an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-IV thus increases the half-life of endogenous GLP-1 by preventing cleavage and inactivation of GLP-1. BYETTA is an injectable medication that exhibits many of the same glucose regulating actions of GLP-1. The overall effect of these compounds is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion,
- 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
- combination therapies combines metformin with members of several of the above-mentioned classes, particularly sulfonylureas and PPARs.

Metformin is a drug that inhibits liver glucose production like CS-917 and MB07803 but does so through an unknown mechanism. Because it does not cause weight gain, metformin is often prescribed as a first line therapy to obese patients with type 2 diabetes, who are reported to comprise more than 90% of patients newly diagnosed with type 2 diabetes. Generic forms of metformin have recently become available. Accordingly, unless CS-917 and MB07803 demonstrate significant benefits when compared to 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 to market CS-917 or 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 to restrict 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 MB07803.

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 marketed products include, but are not limited to the following classes:

- **interferons** mimic interferon, the naturally occurring infection-fighting immune substance produced by the body,
- **nucleoside analogues** chemically engineered nucleoside compounds that are converted inside cells into other compounds that are structurally similar to the building blocks of DNA and RNA that interfere with the replication of HBV, and
- **nucleotide analogues** chemically engineered nucleotide compounds that are converted inside cells into other compounds that are structurally similar to the building blocks of DNA and RNA that interfere with the replication of HBV.

A competitor to pradefovir may be Hepsera (adefovir dipivoxil), which is a nucleotide analogue currently marketed in the U.S. and Europe by Gilead Sciences, Inc. Pradefovir and Hepsera are prodrugs of the same active drug, and therefore may 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, some companies are developing novel therapies specifically for primary liver cancer. Nexavar (sorafenib), a chemotherapy approved for the treatment of kidney cancer, is being evaluated for the treatment of primary liver cancer. The drug's developer, Bayer, recently announced that an ongoing Phase 3 clinical trial of Nexavar for the treatment of primary liver cancer was stopped early because the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar tablets versus those patients receiving placebo. Therefore it is likely that Nexavar will be approved for the treatment of patients with primary liver cancer and it is expected that it will experience significant off-label use prior to its approval.

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 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** lower cholesterol, triglycerides and low density lipoproteins and increase high density lipoproteins,
- **CAIs** 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.

Several 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 and 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, preclinical 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 trials and eventual commercialization. Daiichi Sankyo and Schering-Plough are currently responsible for all clinical and commercial manufacturing of CS-917 and pradefovir, respectively. We have relied on a number of suppliers to manufacture sufficient quantities of MB07803, MB07133 and MB07811 for use in our current clinical trials. Although our suppliers have manufactured other companies' products on a commercial scale, we have not yet determined if they are capable of manufacturing our products on a commercial scale. 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 MB07803, MB07133 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 MB07803, MB07133 or MB07811 may impede the clinical trials of these compounds.

In addition, we, our collaborators or other third-party manufacturers of our products must comply with current good manufacturing practices, or 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. Daiichi Sankyo and Schering-Plough are currently responsible for worldwide marketing and commercialization for CS-917 and pradefovir, 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). Similarly, should our hepatitis C collaboration with Idenix be successful, Idenix will be responsible for worldwide marketing and commercialization of any resulting product candidates. In order to co-promote any of these products, or to commercialize MB07803, MB07133, 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 U.S. 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 type 2 diabetes patients with kidney dysfunction. In addition, CS-917 and HepDirect prodrugs such as pradeфовir, MB07133 and MB07811 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 1 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. While MB07803 has not demonstrated the same metformin interaction risk in clinical trials to date, it may exhibit the same metformin interaction risk and thus may be subject to the same market potential limitations as CS-917. 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 provides a 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 127 as of March 1, 2007. 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, 2006, we had an accumulated deficit of approximately \$108.2 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, grants 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 may raise additional funds through public or private equity offerings, our committed equity financing facility, or CEFF, with Kingsbridge Capital Limited, debt financings, grants or corporate collaboration and licensing arrangements. For example, we have an effective shelf registration statement on file with the Securities and Exchange Commission 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. To date, we have sold approximately \$40 million of our common stock under this registration statement. We have also filed a registration statement with the Securities and Exchange Commission covering the resale

of shares issuable under the CEFF though to date, no shares have been issued under this registration statement. We may sell additional 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,
- our execution of collaborative, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements, and
- changes in the use assumptions or the use of different valuation methods in the application of SFAS No. 123R in future periods.

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.

Our committed equity financing facility with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout or other payments to Kingsbridge and may result in dilution to our stockholders.

In November 2006, we entered into the CEFF with Kingsbridge. The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of 36 months, shares of our common stock for cash consideration up to an aggregate of \$50.0 million, subject to specified conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless specified conditions are met, which include a minimum price for our common stock; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; and the effectiveness of a registration statement registering for resale the shares of common stock to be issued in connection with the CEFF. In addition, among other termination rights, Kingsbridge is permitted to terminate the CEFF by providing written notice to us within 10 business days after it obtains actual knowledge that an event has occurred resulting in a material and adverse effect on our business, operations, properties or financial condition (subject to specified exceptions, including conditions or events that are reasonably expected to occur in the ordinary course of our business). If we are unable to access funds through the CEFF, or if Kingsbridge terminates the CEFF, we may be unable to access capital on favorable terms, or at all.

We are entitled, in certain circumstances, to deliver a "blackout" notice to Kingsbridge to suspend the use of this prospectus and prohibit Kingsbridge from selling shares under this prospectus for a certain period of time. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement of which this prospectus is a part is not effective in circumstances not permitted by our registration rights agreement with Kingsbridge, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of a specified number of shares held by Kingsbridge immediately prior to the blackout period and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the resale registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effect on the holdings of our current stockholders and may result in downward pressure on the price of our common stock. If we draw down amounts under the CEFF, we will issue shares to Kingsbridge at a discount of up to 10% from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our stock price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining stock price will have an even greater dilutive effect than if our stock price were stable or increasing and may further decrease our stock price.

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 HBV 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. 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, in March 2005 two cases of lactic acidosis were 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 to restrict 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. While 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, we

do carry separate pollution legal liability coverage that is intended to cover third party claims for bodily injury, property damage and remediation costs. However, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our insurance and/or 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 Daiichi Sankyo, Schering-Plough, Merck, Idenix 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, have resulted in increased costs to us which are likely to continue and may further increase 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 this annual report on Form 10-K we are 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 requirements including internal control reforms, if any, and how independent auditors are applying these 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 68% of our common stock as of December 31, 2006. 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 4,057,176 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. Under the CEFF, Kingsbridge is committed to purchase up to \$50 million of our common stock over a 36 month period. Sales by these current and potential future 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 Stock 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 Stock Market for the periods indicated.

| | High | Low |
|-------------------------------------|---------|---------|
| Year Ended December 31, 2006 | | |
| Fourth Quarter | \$ 8.39 | \$ 5.15 |
| Third Quarter | \$ 8.29 | \$ 5.05 |
| Second Quarter | \$ 9.30 | \$ 7.45 |
| First Quarter | \$ 9.79 | \$ 7.66 |
| 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 |

As of March 5, 2007, there were 121 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.

Equity Compensation Plan Information

The following table provides certain information as of December 31, 2006, with respect to all of our equity compensation plans in effect on that date.

| | Number of securities to be issued upon exercise of outstanding options, warrants and rights (a) | Weighted-average exercise price of outstanding options, warrants and rights (b) | Number of securities remaining available for issuance under equity compensation plans (excluding securities reflected in column (a)) (c) |
|---|--|--|--|
| Equity compensation plans approved by stockholders(1) | 6,695,459 | \$ 4.70 | 1,840,474 |
| Equity compensation plans not approved by stockholders(2) | | | |
| Total | 6,687,459 | \$ 4.70 | 1,840,474 |

(1) Includes our Amended and Restated 2001 Equity Incentive Plan, our 2004 Non-Employee Directors' Stock Option Plan and our 2004 Employee Stock Purchase Plan. 688,512 shares under column (c) are attributable to our 2004 Employee Stock Purchase Plan.

(2) As of December 31, 2006, we did not have any equity compensation plans that were not approved by our stockholders.

Performance Graph

The material in this section is not soliciting material, is not deemed filed with the Securities and Exchange Commission, and is not to be incorporated by reference into any filing of Metabasis under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

The following graph compares the cumulative 30-month total return to stockholders on our common stock relative to the cumulative total returns of the Nasdaq Composite index and the Nasdaq Biotechnology index. The graph assumes all dividends have been reinvested (to date, we have not declared any dividends). The stock price performance included in the graph is not necessarily indicative of future stock price performance.

**COMPARISON OF 30-MONTH CUMULATIVE TOTAL RETURN*
Among Metabasis Therapeutics, Inc., the Nasdaq Composite Index
and the Nasdaq Biotechnology Index**

* \$100 invested on 6/16/04 in stock or on 5/31/04 in index, including reinvestment of dividends. Fiscal year ending December 31.

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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 annual report on Form 10-K.

| | Years Ended December 31, | | | | |
|---|--------------------------|--------------|--------------|--------------|--------------|
| | 2006 | 2005 | 2004 | 2003 | 2002 |
| (In thousands, except per share amounts) | | | | | |
| Statements of Operations Data: | | | | | |
| Revenue | \$ 4,386 | \$ 3,771 | \$ 6,837 | \$ 9,124 | \$ 2,278 |
| Total operating expenses | 41,195 | 28,438 | 22,112 | 18,507 | 15,163 |
| Loss from operations | (36,809) | (24,667) | (15,275) | (9,383) | (12,885) |
| Other income (expense), net | 3,541 | 1,087 | 303 | (46) | 88 |
| Net loss(1) | (33,268) | (23,580) | (14,972) | (9,429) | (12,797) |
| Preferred stock deemed dividend(2) | | | | (24,900) | |
| Net loss applicable to common stockholders | \$ (33,268) | \$ (23,580) | \$ (14,972) | \$ (34,329) | \$ (12,797) |
| Basic and diluted net loss per share(1) | | | | | |
| Historical | \$ (1.15) | \$ (1.20) | \$ (1.49) | \$ (23.84) | \$ (10.12) |
| Proforma | | | \$ (0.98) | \$ (3.74) | |
| Shares used to compute basic and diluted net loss per share | | | | | |
| Historical | 29,019 | 19,706 | 10,034 | 1,440 | 1,265 |
| Proforma | | | 15,254 | 9,187 | |

(1) 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.

(2) Our Series E preferred stock financing, which closed in October 2003, involved the sale of our Series E preferred stock at a price per share below the initial public offering price of our common stock contemplated in our 2004 initial public filing. Accordingly, pursuant to Emerging Issues Task Force, or EITF, 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, in 2003 we recorded a deemed dividend on our Series E preferred stock of \$24.9 million, which was the difference between the gross proceeds from our Series E preferred stock financing 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 our Series E 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*, we calculated the deemed dividend of \$24.9 million using the most favorable conversion price of \$3.12 per conversion share.

| | As of December 31, | | | | |
|--|--------------------|-----------|-----------|-----------|-----------|
| | 2006 | 2005 | 2004 | 2003 | 2002 |
| | (In thousands) | | | | |
| Balance Sheet Data: | | | | | |
| Cash, cash equivalents and securities available-for-sale | \$ 77,923 | \$ 66,893 | \$ 43,855 | \$ 25,257 | \$ 19,562 |
| Working capital | 69,388 | 60,146 | 40,906 | 22,342 | 13,693 |
| Total assets | 85,855 | 73,878 | 47,860 | 29,110 | 21,733 |
| Long-term obligations (including current portion) | 5,760 | 3,168 | 2,226 | 1,820 | 2,854 |
| Accumulated deficit | (108,213) | (74,945) | (51,365) | (36,393) | (26,964) |
| Total stockholders equity | 68,138 | 59,582 | 41,864 | 23,437 | 8,756 |

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 by applying our proprietary technology, scientific expertise and unique capabilities for targeting the liver and liver pathways. These diseases include metabolic diseases such as diabetes, obesity, and hyperlipidemia, among others, and liver diseases such as hepatitis and primary liver cancer. We have established a broad and growing product pipeline of product candidates and advanced research programs targeting large markets with significant unmet medical needs. We have discovered all of our product candidates internally using our proprietary technologies.

We currently have five product candidates in clinical trials. These five product candidates, by category, and in order from the most advanced in clinical trials within each category, are as follows:

Product Pipeline Metabolic Diseases

| Product Candidates/Programs(1) | Disease/Condition | Partner | Our Commercial Rights | Status |
|--------------------------------|-------------------|----------------|---|----------|
| CS-917 | Diabetes | Daiichi Sankyo | Royalties, North America Co-promotion Option | Phase 2b |
| MB07803 | Diabetes | None | Worldwide | Phase 1 |
| MB07811 | Hyperlipidemia | None | Worldwide | Phase 1 |

Product Pipeline Liver Diseases

| Product Candidates/Programs(1) | Disease/Condition | Partner | Our Commercial Rights | Status |
|--------------------------------|----------------------|-----------------|-----------------------|---------------------|
| Pradefovir | Hepatitis B | Schering-Plough | Royalties | Phase 2b completed |
| MB07133 | Primary Liver Cancer | None | Worldwide | Phase 1/2 completed |

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

We have incurred annual net losses since inception. As of December 31, 2006, our accumulated deficit was approximately \$108.2 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, our private placement of common stock and warrants in October 2005 and our registered direct offering of common stock in March 2006, 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, equity investments from our collaborative partners and, to a lesser extent, the sale of common stock through our stockholder approved equity incentive plans. 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. 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 Schering-Plough. We do not have collaborative partnerships for MB07803, MB07133 or MB07811 and are currently independently developing these product candidates. We retain worldwide commercialization rights to all of the compounds generated from our current research programs, with the exception of product candidates covered by our collaborations with Merck and Idenix. 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 preclinical 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 cash and stock-based compensation and other expenses for research and development personnel, costs associated with preclinical 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 MB07803, MB07133 and MB07811. In addition, research and development activities include work on a variety of compounds in our other discovery research programs. We are responsible for all costs incurred for these product and clinical candidates and in our discovery research programs with the exception of the AMPK and hepatitis C programs partnered with Merck and our hepatitis C program partnered with Idenix. Under the terms of our collaboration agreements with Merck, we had received approximately

\$6.5 million in sponsored research funding through December 31, 2006. Daiichi Sankyo and Schering-Plough are responsible for the costs of clinical development of CS-917 and pradefovir, 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. Other than costs for outsourced services associated with our clinical programs, we generally do not track our research and development expenses by project; rather, we track such expenses by the type of cost incurred. 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 1 clinical trials can be expected to last from 6 to 18 months, Phase 2 clinical trials can be expected to last from 12 to 24 months and Phase 3 clinical trials can be expected to last from 18 to 36 months. However, clinical development timelines vary widely, as do the total costs of clinical trials and the likelihood of success. Although we are currently focused primarily on advancing MB07803, MB07133 and MB07811 through 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, our ongoing assessment of its market potential and considering our available financial resources.

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, stock-based compensation and other related costs for personnel in executive, finance, accounting, business development, investor relations, information systems, legal and human resource functions. Other costs include facility costs not otherwise included in research and development expenses, depreciation and professional fees for legal and accounting services.

We anticipate continued increases in general and administrative expenses to support our expanding research and development activities and 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 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, No. 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:

- 1) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, and
- 2) 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 sponsored research funding are recognized as revenues as the services are performed. Amounts received for sponsored 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.

Stock-Based Compensation. We grant equity based awards under three stockholder-approved share-based compensation plans. We may grant options and restricted stock awards to employees, directors and consultants under our Amended and Restated 2001 Equity Incentive Plan. We also grant awards to non-employee directors under our 2004 Non-Employee Directors Stock Option Plan. All of our employees are eligible to participate in our 2004 Employee Stock Purchase Plan which provides a means for employees to purchase common stock at a discount through payroll deductions. The benefits provided under all of these plans are subject to the provisions of revised Statement of Financial Accounting Standards, or SFAS, No. 123, *Share-Based Payment*, which we adopted effective January 1, 2006. We elected to use the modified

prospective application in adopting SFAS No. 123R and therefore have not restated results for prior periods. The valuation provisions of SFAS No. 123R apply to new awards and to awards that are outstanding on the adoption date and subsequently modified or cancelled. Our results of operations for fiscal 2006 were impacted by the recognition of non-cash expense related to the fair value of our share-based compensation awards. Share-based compensation expense recognized as a result of adoption of SFAS No. 123R for the year ended December 31, 2006 was \$1.9 million. As of December 31, 2006, we had approximately \$7.6 million of unrecognized compensation expense which we expect to recognize over a weighted average period of 1.8 years.

We estimate the fair value of stock options granted using the Black-Scholes Merton, or Black-Scholes option valuation model. This fair value is then amortized over the requisite service periods of the awards. The Black-Scholes option valuation model requires the input of subjective assumptions, including the option's expected life and price volatility of the underlying stock. Expected volatility is based on the weighted average volatility of our stock factoring in daily share price observations and the historical price volatility of certain peers within our industry sector. In computing expected volatility, the length of the historical period used is equal to the length of the expected term of the option and the share purchase right. The expected life of employee stock options represents the average of the contractual term of the options and the weighted average vesting period, as permitted under the simplified method, under Staff Accounting Bulletin No. 107.

As stock-based compensation expense is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. SFAS No. 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures were estimated based on historical experience. We may elect to use different assumptions under the Black-Scholes option valuation model in the future, which could materially affect our net loss and net loss per share. In our pro forma information required under SFAS No. 123, *Accounting for Stock-Based Compensation*, for the periods prior to fiscal 2006, we accounted for forfeitures as they occurred. We had a deferred stock compensation balance of \$3.3 million at December 31, 2005 for options previously issued with an exercise price less than the fair market value of the shares on the date of grant which was eliminated against additional paid-in-capital as a result of adoption of SFAS No. 123R.

Recently Issued Accounting Pronouncements

In February 2006, the Financial Accounting Standards Board, or FASB, issued SFAS No. 155, *Hybrid Instruments*. The statement amends SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities*, and SFAS No. 140, *Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities*. The statement also resolves issues addressed in Statement 133 Implementation Issue No. D1, *Application of Statement 133 to Beneficial Interests in Securitized Financial Assets*. The statement: permits fair value remeasurement for any hybrid financial instrument that contains an embedded derivative that otherwise would require bifurcation; clarifies which interest-only strips and principal-only strips are not subject to the requirements of SFAS No. 133; establishes a requirement to evaluate interests in securitized financial assets to identify interests that are freestanding derivatives or that are hybrid financial instruments that contain an embedded derivative requiring bifurcation; clarifies that concentrations of credit risk in the form of subordination are not embedded derivatives; and amends SFAS No. 140 to eliminate the prohibition on a qualifying special purpose entity from holding a derivative financial instrument that pertains to a beneficial interest other than another derivative financial instrument. We do not believe the adoption of this standard will have an impact on our results of operations or financial position.

In July 2006, the FASB issued Interpretation No., or FIN, 48, *Accounting for Uncertainty in Income Taxes*. This interpretation requires that we recognize in our financial statements, the impact of a tax position, if that position is more likely than not of being sustained on audit, based on the technical merits

of the position. The provisions of FIN 48 are effective for fiscal years beginning after December 15, 2006, with the cumulative effect of the change in accounting principle recorded as an adjustment to retained earnings. We are currently evaluating the impact of FIN 48 on our financial statements, but we do not believe compliance with this guidance will have a significant impact on our results of operations or financial position.

In September 2006, the Securities and Exchange Commission released SAB No. 108, *Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements*. SAB No. 108 provides interpretive guidance on the Securities and Exchange Commission's views regarding the process of quantifying materiality of financial statement misstatements. SAB No.108 is effective for fiscal years ending after November 15, 2006 (beginning with our 2006 fiscal year). The adoption of this statement did not have a material impact on our results of operations or financial position.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*. This standard defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles and expands disclosures about fair value measurements. This statement is effective for financial statements issued for fiscal years beginning after November 15, 2007 (beginning with our 2008 fiscal year), although earlier application is encouraged. We have not begun evaluating the impact of adopting SFAS No. 157 on our results of operation or financial position, however, we intend to evaluate the impact of adoption of this standard during fiscal 2007.

Results of Operations

Please refer to Note 1 to our financial statements for discussion of the reclassification of previously reported financial statements within research and development and general and administrative costs.

Comparison of the Years Ended December 31, 2006 and 2005

Revenues. Revenues were \$4.4 million for the year ended December 31, 2006, compared with \$3.8 million for the year ended December 31, 2005. The \$600,000 increase was mainly due to increased license fee and sponsored research revenues of approximately \$1.8 million from our AMPK collaboration with Merck, which began in the second half of 2005. This increase was partially offset by a decrease of \$1.4 million in sponsored research revenues from our hepatitis C collaboration with Merck, the research portion of which was completed in 2005. We expect an increase in sponsored research revenues in 2007 compared to 2006 as we begin efforts under the sponsored research portion of our agreement with Idenix and continue efforts under our AMPK collaboration with Merck. In addition, we expect an increase in license fee revenue in 2007 as a result of the up-front license fee we received from Schering-Plough and our hepatitis C collaboration with Idenix.

Research and Development Expenses. Research and development expenses were \$30.3 million for the year ended December 31, 2006, compared with \$21.3 million for the year ended December 31, 2005. The \$9.0 million increase was mainly due to increased spending of \$3.2 million in payroll and related benefits as a result of a higher average number of employees in 2006, a \$2.9 million increase in clinical development expense for MB07803, MB07133 and MB07811, a \$2.1 million increase in occupancy costs related to our new facility, increased travel, supplies and insurance expense and an increase of \$800,000 in stock-based compensation expense. We expect continued increases in research and development costs as we continue to advance MB07803, MB07133 and MB07811 through clinical development.

General and Administrative Expenses. General and administrative expenses were \$10.9 million for the year ended December 31, 2006, compared with \$7.2 million for the year ended December 31, 2005. The \$3.7 million increase primarily relates to an increase of \$1.3 million in professional services related to legal costs associated with patent and corporate related matters and consulting services, increased stock-based compensation expense of \$1.2 million as a result of the implementation of SFAS No. 123R, higher payroll

and related benefits costs of \$800,000 as a result of a higher average number of employees in 2006 and increased travel, occupancy and public company costs of \$400,000. We anticipate continued increases in general and administrative expenses for investor relations and other activities associated with operating as a publicly-traded company.

Net Interest Income. Net interest income was \$3.5 million for the year ended December 31, 2006, compared to net interest income of \$1.1 million for the year ended December 31, 2005. The \$2.4 million increase was due to increased interest income as a result of higher average cash balances for the twelve months ended December 31, 2006 as compared to the same period in 2005 as well as increased yields on investments. Our average cash balances were higher in 2006 as compared to 2005 due to the net proceeds from our October 2005 and March 2006 stock offerings.

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 revenues from our AMPK collaboration agreement entered into with Merck in June 2005 which included sponsored research revenue of \$1.1 million and license fee revenue of \$0.4 million.

Research and Development Expenses. Research and development expenses were \$21.3 million for the year ended December 31, 2005, compared with \$17.2 million for the year ended December 31, 2004. The \$4.1 million increase was mainly due to increased spending of \$1.1 million in preclinical development expenses for MB07803, increased research and development services expense of \$1.1 million, an increase of \$1.0 million in payroll and related benefits as a result of a higher average number of employees in 2005, increased occupancy costs related to our new facility of \$0.5 million and increased travel, supplies and insurance expense of \$0.4 million.

General and Administrative Expenses. General and administrative expenses were \$7.2 million for the year ended December 31, 2005, compared with \$4.9 million for the year ended December 31, 2004. The \$2.3 million increase was primarily a result of an increase in payroll and related benefits costs of \$0.8 million as a result of a higher average number of employees in 2005, increased travel and occupancy, public company costs of \$0.9 million and increased professional services expense of \$0.6 million.

Net Interest Income. 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 October 2005 common stock offering, as well as higher investment yields.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily with \$55.8 million in private equity financings and \$107.5 million in net proceeds from our initial public offering in June 2004, a private placement of common stock and warrants in October 2005 and a registered direct offering of common stock in March 2006.

In November 2006, we entered into a Committed Equity Financing Facility, or CEFF, with an institutional investor. Under the terms of the CEFF the investor is committed to providing us up to \$50 million in funding over a three-year term through the purchase of newly-issued shares of our common stock. We may access capital under the CEFF in tranches of up to the lesser of \$10 million or from between 0.75% to 1.5% of our market capitalization at the time of the draw down of such tranche, subject to certain conditions. The investor will purchase shares of our common stock pursuant to the CEFF at

discounts ranging from 6% to 10%, depending on the average market price of our common stock during an eight-day pricing period, provided that the minimum acceptable purchase price for any shares to be issued to the investor during the eight-day pricing period is determined by the higher of \$2.25 or 90% of our share price the day before the commencement of each draw down. Pursuant to the agreement we filed a registration statement with the Securities and Exchange Commission for the resale of the shares of common stock issuable in connection with the CEFF and the shares of common stock underlying the warrant discussed below which became effective on December 22, 2006.

In connection with the CEFF, we issued a warrant to the investor to purchase up to 260,000 shares of our common stock at an exercise price of \$9.26, which represents a 30% premium over the average of the closing prices of our common stock during the five days preceding the signing of the agreement. The warrant will become exercisable after the six-month anniversary of the effective date of the agreement and will remain exercisable, subject to certain exceptions, until five years after the effective date of the agreement.

In October 2006, we entered into a collaboration agreement with Idenix to apply our HepDirect technology to certain Idenix lead compounds with the goal of improving the safety and efficacy of these compounds for the treatment of hepatitis C. The research term will be for two years and may be extended beyond two years by mutual agreement of the parties. In addition, Idenix will have the option to terminate the research term upon the first anniversary of the effective date of the agreement or upon the achievement of certain preclinical and clinical development milestones during the research term. As part of this collaboration, Idenix paid us an initial, non-refundable license fee of \$2.0 million in the fourth quarter of 2006 and agreed to provide us research funding of up to \$1.7 million per year during the research term. Idenix will also pay us milestones if specified preclinical and clinical development and regulatory events occur and royalties on product sales that result from the collaboration. If all milestones are achieved, and including the \$2.0 million license fee and up to \$1.7 million per year in research funding over the term, we may be entitled to payments which total up to \$68.8 million, plus royalties. Idenix is solely responsible for conducting and funding all development work for compounds resulting from this collaboration.

In March 2006, we raised approximately \$40.0 million in gross proceeds in a registered direct offering involving the sale of approximately 4.9 million shares of common stock at a price of \$8.10 per share. Placement agency fees and other offering expenses were approximately \$2.7 million.

In October 2005, we raised gross proceeds of 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.

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 NASH by activating AMPK. As part of this collaboration, Merck paid an initial non-refundable license fee of \$5.0 million in July 2005 and will provide sponsored research funding of a minimum of \$2.1 million each year during the three-year research term.

In June 2004, we completed an initial public offering of our common stock in which we sold approximately 5.0 million shares of common stock for proceeds of \$30.6 million, net of underwriting discounts and commissions and offering expenses. In July 2004, the underwriters exercised their over-allotment option, resulting in the sale of an additional 75,000 shares of common stock, which resulted in proceeds of \$0.5 million, net of underwriting discounts and commissions.

Additionally, we have received cumulative SBIR grant funding of approximately \$1.6 million through December 31, 2006. We do not expect additional funding under SBIR grants in fiscal 2007 as we have discontinued further work under this program.

As of December 31, 2006, we had \$77.9 million in cash and cash equivalents and securities available-for-sale as compared to \$66.9 million as of December 31, 2005, an increase of \$11.0 million. The increase is primarily a result of net proceeds of \$37.3 million raised from our registered direct offering in March 2006 and a \$2.0 million non-refundable license payment under our collaboration with Idenix which was offset by net cash used in operations of \$27.3 million and net cash used in investing activities of \$33.8 million for the year ended December 31, 2006 resulting from net purchases of investments of \$30.6 million and \$3.2 million of equipment purchases.

As of December 31, 2006, we have financed through leases and loans the purchase of equipment and leasehold improvements totaling approximately \$10.1 million, of which \$5.8 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. We currently anticipate investing approximately \$3.5 million to \$4.5 million in cash in 2007 for leasehold improvements and capital equipment necessary to support our clinical development efforts, research programs and to support all other operations. We expect to continue to finance our capital expenditures through the use of debt.

In November 2006, we entered into a CEFF with an institutional investor. Under the terms of the agreement the investor is committed to providing us up to \$50 million in funding over a three-year term through the purchase of newly-issued shares of our common stock as described above. As of December 31, 2006, we have not exercised our option to sell shares under this agreement. In the event we determine that the need for an equity financing is necessary to pursue specific strategic initiatives, and we determine that an equity offering under this agreement provides for more favorable terms and results than what may be available through other financing vehicles at the time, and we determine that the market will favorably support the additional equity available, we may utilize our option to sell shares of common stock under this agreement.

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. We expect to continue to increase our use of cash resources in fiscal 2007 for the further advancement of our current product candidates. This includes, but is not limited to, expenditures for additional personnel to further our preclinical, clinical and regulatory efforts, increased consulting services and increases in facilities and general and administrative support costs. Excluding potential cash inflows from financing activities or additional collaborations and net of anticipated cash inflows from existing collaborations, we currently anticipate utilizing approximately \$43.0 million to \$48.0 million in cash during 2007 to support the further development of our current product candidates, research programs and in support of all other operations. Based on our expected 2007 cash utilization, we expect to raise additional cash to fund our cash needs beyond the next twelve months through the sale of our common stock, including by the exercise of our option under the CEFF, and/or by entering into additional collaborations in 2007.

Until we can generate significant cash from our operations, we expect to continue to fund our operations with existing cash resources that were primarily generated from the proceeds of additional offerings of our equity securities, cash payments under our strategic collaborations, our CEFF and debt financing arrangements. In addition, we may finance future cash needs through the sale of other equity securities, entering into additional strategic collaboration agreements and debt financing. However, we may not be successful in obtaining additional collaboration agreements, or in receiving milestone or royalty payments under current or future agreements. In addition, we cannot be sure that our existing cash, cash equivalents and securities available-for-sale 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.

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 rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us.

The following summarizes our long-term contractual obligations as of December 31, 2006 (in thousands):

| Contractual Obligations | Payments Due by Period | | | | |
|-------------------------|------------------------|------------------|--------------|--------------|---------------|
| | Total | Less than 1 Year | 1 to 3 Years | 4 to 5 Years | After 5 Years |
| Operating leases | \$ 26,206 | \$ 1,760 | \$ 5,086 | \$ 6,265 | \$ 13,094 |
| Equipment financing | 5,669 | 1,762 | 3,064 | 699 | 144 |
| Purchase commitments | 1,277 | 1,277 | | | |
| Capital leases | 91 | 20 | 46 | 25 | |
| Total | \$ 33,243 | \$ 4,819 | \$ 8,196 | \$ 6,990 | \$ 13,238 |

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. In addition, under certain agreements, we may be subject to penalties in the event we prematurely discontinue performance under these agreements. At this time, due to the variability associated with these agreements, we are unable to estimate with certainty the future costs we will incur.

We have entered into employment agreements with our executive officers and certain other key employees that, under certain circumstances, provide for the continuation of salary and certain other benefits if terminated under specified circumstances. These agreements generally expire upon termination for cause or when the Company has met its obligations under these agreements. As of December 31, 2006, no events have occurred resulting in the obligation of any such payments.

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.

Environmental Risk

Our research and development activities involve the use of biological and hazardous materials. We incurred approximately \$435,000, \$409,000 and \$132,000 for the years ended December 31, 2006, 2005 and 2004, respectively, of costs associated with managing hazardous substances and pollution in ongoing operations.

Off-Balance Sheet Arrangements

As of December 31, 2006, 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 annual report on Form 10-K, Certain Relationships and Related Transactions, and Director Independence.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our exposure to market risk for changes in interest rates relates primarily to the increase or decrease in the amount of interest income we can earn on our investment portfolio. Our risk associated with fluctuating interest income is limited to our investments in interest rate sensitive financial instruments. Under our current policies, we do not use interest rate derivative instruments to manage this exposure to interest rate changes. We seek to ensure the safety and preservation of our invested principal by limiting default risk, market risk, and reinvestment risk. We mitigate default risk by investing in short-term investment grade securities. A 100 basis point increase or decrease in interest rates would increase or decrease our current investment balance by approximately \$140,000 annually. While changes in our interest rates may affect the fair value of our investment portfolio, any gains or losses are not recognized in our statement of operations until the investment is sold or if a reduction in fair value is determined to be a permanent impairment.

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 annual report on 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 timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, a control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

As of the end of the period covered by this annual report on Form 10-K, 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 defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2006, at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

An evaluation was also performed under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. There was no change in our internal control over financial reporting during our latest fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) of the Securities and Exchange Act of 1934, as amended. Under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2006 based on the framework in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on our evaluation under the framework in *Internal Control - Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2006.

Our management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

**Report of Independent Registered Public Accounting Firm
on Internal Control Over Financial Reporting**

The Board of Directors and Stockholders
Metabasis Therapeutics, Inc.

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that Metabasis Therapeutics, Inc. maintained effective internal control over financial reporting as of December 31, 2006, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Metabasis Therapeutics' management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, management's assessment that Metabasis Therapeutics, Inc. maintained effective internal control over financial reporting as of December 31, 2006, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Metabasis Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2006, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets as of December 31, 2006 and 2005, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2006 of Metabasis Therapeutics, Inc. and our report dated March 5, 2007 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California
March 5, 2007

Item 9B. Other Information

On March 7, 2007, 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 2007 base salary and the number of shares of common stock underlying the stock option grants for these executive officers:

| Name | 2007 Base Salary | Stock Options |
|-----------------------------------|-------------------------|----------------------|
| Paul K. Laikind, Ph.D. | \$ 379,000 | 100,000 |
| Mark D. Erion, Ph.D. | \$ 325,000 | 75,000 |
| John W. Beck, C.P.A. | \$ 258,000 | 60,000 |
| Edgardo Baracchini, Ph.D., M.B.A. | \$ 263,000 | 60,000 |

The stock options described above (i) were granted pursuant to our Amended and Restated 2001 Equity Incentive Plan, (ii) terminate ten years after March 7, 2007, 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 \$7.60, or the closing price of our common stock as reported on the Nasdaq Stock Market on the date of grant. 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.

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

| Name | 2006 Bonus |
|-----------------------------------|-------------------|
| Paul K. Laikind, Ph.D. | \$ 108,187 |
| Mark D. Erion, Ph.D. | \$ 78,947 |
| John W. Beck, C.P.A. | \$ 62,790 |
| Edgardo Baracchini, Ph.D., M.B.A. | \$ 66,099 |

Also on March 7, 2007, the compensation committee approved our Employee Incentive Compensation Plan for 2007, which is attached hereto as Exhibit 10.34 and incorporated herein by reference, and established 2007 target bonuses, as a percentage of base salary, for certain of our executive officers as follows:

| Name | 2007 Target Bonus % |
|-----------------------------------|----------------------------|
| Paul K. Laikind, Ph.D. | 50 % |
| Mark D. Erion, Ph.D. | 35 % |
| John W. Beck, C.P.A. | 35 % |
| Edgardo Baracchini, Ph.D., M.B.A. | 35 % |

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item will be set forth in the sections entitled Election of Directors, 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, or the Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2006, and is incorporated in this report by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer and principal financial and accounting officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at <http://www.mbasis.com>. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website, as well as via any other means as required by Nasdaq listing standards or applicable law. Stockholders may request a free copy of the Code of Business Conduct and Ethics from:

Metabasis Therapeutics, Inc.
Attention: Investor Relations
11119 North Torrey Pines Road
La Jolla, CA 92037
(858) 587-2770
Bienfait@mbasis.com

Item 11. Executive Compensation

The information required by this item will be set forth in the sections entitled Compensation of Executive Officers, Compensation Committee Report and Compensation Committee Interlocks and Insider Participation 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, and Director Independence

The information required by this item will be set forth in the sections entitled Election of Directors and 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, 2006 and 2005
- Statements of operations for the years ended December 31, 2006, 2005 and 2004
- Statements of stockholders' equity for the years ended December 31, 2006, 2005 and 2004
- Statements of cash flows for the years ended December 31, 2006, 2005 and 2004
- 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. |

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- 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.
- 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.
- 4.14(12) Common Stock Purchase Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited.
- 4.15(13) Registration Rights Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited.
- 4.16(14) Warrant dated November 2, 2006 issued by the Company to Kingsbridge Capital Limited.
- 10.1(1) Form of Indemnity Agreement.
 - 10.2 Amended and Restated 2001 Equity Incentive Plan and Form of Stock Option Agreement thereunder.
 - 10.3 2004 Non-Employee Directors Stock Option Plan and Form of Stock Option Agreement thereunder.
 - 10.4 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(7) Amended and Restated Severance Agreement dated July 19, 2006 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 Sicom 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^ Amended and Restated Development and License Agreement dated December 13, 2006 between the Company and Schering-Plough Corporation.
- 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(8)^ 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(8)^ Amendment dated November 2, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
- 10.31(9)^ Amendment dated May 1, 2006 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
- 10.31(10) Amendment dated May 16, 2006 to Lease Agreement dated December 21, 2004 between the Company and CarrAmerica Realty, L.P.
- 10.31(11) Offer Letter dated September 12, 2006 by and between the Company and David F. Hale.
- 10.32^ Exclusive License and Research Collaboration Agreement dated October 24, 2006 by and between the Company and Idenix Pharmaceuticals, Inc.
- 10.33(2) Assignment and Assumption Agreement dated December 13, 2006 by and among the Company, Valeant Research & Development and Schering Corporation.
- 10.34 Metabasis Employee Incentive Compensation Plan.
- 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.
 - 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 10.35 to the Valeant Pharmaceuticals International Annual Report on Form 10-K for the fiscal year ended December 31, 2006.

(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.

(7) Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 25, 2006.

(8) Incorporated by reference to the exhibit of the same number to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2005.

(9) Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2006.

(10) Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2006.

(11) Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 12, 2006.

(12) Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 2, 2006.

(13) Incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on November 2, 2006.

(14) Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on November 2, 2006.

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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.

Dated: March 12, 2007

METABASIS THERAPEUTICS, INC.
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 Paul K. Laikind, Ph.D. | Chief Executive Officer, President, Secretary and Director (Principal Executive Officer) | March 12, 2007 |
| /s/ JOHN W. BECK John W. Beck, C.P.A. | Senior Vice President of Finance, Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer) | March 12, 2007 |
| /s/ MARK D. ERION Mark D. Erion, Ph.D. | Executive Vice President of Research and Development, Chief Scientific Officer and Director | March 12, 2007 |
| /s/ DAVID F. HALE David F. Hale | Chairman of the Board of Directors | March 12, 2007 |
| /s/ DANIEL D. BURGESS Daniel D. Burgess, M.B.A. | Director | March 12, 2007 |
| /s/ LUKE B. EVNIN Luke B. Evnin, Ph.D. | Director | March 12, 2007 |
| /s/ ARNOLD L. ORONSKY Arnold L. Oronsky, Ph.D. | Director | March 12, 2007 |
| /s/ WILLIAM R. ROHN William R. Rohn | Director | March 12, 2007 |
| /s/ HEINZ GSCHWEND Heinz Gschwend, Ph.D. | Director | March 12, 2007 |

METABASIS THERAPEUTICS, INC.
INDEX TO FINANCIAL STATEMENTS

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F-1

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Metabasis Therapeutics, Inc.

We have audited the accompanying balance sheets of Metabasis Therapeutics, Inc. as of December 31, 2006 and 2005, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2006. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Metabasis Therapeutics, Inc. at December 31, 2006 and 2005, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2006, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 1 to the financial statements, Metabasis Therapeutics, Inc. changed its method of accounting for share-based payments in accordance with Statement of Financial Accounting Standards No. 123 (revised 2004) on January 1, 2006.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Metabasis Therapeutics Inc.'s internal control over financial reporting as of December 31, 2006, based on the criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 5, 2007, expressed an unqualified opinion on management's assessment and an unqualified opinion on the effectiveness of internal control over financial reporting.

/s/ ERNST & YOUNG LLP

San Diego, California

March 5, 2007

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METABASIS THERAPEUTICS, INC.
BALANCE SHEETS
(in thousands, except par value data)

| | December 31, 2006 | 2005 |
|---|----------------------|-----------|
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 12,052 | \$ 32,597 |
| Securities available-for-sale | 65,871 | 34,296 |
| Trade accounts receivable | 187 | 199 |
| Prepays and other current assets | 1,303 | 1,970 |
| Total current assets | 79,413 | 69,062 |
| Property and equipment, net | 6,263 | 4,664 |
| Other assets | 179 | 152 |
| Total assets | \$ 85,855 | \$ 73,878 |
| Liabilities and stockholders equity | | |
| Current liabilities: | | |
| Accounts payable | \$ 1,053 | \$ 1,745 |
| Accrued liabilities | 3,999 | 3,937 |
| Deferred revenue, current portion | 3,192 | 2,192 |
| Current portion of long-term debt | 1,761 | 1,024 |
| Current portion of capital lease obligations | 20 | 18 |
| Total current liabilities | 10,025 | 8,916 |
| Deferred revenue, net of current portion | 1,630 | 2,463 |
| Deferred rent | 1,566 | 330 |
| Long-term debt | 3,908 | 2,067 |
| Capital lease obligations, net of current portion | 71 | 59 |
| Other long-term liabilities | 517 | 461 |
| Total liabilities | 17,717 | 14,296 |
| Stockholders equity: | | |
| Preferred stock, \$0.001 par value; 5,000 shares authorized at December 31, 2006 and December 31, 2005, no shares issued or outstanding | | |
| Common stock, \$0.001 par value; 100,000 shares authorized at December 31, 2006 and December 31, 2005; 30,493 and 25,313 shares issued and outstanding at December 31, 2006 and December 31, 2005, respectively | 30 | 25 |
| Additional paid-in capital | 176,298 | 137,822 |
| Deferred compensation | | (3,266) |
| Accumulated deficit | (108,213) | (74,945) |
| Accumulated other comprehensive loss | 23 | (54) |
| Total stockholders equity | 68,138 | 59,582 |
| Total liabilities and stockholders equity | \$ 85,855 | \$ 73,878 |

See accompanying notes.

METABASIS THERAPEUTICS, INC.
STATEMENTS OF OPERATIONS
(in thousands, except per share data)

| | Years Ended December 31, | | |
|---|--------------------------|--------------|--------------|
| | 2006 | 2005 | 2004 |
| Revenues: | | | |
| Sponsored research | \$ 2,210 | \$ 2,493 | \$ 1,375 |
| License fees | 1,984 | 871 | 458 |
| Other revenue | 192 | 407 | 504 |
| Milestones | | | 4,500 |
| Total revenues | 4,386 | 3,771 | 6,837 |
| Operating expenses: | | | |
| Research and development | 30,305 | 21,252 | 17,226 |
| General and administrative | 10,890 | 7,186 | 4,886 |
| Total operating expenses | 41,195 | 28,438 | 22,112 |
| Loss from operations | (36,809) | (24,667) | (15,275) |
| Other income (expense): | | | |
| Interest income | 3,932 | 1,297 | 531 |
| Interest expense | (391) | (210) | (228) |
| Total other income | 3,541 | 1,087 | 303 |
| Net loss | \$ (33,268) | \$ (23,580) | \$ (14,972) |
| Basic and diluted net loss per share | \$ (1.15) | \$ (1.20) | \$ (1.49) |
| Shares used to compute basic and diluted net loss per share | 29,019 | 19,706 | 10,034 |
| Proforma net loss per common share assuming conversion of preferred stock, basic and diluted | | | \$ (0.98) |
| Shares used to compute proforma net loss per common share assuming conversion of preferred stock, basic and diluted | | | 15,254 |

See accompanying notes.

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METABASIS THERAPEUTICS, INC.
STATEMENTS OF STOCKHOLDERS EQUITY
(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional Paid-In Capital | Deferred Compensation | Accumulated Deficit | Accumulated Other Comprehensive Income (Loss) | Total Stockholders Equity |
|--|-----------------------------|-----------|--------------|------------|----------------------------|-----------------------|---------------------|---|---------------------------|
| | Shares | Amount | Shares | Amount | | | | | |
| 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, 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 | | | | | | | | | (23,580) |
| 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 of 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 | |
| Net loss | | | | | | | (33,268) | | (33,268) |
| Unrealized gain on short-term investments | | | | | | | | 77 | 77 |
| Net comprehensive loss | | | | | | | | | (33,191) |
| Issuance of common stock in registered direct offering, net of | | | 4,938 | 5 | 37,299 | | | | 37,304 |

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| | | | | | | | | | | | | |
|---|-----|--------|---------|----|-------|---------|----|-----------|----|----|----|--------|
| offering costs of \$2,696 | | | | | | | | | | | | |
| Issuance of common stock for option exercises | 44 | | 95 | | | | | 95 | | | | |
| Issuance of common stock pursuant to the Employee Stock Purchase Plan | 198 | | 603 | | | | | 603 | | | | |
| Reclass of deferred compensation | | | (3,266) | | 3,266 | | | | | | | |
| Stock-based compensation | | | 3,745 | | | | | 3,745 | | | | |
| Balance at December 31, 2006 | \$ | 30,493 | \$ | 30 | \$ | 176,298 | \$ | (108,213) | \$ | 23 | \$ | 68,138 |

See accompanying notes.

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METABASIS THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

| | Years Ended December 31, | | |
|---|---------------------------------|--------------|--------------|
| | 2006 | 2005 | 2004 |
| Operating activities | | | |
| Net loss | \$ (33,268) | \$ (23,580) | \$ (14,972) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Stock-based compensation | 3,745 | 1,938 | 1,811 |
| Depreciation and amortization | 1,602 | 910 | 699 |
| Deferred rent | 1,236 | 263 | (55) |
| Loss on disposal of assets | 29 | | |
| Amortization of discount on equipment loan | | 5 | 15 |
| Realized gain on investments | (1) | (2) | |
| Amortization of discount and premium on securities available-for-sale | (924) | 528 | 561 |
| Change in operating assets and liabilities: | | | |
| Trade accounts receivable | 12 | (403) | 432 |
| Other current assets | 667 | (115) | (660) |
| Other assets | (27) | (152) | 199 |
| Deferred revenue | 167 | 4,655 | (458) |
| Accounts payable | (692) | 881 | 97 |
| Accrued liabilities and other long-term liabilities | 118 | 1,559 | 333 |
| Net cash flows used in operating activities | (27,336) | (13,513) | (11,998) |
| Investing activities | | | |
| Purchases of securities available-for-sale | (134,752) | (36,785) | (40,327) |
| Sales/maturities of securities available-for-sale | 104,179 | 34,897 | 21,024 |
| Purchases of property and equipment | (3,230) | (3,220) | (1,326) |
| Net cash flows used in investing activities | (33,803) | (5,108) | (20,629) |
| Financing activities | | | |
| Issuance of common stock, net | 38,002 | 39,380 | 32,140 |
| Principal payments on debt and capital lease obligations | (1,486) | (870) | (788) |
| Repurchase unvested common stock | | (20) | |
| Proceeds received from debt and capital lease obligations | 4,078 | 1,807 | 1,179 |
| Net cash flows provided by financing activities | 40,594 | 40,297 | 32,531 |
| (Decrease) increase in cash and cash equivalents | (20,545) | 21,676 | (96) |
| Cash and cash equivalents at beginning of year | 32,597 | 10,921 | 11,017 |
| Cash and cash equivalents at end of period | \$ 12,052 | \$ 32,597 | \$ 10,921 |
| Supplemental disclosure of cash flow information: | | | |
| Interest paid | \$ 405 | \$ 205 | \$ 214 |
| Supplemental schedule of noncash investing and financing activities: | | | |
| Reclass of deferred compensation | \$ 3,266 | \$ | \$ |
| Fair value of warrant issued in connection with the Committed Equity Financing Facility | \$ 1,098 | \$ | \$ |
| Unrealized gain (loss) on short-term investments | \$ 77 | \$ | \$ (48) |
| Conversion of convertible preferred stock to common stock upon initial public offering | \$ | \$ | \$ 64 |

See accompanying notes.

METABASIS THERAPEUTICS, INC.
NOTES TO FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

Organization and Basis of Presentation

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. The Company was incorporated in Delaware in April 1997 as a wholly owned subsidiary of Gensia Sicom Inc., now Sicom Inc., which became an indirect wholly owned subsidiary of Teva Pharmaceutical Industries Limited in January 2004. In December 1997, Sicom assigned the Company specified assets and liabilities relating to its then existing business of discovering and developing proprietary pharmaceutical products. In June 1999 the Company completed a corporate restructuring and management stock purchase in which the Company became an independent company.

Certain prior year amounts have been reclassified to be consistent with current year presentation. In the fourth quarter of 2006, the Company began reporting all legal costs associated with patent related activities as general and administrative costs. All general and administrative and research and development costs referred to within this Form 10-K have been reclassified to give effect of the reclassification of these costs. The cumulative adjustment for the reclassification of these costs for the nine months ended September 30, 2006 totaled \$1.5 million, and \$1.4 million and \$587,000, for the twelve months ended December 31, 2005 and 2004, respectively. There is no impact on retained earnings, total operating expenses, net cash used for operating activities, net loss or earnings per share as a result of the classification of these costs. In addition, the Company recorded other immaterial reclassifications within its prior year balance sheet to conform to current year presentation. None of these additional reclassifications had an impact to total assets, total liabilities or net cash used in operating or investing activities for the period presented herein.

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

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is based on the specific-identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

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

| | December 31, 2006 | | | |
|----------------------------|---------------------------|---------------------------------------|--|-------------------------------------|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
| Corporate debt securities | \$ 55,074 | \$ 22 | \$ (1) | \$ 55,095 |
| Mortgage-backed securities | 10,774 | 2 | | 10,776 |
| Total | \$ 65,848 | \$ 24 | \$ (1) | \$ 65,871 |

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

Gross realized gains and losses on available-for-sale securities were immaterial during the years ended December 31, 2006, 2005 and 2004. All realized gains and losses are reclassified out of other comprehensive income (loss) in the period recognized. Proceeds from the sale of short-term investments totaled \$104.2 million, \$35.4 million and \$21.6 million for the years ended December 31, 2006, 2005 and 2004, respectively. All available-for-sale securities at December 31, 2006 have a contractual maturity of one year or less.

Investments considered to be temporarily impaired at December 31, 2006 are as follows:

| | Number of Investments | Less than 12 months of temporary impairment | |
|--|----------------------------------|--|------------------------------|
| | | Fair Value | Unrealized Losses |
| Corporate debt securities | 2 | \$ 5,247 | \$ (1) |
| Total temporary impaired securities | 2 | \$ 5,247 | \$ (1) |

There are no investments held at December 31, 2006, which are considered to be temporarily impaired beyond 12 months. The Company regularly monitors and evaluates the realizable value of its marketable securities. When assessing marketable securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost and the market in general.

The Company believes that the decline in value of its marketable securities is temporary and related to the change in market interest rates since purchase. The decline is not related to any company or industry specific event, and all portfolio investments are investment grade quality. The Company anticipates full recovery of amortized cost with respect to these securities at maturity or sooner in the event of a change in the market interest rate environment.

Fair Value of Financial Instruments

The carrying amount of cash and cash equivalents, securities available-for-sale, accounts receivable, accounts payable, accrued liabilities and deferred revenue 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 86% and 90% of total revenues during the years ended December 31, 2006, and 2005, respectively and a different collaborative partner individually accounted for 51% of total revenues during the year ended December 31, 2004 (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.

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

| | December 31, | |
|---|---------------------|-------------|
| | 2006 | 2005 |
| Laboratory equipment | \$ 9,849 | \$ 7,561 |
| Computers and electronics | 3,117 | 2,322 |
| Office furniture and fixtures | 1,197 | 987 |
| Leasehold improvements | 1,120 | 943 |
| Construction in progress | 150 | 456 |
| | 15,433 | 12,269 |
| Less: accumulated depreciation and amortization | (9,170) | (7,605) |
| | \$ 6,263 | \$ 4,664 |

Depreciation and amortization expenses, which include assets held under capital leases, were \$1.6 million, \$910,000 and \$699,000 for the years ended December 31, 2006, 2005 and 2004, respectively. Assets held under capital leases and equipment loans totaled approximately \$5.8 million and \$3.2 million at December 31, 2006 and 2005, respectively. The related accumulated amortization was approximately \$4.0 million and \$2.4 million at December 31, 2006 and 2005, respectively. Maintenance and repairs are charged to operations as incurred.

Impairment of Long-Lived Assets

The Company assesses potential impairment to its long-lived and intangible assets in accordance with 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, 2006.

Revenue Recognition

The Company's revenue recognition policies are in accordance with the SAB No. 104, *Revenue Recognition*, and Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables*. 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 of performance obligation. 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, stock-based compensation expense, outside service providers, facilities costs, fees paid to consultants, professional services, travel costs, dues and subscriptions, depreciation 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.

Stock-Based Compensation

In December 2004, the Financial Accounting Standards Board (FASB) issued SFAS No. 123R, *Share-Based Payment*. SFAS No. 123R requires all share-based payments to employees or non-employee directors as compensation for service on the Board of Directors, to be recognized as compensation expense in the financial statements based on the fair values of such payments.

The Company maintains three shareholder-approved share-based compensation plans that are subject to the requirements of SFAS No. 123R. The Amended and Restated 2001 Equity Incentive Plan (Equity Incentive Plan) provides for the grant of stock options and restricted stock to officers, directors and employees of, and consultants and advisors to, the Company. The 2004 Non-Employee Directors' Stock Option Plan (Directors' Stock Option Plan) provides for the grant of non-statutory stock options to non-employee directors. The 2004 Employee Stock Purchase Plan (Employee Stock Purchase Plan) provides

a means by which employees may purchase common stock at a discount through payroll deductions and is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Internal Revenue Code.

Grants under the Equity Incentive Plan and the Directors' Stock Option Plan are primarily in the form of options that allow a grantee to purchase a fixed number of shares of the Company's common stock at a fixed exercise price equal to the market price of the shares at the date of the grant. Grants under the Equity Incentive Plan are incentive stock option grants or non-qualified stock option grants if they are granted to employees and non-qualified stock option grants if granted to non-employees. Grants under the Directors' Stock Option Plan are non-qualified stock option grants. Options under both the Equity Incentive Plan and the Directors' Stock Option Plan may vest on a single date or in tranches over a period of time, but normally they do not vest unless the grantee is still employed by or a director of the Company on the vesting date. Options under the Equity Incentive Plan generally vest over a four year period: 1/4th on the first year anniversary of the date of grant and in equal monthly installments over the remaining three years and expire ten years from the date of grant. Options under the Directors' Stock Option Plan generally vest from one to two years, and expire ten years from the date of grant. The Company made no modifications to outstanding options with respect to vesting periods or exercise prices prior to adopting SFAS No. 123R. Rights to purchase shares under the Employee Stock Purchase Plan allow participating employees to purchase stock at a discount during offering periods of 6, 12, 18 or 24 months with purchases occurring every six months.

In March 2005, the Securities and Exchange Commission issued SAB No. 107, *Share-Based Payments*, which provides guidance on the implementation of SFAS No. 123R. The Company applied the principles of SAB No. 107 in conjunction with its adoption of SFAS No. 123R.

The Company adopted SFAS No. 123R effective January 1, 2006, using the modified-prospective transition method. Under this transition method, compensation expense under both the Equity Incentive Plan and the Directors' Stock Option Plan will be recognized based on the grant date fair value estimated in accordance with the provisions of SFAS No. 123R for all new grants effective January 1, 2006, and for options granted prior to but not vested as of December 31, 2005, compensation will be recognized based on the grant date fair value as estimated in accordance with SFAS No. 123. Compensation expense will be recognized over the requisite service period which is typically the period over which the stock-based compensation awards vest. Compensation expense under the Employee Stock Purchase Plan will be recognized based on the fair value on the date that the purchase rights were granted in accordance with the provisions of SFAS No. 123R for all new grants effective January 1, 2006, and for share purchase rights granted prior to but not vested as of December 31, 2005, and will be recognized over the remaining period of each grant's respective offering period.

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Prior periods were not restated to reflect the impact of adopting the new standard and therefore do not include compensation expense related to qualified stock option grants for those periods. In accordance with SFAS No. 123R, the Company recognized share-based compensation expense for all three plans as follows (in thousands):

| | Twelve months ended December 31, 2006 |
|--|--|
| Stock-based compensation expense: | |
| Research and development | \$ 1,936 |
| General and administrative | 1,809 |
| Total stock-based compensation expense | \$ 3,745 |
| Net effect on net loss | \$ 3,745 |
| Effect on loss per share: | |
| Basic and diluted | \$ 0.13 |

As a result of adopting SFAS No. 123R on January 1, 2006, the Company's net loss for the twelve months ended December 31, 2006 is approximately \$1.9 million greater than if the Company had continued to account for share-based compensation under Accounting Principles Board (APB) Opinion No. 25, *Accounting for Stock Issued to Employees*. Basic and diluted net loss per share for the twelve months ended December 31, 2006 is \$0.07 greater, than if the Company had continued to account for share-based compensation under APB Opinion No. 25.

Compensation expense for all options granted under the Equity Incentive Plan and the Directors' Stock Option Plan during the twelve-month period ended December 31, 2006 was recognized on a straight-line basis over the vesting period of each grant, net of estimated forfeitures. The Company's estimated forfeiture rates are based on its historical experience. The estimated fair value of the options and share purchase rights granted during 2006 and in prior years was calculated using a Black-Scholes Merton option-pricing model (Black-Scholes model). The following summarizes the assumptions used in the Black-Scholes model as applied in 2006:

| | Equity Incentive Plan and Directors' Stock Option Plan | | Employee Stock Purchase Plan | |
|--|---|---|---------------------------------|---|
| Risk-free interest rate(1) | 4.7 | % | 4.7 | % |
| Volatility(2) | 69.0 | % | 67.5 | % |
| Dividend yield(3) | 0.0 | % | 0.0 | % |
| Expected Life(4) | 6 years | | 1.3 years | |
| Weighted average fair value at date of grant | \$ 4.84 | | \$ 2.11 | |

(1) The risk-free interest rate is based on U.S. Treasury debt securities with maturities close to the expected term of the option and the share purchase right.

(2) Expected volatility is based on the weighted average volatility of the Company's stock factoring in daily share price observations and the historical price volatility of certain peers within the Company's industry sector. In computing expected volatility, the length of the historical period used is equal to the length of the expected term of the option and the share purchase right.

(3) No cash dividends have been declared on the Company's common stock since the Company's inception, and the Company currently does not anticipate paying cash dividends over the expected term of the option and the share purchase right.

(4) The expected life of employee stock options represents the average of the contractual term of the options and the weighted average vesting period, as permitted under the simplified method, under SAB No. 107.

Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Forfeitures were estimated to be \$68,831 for the options granted during the twelve months ended December 31, 2006, based on historical experience. In the Company's pro forma information required under SFAS No. 123, *Accounting for Stock-Based Compensation*, for the periods prior to fiscal 2006, the Company accounted for forfeitures as they occurred.

The Employee Stock Purchase Plan permits for the modification of the original rate of contribution an employee elects upon enrollment. The Company accounts for each increase from the original rate of contribution, during an offering period, as a modification of the original award and recognizes the incremental change in compensation expense as a result of the change in fair value from the modification. The incremental effect to stock compensation as a result of modifications to these awards during the twelve months ended December 31, 2006, was immaterial.

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The following is a summary of stock option activity under the Equity Incentive Plan and the Directors' Stock Option Plan as of December 31, 2005, and changes during the twelve months ended December 31, 2006 (in thousands, except per share data):

| | Number of Options | Weighted average exercise price |
|----------------------------------|-------------------------|---------------------------------------|
| 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 |
| Granted | 1,338 | \$ 8.05 |
| Exercised | (44) | \$ 2.17 |
| Canceled | (61) | \$ 6.40 |
| Outstanding at December 31, 2006 | 2,638 | \$ 5.58 |
| Exercisable at December 31, 2006 | 1,025 | \$ 3.01 |

The intrinsic value of options exercised during the twelve months ended December 31, 2006 was \$254,000. The aggregate intrinsic value of stock options exercisable and outstanding as of December 31, 2006 was \$3.1 million and \$14.7 million, respectively. The weighted average contractual life for options outstanding as of December 31, 2006 was 8.2 years. The weighted average contractual life for options exercisable as of December 31, 2006 was 6.9 years. The weighted average fair value of options vested during fiscal 2006 was \$5.39.

The following is a summary of activity for non-vested stock options under the Equity Incentive Plan and the Directors' Stock Option Plan as of December 31, 2005, and changes during the twelve months ended December 31, 2006 (in thousands, except per share data):

| | Number of Options | Weighted Average Fair Value Price Per Share |
|--------------------------------|-------------------------|---|
| Nonvested at December 31, 2005 | 737 | \$ 5.68 |
| Granted | 1,338 | \$ 4.84 |
| Vested | (394) | \$ 5.58 |
| Forfeited | (61) | \$ 3.36 |
| Nonvested at December 31, 2006 | 1,620 | \$ 5.07 |

As of December 31, 2006, the Company had approximately \$7.6 million of unrecognized compensation expense of which \$7.4 million related to stock options under the Equity Incentive Plan and the Directors' Stock Option Plan and \$172,000 related to share purchase rights under the Employee Stock Purchase Plan. The expense is expected to be recognized over a weighted average period of approximately 1.8 years. The resulting effect on net loss and net loss per share is not likely to be representative of the effects in future periods due to additional grants, subsequent periods of vesting and changes in volatility and expected life.

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Prior to January 1, 2006, the Company accounted for its stock-based compensation plans under APB Opinion No. 25. In accordance with APB Opinion No. 25, the Company recognized no compensation expense for incentive stock option grants where the exercise price was equal to the market price on the date of grant. For options issued with an exercise price less than the fair market value of the shares at the date of grant, the Company recognized the difference between the exercise price and fair market value as compensation expense in accordance with APB Opinion No. 25. Compensation expense was recognized and amortized on a straight-line basis over the vesting period of the related options, generally four years. The Company had a deferred stock compensation balance of \$3.3 million at December 31, 2005 for options previously issued with an exercise price less than the fair market value of the shares on the date of grant. Upon adoption of SFAS No. 123R, deferred stock compensation was eliminated against additional paid-in-capital.

Prior to January 1, 2006, the Company provided pro forma disclosure amounts in accordance with SFAS No. 123, as amended by SFAS No. 148, *Accounting for Stock-Based Compensation Transition and Disclosure*. In the Company's pro forma information required under SFAS No. 123 for periods prior to the fiscal year ended 2006, the Company accounted for forfeitures as they occurred. The fair value of these options was estimated at the date of grant using the Black-Scholes model with the following weighted average assumptions used for option grants:

| | Years Ended | |
|--------------------------------|--------------|--------|
| | December 31, | |
| | 2005 | 2004 |
| Risk-free interest rate | 4.4 % | 3.6 % |
| Dividend yield | 0.0 % | 0.0 % |
| Volatility factor | 70.0 % | 70.0 % |
| Weighted average life in years | 6.3 | 5.0 |

The following table illustrates the effect on net loss and net loss per share if the Company had applied the fair value recognition provisions of SFAS No. 123 to stock-based employee compensation in the prior fiscal year 2005 and 2004 (in thousands, except per share data):

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

The Company accounts for stock options granted to non-employees for acquiring, or in conjunction with selling, goods and services in accordance with SFAS No. 123 and EITF 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 accordingly recognizes as expense the estimated fair value of such options as calculated using the Black-Scholes model. The fair value is remeasured during the service period and is amortized over the vesting period of each option or the recipient's contractual arrangement, if shorter. Expense recognized for acquiring, or in conjunction with selling, goods or services for the twelve months ended December 31, 2006, 2005 and 2004 were not material.

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 non-owner sources. The Company's other comprehensive loss for December 31, 2006, 2005 and 2004 consisted of unrealized gains and losses on available-for-sale securities and is reported in stockholders' equity.

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 total number of shares issuable upon exercise of stock options and warrants excluded from the calculation of diluted earnings per share since they are anti-dilutive were 5,142,606, 2,622,617 and 1,679,518 in 2006, 2005 and 2004, respectively.

Years Ended December 31,
2006 2005 2004
(in thousands, except per share amounts)

| Actual: | | | |
|---|--------------|--------------|--------------|
| <i>Numerator:</i> | | | |
| Net loss | \$ (33,268) | \$ (23,580) | \$ (14,972) |
| <i>Denominator:</i> | | | |
| Weighted average common shares | 29,152 | 19,981 | 10,452 |
| Weighted average unvested common shares subject to repurchase | (133) | (275) | (418) |
| Denominator for basic and diluted net loss per share | 29,019 | 19,706 | 10,034 |
| Basic and diluted net loss per share | \$ (1.15) | \$ (1.20) | \$ (1.49) |
| Pro forma: | | | |
| <i>Numerator:</i> | | | |
| Proforma net loss | \$ (33,268) | \$ (23,580) | \$ (14,972) |
| <i>Denominator:</i> | | | |
| Shares used above | 29,019 | 19,706 | 10,034 |
| Pro forma adjustments to reflect assumed weighted average effect of conversion of preferred stock | | | 5,220 |
| Pro forma shares used to compute basic net loss per share | 29,019 | 19,706 | 15,254 |
| Basic and diluted net loss per share | \$ (1.15) | \$ (1.20) | \$ (0.98) |

Warrants

The Company issues warrants to purchase the Company's shares of common stock in connection with financing arrangements. Generally, the warrants are provided as additional consideration to an investor for the purchase of the Company's common stock through a structured offering. The terms of the warrants may vary, however, generally include an exercise price equal to a specific premium over the value of the common stock at the time of the financing. They are generally required to be settled in cash, however,

under rare and certain circumstances, such as in a default of funding by the investor, may require the Company to repurchase common stock obtained through the exercise of the warrant. The Company accounts for these financial instruments in accordance with SFAS No. 150, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*, and EITF Issue No. 00-19, *Accounting for Derivative Financial Instruments Indexed to and Potentially Settled in a Company's Own Stock*. Where the instrument qualifies as a freestanding financial instrument and does not represent an obligation or where the monetary value of the instrument changes in the same direction as the shares of common stock, the Company will assess the terms of the instrument against the criteria within EITF Issue No. 00-19 to determine the appropriate classification as equity or a liability. As of December 31, 2006, all warrants issued are classified as equity.

Recent Accounting Pronouncements

In February 2006, the FASB issued SFAS No. 155, *Hybrid Instruments*. The statement amends SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities*, and SFAS No. 140, *Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities*. The statement also resolves issues addressed in Statement 133 Implementation Issue No. D1, *Application of Statement 133 to Beneficial Interests in Securitized Financial Assets*. The statement: permits fair value remeasurement for any hybrid financial instrument that contains an embedded derivative that otherwise would require bifurcation; clarifies which interest-only strips and principal-only strips are not subject to the requirements of SFAS No. 133; establishes a requirement to evaluate interests in securitized financial assets to identify interests that are freestanding derivatives or that are hybrid financial instruments that contain an embedded derivative requiring bifurcation; clarifies that concentrations of credit risk in the form of subordination are not embedded derivatives, and; amends Statement 140 to eliminate the prohibition on a qualifying special purpose entity from holding a derivative financial instrument that pertains to a beneficial interest other than another derivative financial instrument. The Company believes the adoption of this standard will not have an impact on its results of operations or financial position.

In July 2006, the FASB issued Interpretation, or FIN, No. 48, *Accounting for Uncertainty in Income Taxes*. This interpretation requires that we recognize in our financial statements, the impact of a tax position, if that position is more likely than not of being sustained on audit, based on the technical merits of the position. The provisions of FIN 48 are effective for fiscal years beginning after December 15, 2006, with the cumulative effect of the change in accounting principle recorded as an adjustment to opening retained earnings. The Company is currently evaluating the impact of the adoption of FIN 48 on its financial statements.

In September 2006, the Securities and Exchange Commission released SAB No. 108, *Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements*. SAB 108 provides interpretive guidance on the Securities and Exchange Commission's views regarding the process of quantifying materiality of financial statement misstatements. SAB 108 is effective for fiscal years ending after November 15, 2006 (beginning with our 2006 fiscal year). The adoption of this guidance did not have a material impact on the Company's results of operations or financial position.

In September 2006, the FASB issued FAS 157, *Fair Value Measurements*. This standard defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles, and expands disclosures about fair value measurements. This statement is effective for financial statements issued for fiscal years beginning after November 15, 2007 (beginning with our 2008 fiscal year), although earlier application is encouraged. The Company has not yet evaluated the impact of adopting SFAS 157 on its financial statements, however, the Company expects to assess the impact of adoption of this standard will have on its results of operations and financial position.

2. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

| | December 31, | |
|-------------------------------|---------------------|-------------|
| | 2006 | 2005 |
| Accrued development expenses | \$ 1,464 | \$ 1,008 |
| Accrued bonuses | 1,169 | 700 |
| Other accrued liabilities | 621 | 864 |
| Accrued employee benefits | 542 | 752 |
| Accrued legal and patent fees | 203 | 613 |
| | \$ 3,999 | \$ 3,937 |

3. Commitments and Contingencies*Lease Commitments*

The Company leases its office and research facilities and certain laboratory and electronic equipment under operating and capital lease agreements, which expire at varying dates through 2015. 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 \$26.2 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 \$2.8 million, \$1.4 million and \$1.3 million for each of the years ended December 31, 2006, 2005 and 2004, respectively.

Debt

In 2001, the Company entered into a \$650,000 equipment loan agreement with a financing company, which was subsequently amended two times to increase the amount available under the agreement to \$2.1 million. The Company utilized approximately \$1.7 million before the amended agreement expired on December 31, 2002. The proceeds from the loan were used to purchase laboratory, computer and electronic equipment, tenant improvements and furniture which also served as collateral to the loan. Each borrowing was payable over 48 months with an interest rate fixed at the funding date of each borrowing ranging from 9.58% to 12.05%. The weighted average interest rate during 2006 was 10%. The outstanding balance of this loan is \$0 and \$178,000 at December 31, 2006 and 2005, respectively.

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.

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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 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. There are no amounts outstanding under this agreement at December 31, 2006.

In August 2003, the Company entered into a \$1.4 million equipment loan agreement with a different financing company. This agreement was subsequently amended two times to increase the amount available to \$7.6 million. The proceeds are used to finance lab equipment, computer and electronic equipment and furniture, which serve as collateral under the loan. As of December 31, 2006, the Company has utilized the total amount available under the equipment loan agreement. Each borrowing is payable over 48 months with the interest rate fixed at the funding date of each borrowing ranging from 8.62% to 10.96%. The weighted average interest rate in 2006 was 9%. No warrants were issued in connection with this equipment loan agreement. The outstanding balance of this loan is \$5.4 million and \$2.6 million at December 31, 2006 and 2005, respectively.

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. The outstanding balance of this loan is \$276,000 and \$297,000 at December 31, 2006 and 2005, respectively.

Licensing and Purchase Commitments

Payment schedules for commitment and contractual obligations at December 31, 2006, are as follows (in thousands):

| | Capital Leases | Equipment Financing | Operating Leases |
|---|---------------------------|--------------------------------|-----------------------------|
| 2007 | \$ 29 | \$ 2,244 | \$ 1,760 |
| 2008 | 29 | 1,911 | 2,306 |
| 2009 | 28 | 1,638 | 2,781 |
| 2010 | 22 | 711 | 3,088 |
| 2011 | 5 | 44 | 3,178 |
| Thereafter | | 167 | 13,093 |
| Total minimum payments | 113 | 6,715 | \$ 26,206 |
| Less amount representing interest | (22) | (1,046) | |
| Present value of net minimum payments | 91 | 5,669 | |
| Less current portion | (20) | (1,761) | |
| Long-term debt and capital lease obligations | \$ 71 | \$ 3,908 | |

The Company also has open purchase orders from time to time for the purchase of capital expenditures, consulting services, subscriptions and materials. Obligations under these open purchase orders totaled \$1.3 million at December 31, 2006. These purchase commitments expire at varying dates through December 31, 2007.

Executive Severance Agreements

The Company has entered into employment agreements with our executive officers and certain other key employees that, under certain circumstances, provide for the continuation of salary and certain other benefits if terminated under specified circumstances.

These agreements generally expire upon termination for cause or when the Company has met its obligations under these agreements. As of December 31, 2006, no events have occurred resulting in the obligation of any such payments.

Clinical Development Agreements

The Company has entered into agreements with various vendors for the preclinical and clinical development of its product candidates, which are generally cancelable at the option of the Company at any time. Under the terms of these agreements, the vendors provide a variety of services including conducting preclinical development research, manufacturing clinical compounds, enrolling patients, recruiting patients, monitoring studies, data analysis and regulatory filing assistance. Payments under these agreements typically include fees for services and reimbursement of expenses. In addition, under certain agreements, we are subject to penalties in the event we prematurely discontinue performance under these agreements.

4. Collaborative Research and Development Agreements

Idenix

In October 2006, the Company entered into a non-exclusive collaboration agreement with Idenix, Inc. (Idenix) to apply its HepDirect technology to certain Idenix lead compounds with the goal of improving the safety and efficacy of these compounds for the treatment of hepatitis C. The research term will be for two years and may be extended beyond two years by mutual agreement of the parties. In addition, Idenix will have the option to terminate the research term upon the first anniversary of the effective date of the agreement or upon the achievement of certain preclinical and clinical development milestones during the research term. As part of this collaboration, Idenix paid the Company an initial, non-refundable license fee of \$2.0 million in the fourth quarter of 2006 and agreed to provide sponsored research funding of up to \$1.7 million per year during the research term. Idenix will also pay the Company milestones if specified preclinical and clinical development and regulatory events occur and royalties on product sales that result from the collaboration. If all milestones are achieved, and including the \$2.0 million license fee and the up to \$1.7 million per year in sponsored research funding over the term, the Company may be entitled to payments which total up to \$68.8 million, plus royalties. Idenix is solely responsible for conducting and funding all development work for compounds resulting from this collaboration.

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. As of December 31, 2006, 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.

Schering-Plough

In January 2007, Valeant assigned its rights, interests and obligations under the development and license agreement to Schering-Plough and further granted Schering-Plough a license to its intellectual

property related to pradefovir. Concurrently, the Company and Schering-Plough entered into an amended and restated development and license agreement for the continued future development and commercialization of pradefovir. Under the amended and restated development and license agreement and pursuant to Valeant's assignment, Schering-Plough was granted exclusive worldwide rights to develop and commercialize pradefovir during the term of the agreement. The Company received a non-refundable license fee of \$1.8 million in January 2007 from Schering-Plough and will receive future milestone payments upon the occurrence of specified development, regulatory and commercial milestones as well as royalties on sales of products resulting from the collaboration. If all development, regulatory and commercial milestones are achieved, and including the \$1.8 million non-refundable license fee, the Company will be entitled to payments totaling up to \$25 million, plus royalties under the agreement with Schering-Plough. In addition, Schering-Plough is solely responsible for conducting and funding all development work.

The term of the development and license agreement will continue until all of Schering-Plough'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 for material breach of the other party which remains uncured. Schering-Plough has the sole right to terminate the agreement in its entirety or in certain countries by providing at least 180 days written notice to the Company.

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 the clinical development of 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, 2006, the Company has achieved three developmental milestones triggering a total of \$6.5 million in payments, including \$3.5 million received in 2004 and none in 2005 and 2006 from Daiichi Sankyo. In 2003, Daiichi Sankyo chose not to exercise an option with the Company to negotiate a new agreement for next generation compounds to treat diabetes. Because the Company concluded that it therefore had no future performance obligation remaining it recognized \$7.6 million related to a previously unamortized option fee. 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 non-exclusive 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 has supplied 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 totaling \$2.7 million during 2004 and 2005. Revenue recognized under the agreement was \$1.4 million and \$1.8 million for the years ended December 31, 2005 and 2004, respectively. Merck is also obligated to pay preclinical and clinical milestone payments if

specified development and regulatory events occur and royalties on sales of products resulting from the collaboration. If all preclinical 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 \$25.3 million 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 NASH 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 preclinical and clinical development and regulatory events occur and pay royalties on sales of any product resulting from this collaboration. As of December 31, 2006, 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 preclinical 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 \$3.8 million and \$1.9 million for the years ended December 31, 2006 and 2005, respectively. Deferred revenue of \$3.0 million is reflected on the balance sheet as of December 31, 2006, relating to this agreement.

5. Committed Equity Financing Facility (CEFF)

In November 2006, the Company entered into a CEFF with an institutional investor. Under the terms of the agreement the investor is committed to providing the Company up to \$50 million in funding, or up to a maximum of 6,046,071 of shares of common stock, over a three-year term through the purchase of newly-issued shares of the Company's common stock. The Company may access capital under the CEFF in tranches of up to the lesser of \$10 million or from between 0.75% to 1.5% of the Company's market capitalization at the time of the draw down of such tranche, subject to certain conditions. The investor will purchase shares of the Company's common stock pursuant to the CEFF at discounts ranging from 6% to 10%, depending on the average market price of the common stock during the eight-day pricing period, provided that the minimum acceptable purchase price for any shares to be issued to the investor during the eight-day pricing period is determined by the higher of \$2.25 or 90% of the Company's share price the day before the commencement of each draw down. In accordance with SFAS No. 133 Implementation Issue A6, the Company determined the option to sell shares of the Company's common stock does not qualify as a derivative as the notional amount, the sales price of the stock, is variable and therefore undeterminable. In addition, this arrangement does not require a minimum number of shares to be sold and is restricted to a maximum number of shares to be sold.

In connection with the CEFF, the Company issued a warrant to the investor to purchase up to 260,000 shares of common stock at an exercise price of \$9.26 which represents a 30% premium over the average of the closing prices of the Company's common stock during the 5 days preceding the signing of the agreement. The warrant will become exercisable after the six-month anniversary of the effective date of the agreement and will remain exercisable, subject to certain exceptions, until November 2, 2011. In accordance with EITF Issue No. 00-19, the warrant met all criteria within the guidance providing for the

classification of this financial instrument as equity. The fair value of this warrant, totaling \$1.1 million, was determined using the Black-Scholes model using the following assumptions: risk-free interest rates of 4.84%; dividend yield of 0%; expected volatility of 74%; and a term of 5.5 years. The net effect of recording the fair value to equity is zero at December 31, 2006.

The Company filed a registration statement with the Securities and Exchange Commission for the resale of the shares of common stock issuable in connection with the CEFF and the shares of common stock underlying the warrant in accordance with a registration rights agreement entered into concurrently with the above agreements. The registration rights agreement maintains penalty and make-whole provisions in the event the registration statement does not become effective within an allotted time frame and where the investor may be restricted, due to black out periods, from trading shares of the Company's common stock purchased pursuant to the CEFF or by the exercise of the warrant. In accordance with SFAS 133, *Accounting for Derivative Instruments and Hedging Activities*, and EITF Issue No. 00-19-2, *Accounting for Registration Payment Arrangements*, the Company accounts for these provisions under SFAS No.5, *Accounting for Contingencies* and will record the fair value of the liability in the event such a penalty is measurable and probable. As of December 31, 2006, an effective registration statement was filed with the Securities and Exchange Commission and the Company had not utilized this financial instrument.

6. Stockholders' Equity

Common Stock

In March 2006, the Company raised approximately \$40.0 million in gross proceeds in a registered direct offering involving the sale of approximately 4.9 million shares of common stock at a price of \$8.10 per share. Placement agency fees and other offering expenses were approximately \$2.7 million. These shares were offered pursuant to an effective registration statement that the Company had previously filed with the Securities and Exchange Commission.

In October 2005, the Company raised gross proceeds of 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.

In June 2004, the Company completed an initial public offering of its common stock in which it sold approximately 5.0 million shares of common stock for proceeds of \$30.6 million, net of underwriting discounts and commissions and offering expenses. In July 2004, the underwriters exercised their over-allotment option resulting in the sale of an additional 75,000 shares which resulted in proceeds of \$0.5 million, net of underwriting discounts and commissions.

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 2000 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 2001 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 Stock 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 equipment loans (see Note 3) and in connection with the Company's CEFF (see Note 5).

None of the above issued warrants had been exercised through December 31, 2006.

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 Equity Incentive Plan. Approximately 915,000 and 619,000 shares were added to the Equity Incentive Plan on January 1, 2006 and 2005, respectively, pursuant to an evergreen provision contained in the Equity Incentive Plan. The Equity Incentive 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 Equity Incentive Plan may be designated as incentive stock options or non-statutory 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, 2006 and 2005 were approximately 834,000 and 580,000, 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 Directors' Stock Option Plan. On January 1, 2006 and 2005, 100,000 shares were added to the plan pursuant to an evergreen provision contained in the Directors' Stock Option Plan. The Directors' Stock Option Plan provides for the grant of stock options and restricted stock to directors of the Company. Options under the Directors' Stock Option Plan are designated as non-statutory 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' Stock Option 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, 2006 and 2005 were approximately 188,000 and 109,000, respectively.

The weighted-average remaining contractual life of the options outstanding under both plans at December 31, 2006 was approximately 8.2 years. The estimated weighted average fair value of stock options granted during 2006, 2005 and 2004 was \$4.84, \$2.38 and \$6.32, respectively.

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The following is a further breakdown of the options outstanding as of December 31, 2006 (in thousands, except per share data):

| Ranges of Exercise Prices | Number of Options | Options Outstanding | | Options Vested and Exercisable | |
|---------------------------|-------------------|---|---------------------------------|--------------------------------|---------------------------------|
| | | Weighted Average Remaining Contractual Life | Weighted Average Exercise Price | Number of Options | Weighted Average Exercise Price |
| \$0.30 to \$2.00 | 705 | 6.4 | \$ 1.40 | 597 | \$ 1.39 |
| \$2.01 to \$4.00 | 227 | 7.5 | \$ 2.82 | 156 | \$ 2.80 |
| \$4.01 to \$6.00 | 299 | 8.7 | \$ 5.66 | 74 | \$ 5.56 |
| \$6.01 to \$8.00 | 551 | 8.9 | \$ 7.34 | 163 | \$ 6.80 |
| \$8.01 to \$9.22 | 856 | 9.3 | \$ 8.59 | 35 | \$ 8.51 |
| Total | 2,638 | 8.2 | \$ 5.58 | 1,025 | \$ 3.01 |

There were approximately 9,000 and 24,000 shares of common stock outstanding at December 31, 2006 and 2005, respectively, 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 Employee Stock Purchase Plan. Approximately 305,000 and 206,000 shares were added to the plan on January 1, 2006 and 2005, respectively, pursuant to an evergreen provision contained in the Employee Stock Purchase Plan. The Employee Stock Purchase Plan 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 Employee Stock Purchase Plan shares. The following shares were issued under the Employee Stock Purchase Plan during the year ending December 31:

| | Number of Shares Purchased | Weighted Average Price | Total Proceeds |
|------|----------------------------|------------------------|----------------|
| 2006 | 198,158 | \$ 3.04 | \$ 602,961 |
| 2005 | 104,551 | \$ 2.67 | 279,369 |
| 2004 | 29,656 | \$ 5.98 | 177,453 |
| | 332,365 | | \$ 1,059,783 |

Shares Reserved For Future Issuance

The following shares of common stock were reserved for future issuance at December 31, 2006 (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 |
| Warrants to purchase shares in conjunction with the CEFF | 260 |
| Common stock options: | |
| Granted and outstanding | 2,638 |
| Reserved for future issuance | 1,152 |
| Employee stock purchase plan | 689 |
| | 8,537 |

7. Income Taxes

Significant components of the Company's deferred tax assets as of December 31, 2006 and 2005 are shown below (in thousands). A valuation allowance of \$46.6 million and \$32.9 million has been established at December 31, 2006 and 2005, respectively, to offset the net deferred tax assets as realization is uncertain.

| | December 31, | |
|---|--------------|-----------|
| | 2006 | 2005 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | \$ 37,406 | \$ 27,874 |
| Research and development credits | 5,890 | 4,601 |
| Deferred revenue | 1,964 | |
| Other, net | 1,403 | 557 |
| Total deferred tax assets | 46,663 | 33,032 |
| Deferred tax liabilities: | | |
| Deferred compensation | (28) | (97) |
| Valuation allowance for deferred tax assets | (46,635) | (32,935) |
| Net deferred assets | \$ | \$ |

At December 31, 2006, the Company had federal and California net operating loss carryforwards of \$91.9 million and \$91.6 million, respectively, which will begin to expire in 2019 and 2009, respectively, unless previously utilized. The Company also had federal and state research and development tax credit carryforwards of approximately \$3.7 million and \$3.2 million respectively. The federal research and development tax credit carryforwards will begin expiring in 2019 unless previously utilized and the state credits do not expire.

Pursuant to Internal Revenue Code Sections 382 and 383, use of the Company's net operating loss and credit carryforwards may be limited in the event cumulative changes in ownership of more than 50% have occurred.

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The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2006, 2005 and 2004, due to the following (in thousands):

| | 2006 | 2005 | 2004 |
|---|--------------|-------------|-------------|
| Federal income taxes at 35% | \$ (11,644) | \$ (8,253) | \$ (5,240) |
| State income tax, net of Federal benefit | (1,751) | (1,268) | (766) |
| Tax effect on non-deductible expenses and credits | (305) | (556) | (364) |
| Increase in valuation allowance | 13,700 | 10,077 | 6,370 |
| | \$ | \$ | \$ |

8. 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. Matching contributions have not been approved or made since the inception of the 401(k) Plan. Plan administration costs totaled \$6,850, \$6,500 and \$6,500 for the years ended December 31, 2006, 2005 and 2004, respectively.

9. Related Party Transactions

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 are covered by a claim of an issued, valid and unexpired patent or a patent application, that was in existence or based on any 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 of the Company's current product candidates and drug compounds from our research programs may be subject to these royalty provisions. The determination of any potential obligations will be assessed at the time such products are commercially available.

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10. Summary of Quarterly Financial Data (Unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2006 and 2005 (in thousands, except for net loss per share data):

| | Quarters Ended | | | | Year Ended Dec 31(1) |
|--|------------------|-------------------|------------------|-------------------|-------------------------|
| | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | |
| 2006 | | | | | |
| Revenue | \$ 973 | \$ 942 | \$ 1,055 | \$ 1,416 | \$ 4,386 |
| Research and development(2) | 6,791 | 6,820 | 7,715 | 8,979 | 30,305 |
| General and administrative(2) | 2,248 | 2,725 | 2,779 | 3,138 | 10,890 |
| Total operating expenses | 9,039 | 9,545 | 10,494 | 12,117 | 41,195 |
| Net loss attributable to common stockholders | (7,466) | (7,645) | (8,410) | (9,747) | (33,268) |
| Basic and diluted net loss per share: | (0.30) | (0.25) | (0.28) | (0.32) | (1.15) |
| 2005 | | | | | |
| Revenue | \$ 397 | \$ 617 | \$ 1,395 | \$ 1,362 | \$ 3,771 |
| Research and development(3) | 5,115 | 4,869 | 4,989 | 6,279 | 21,252 |
| General and administrative(3) | 1,722 | 1,680 | 1,721 | 2,063 | 7,186 |
| Total operating expenses | 6,837 | 6,549 | 6,710 | 8,342 | 28,438 |
| Net loss income attributable 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) |

-
- (1) The sum of the four quarters may not necessarily agree to the year total due to rounding within a quarter.
- (2) Approximately \$0.4, \$0.6, and \$0.5 related to patent and patent related activities were reclassified from research and development to general and administrative for the first, second, and third quarter of 2006, respectively.
- (3) Approximately \$0.3, \$0.4, \$0.4, and \$0.3 related to patent and patent related activities were reclassified from research and development to general and administrative for the first, second, third and fourth quarters of 2005, respectively.