METABASIS THERAPEUTICS INC
Form 10-K
March 31, 2009
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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)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2008

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 000-50785

METABASIS THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

(858) 587-2770

(Registrant s telephone number, including area code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.001 per share	**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 x

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 x

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

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

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

Large accelerated filer ¨ Accelerated filer ¨ Non-accelerated filer ¨ Smaller reporting company x

(Do not check if a smaller reporting company)

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

As of June 30, 2008, 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 $32.5 million, based on the closing price of the registrant s common stock on the Nasdaq Stock Market on June 30, 2008 of $1.55 per share. Shares of common stock held by executive officers, directors and 10% or greater stockholders of the registrant have been excluded from such calculation 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 25, 2009 was 35,152,359.

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, 2008 are incorporated by reference into Part III of this report.

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METABASIS THERAPEUTICS, INC.

FORM 10-K ANNUAL REPORT

FOR THE YEAR ENDED DECEMBER 31, 2008

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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, future collaborations, 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, potentia projects, should, will, would 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 committed to the discovery, development and commercialization of novel drugs for metabolic diseases using our proprietary technology and our knowledge of processes and pathways within the liver that are useful for liver-selective drug targeting and treatment of metabolic diseases. We have established a broad pipeline of product candidates and advanced discovery programs targeting large markets with significant unmet needs. Our product pipeline includes clinical-stage product candidates and advanced discovery programs for the treatment of metabolic diseases such as diabetes and hyperlipidemia, which we refer to as our core assets, as well as product candidates and advanced discovery programs for the treatment of liver diseases such as hepatitis and primary liver cancer, which we refer to as our non-core assets. All of our product candidates were developed internally using our proprietary technology and know-how.

Our current financial resources will support our on-going planned operating expenses into July 2009. In January 2009, we announced a plan to restructure our organization which followed the initiation of a separate restructuring plan that we announced in November 2008. The two restructuring plans resulted in an approximately 60% reduction of our workforce.

As part of the January 2009 plan, we narrowed our research and development efforts and intend to utilize a significant portion of our existing resources on the planned Phase 2 clinical trial for MB07811, our clinical-stage product candidate for the treatment of hyperlipidemia, which we believe will provide significant value for stockholders. In addition, we continue to support our on-going sponsored research programs in collaboration with Merck & Co., or Merck and Hoffmann-La Roche Inc., F. Hoffmann-La Roche LTD and Roche Palo Alto LLC, or collectively Roche.

To a lesser extent, we have committed resources towards the advancement of our second generation beta-subtype selective thyroid hormone receptor, or TRß, agonist and our glucagon antagonist discovery programs to the preparatory stage of preclinical development. We believe the second generation TRß agonist discovery program could result in one or more compounds that could enhance the overall value of our hyperlipidemia program to potential strategic partners. Additionally, we believe the advancement of the glucagon antagonist program will improve our ability to secure additional financial resources under a collaborative arrangement.

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Our pipeline of clinical-stage product candidates also consists of our core asset, MB07803, a product candidate for the treatment of type 2 diabetes, and our non-core assets, pradefovir and MB07133, developed for the treatment of hepatitis B and primary liver cancer, respectively. As part of our near-term strategic focus, we have not committed resources for the further development of these product candidates as we intend to establish a strategic partnership with respect to MB07803 and, in the case of our non-core assets, license or monetize these product candidates to secure additional financial resources. In addition, we have suspended all activities related to various other metabolic disease advanced discovery programs.

Completion of the MB07811 Phase 2 clinical trial, currently anticipated by the end of 2009, is dependent upon our ability to raise significant additional capital to continue operations beyond July 2009 through the achievement of milestones from existing collaboration agreements, the entry into new strategic collaborations with respect to one or more of our core assets or the license or monetization of our non-core assets, potential equity financings and/or other funding sources. In the event we are not able to generate sufficient capital through the attainment of contractual milestones, other business development activities, potential equity financings and/or other funding sources, we will be required to seek additional resources by pursuing other strategic alternatives, including the merger with, or sale of some or all of our assets to, another company, or cease our operations entirely.

The following table summarizes our product candidates currently in clinical development and our advanced discovery programs:

Clinical-Stage Product Candidates or Advanced Discovery Programs(1)	Disease/Condition	Partner	Our Commercial Rights	Status(4)
Core Assets:				
MB07811	Hyperlipidemia	None	Worldwide	Phase 2
MB07803	Diabetes	None	Worldwide	Phase 2
AMPK Activators(2)	Diabetes	Merck	Royalties	Lead Optimization(5)
Glucagon Antagonist	Diabetes	None	Worldwide	Lead Optimization(5)
TRß Agonist	Hyperlipidemia	None	Worldwide	Lead Optimization(5)
Non-Core Assets:				
Pradefovir	Hepatitis B	None	Worldwide	Phase 3
MB07133	Liver Cancer	None	Worldwide	Phase 2
Unnamed(3)	Hepatitis C	Roche	Royalties	Lead Optimization(5)

(1) None of our clinical-stage product candidates have received regulatory approval in the U.S. or in foreign countries. An advanced discovery program is a program that has yielded compounds with the appropriate potency, selectivity and pharmacokinetics to allow the demonstration of target engagement and efficacy in preclinical models.

(2) We are collaborating with Merck on developing an adenosine 5 monophosphate activated protein kinase, or AMPK, activator for treating type 2 diabetes and potentially other metabolic diseases.

(3) We are collaborating with Roche to apply our HepDirect technology to certain compounds for treating hepatitis C infection.

(4) The clinical trial phase denoted for a compound either represents the most advanced trial phase tested to date or the phase of the next planned trial, e.g. pradefovir is listed as a Phase 3 compound because it has completed a 48-week Phase 2 trial and end of Phase 2 meetings with both the Federal Drug Administration, or FDA, and European Medicines Evaluation Agency, or EMEA.

(5) Lead optimization is a stage within the discovery process during which the physical properties and biological activity of various structural analogs of a lead compound are evaluated to determine those analogs with the greatest potential to be developed into safe and effective medicines.

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Core Assets Metabolic Disease Product Candidates

Our metabolic disease-related clinical-stage product candidates are as follows:

MB07811, a Phase 2 product candidate for treating hyperlipidemia. MB07811 uses our HepDirect prodrug technology and other structural characteristics to target a TRß agonist to the liver for the treatment of hyperlipidemia. We completed a rising multiple-dose Phase 1 clinical trial of MB07811 in 2008. A 12-week Phase 2 clinical trial in subjects with high cholesterol is planned for initiation in the first half of 2009, and we expect to complete the study by the end of 2009.

MB07803, a Phase 2 product candidate for treating type 2 diabetes. MB07803 is a second-generation fructose-1,6-bisphosphatase, or FBPase, inhibitor we discovered for treating type 2 diabetes. We have completed five Phase 1 clinical trials in healthy volunteers with MB07803 and a four-week randomized initial proof-of-concept Phase 2 clinical trial. We recently completed a 14-day, multi-dose safety and pharmacokinetic trial of MB07803 in patients with type 2 diabetes.

Core Assets Metabolic Disease Advanced Discovery Programs

Our metabolic disease-related advanced discovery programs are as follows:

AMPK, a metabolic disease program, in collaboration with Merck, that is focused on developing drug candidates that activate AMPK for treating type 2 diabetes and potentially other metabolic diseases.

Glucagon Antagonist, a program focused on identifying potent, orally bioavailable glucagon antagonists for treating type 2 diabetes.

TRß agonist, a second-generation program to identify drug candidates for treating hyperlipidemia.

Non-Core Assets Liver Disease Product Candidates and Other Programs

Our liver disease-related product candidates and advanced discovery programs are as follows:

Pradefovir, a Phase 3 product candidate for treating chronic hepatitis B. Pradefovir is a HepDirect prodrug designed to deliver high concentrations of a potent antiviral nucleotide analog to the liver for the treatment of chronic hepatitis B. We have completed eleven Phase 1 and Phase 2 clinical trials of pradefovir, including a 48-week Phase 2 clinical trial.

MB07133, a Phase 2 product candidate for treating primary liver cancer. MB07133 is a HepDirect prodrug of the intermediate form of a known oncolytic, which is designed to deliver high concentration of the active form of the drug to the liver tumor. We have completed a repeat cycle Phase 1/2 clinical trial of MB07133.

Our liver disease-related programs also include a collaboration with Roche to apply our HepDirect technology to certain compounds for treating hepatitis C infection.

HepDirect Technology

Our HepDirect technology is a proprietary technology used to target drugs to the liver. We are using this proprietary technology, our knowledge of liver diseases and our expertise in pathways and proteins residing in the liver that significantly contribute to metabolic diseases in order to discover new drug therapies. We have used this technology, knowledge and expertise to discover product candidates such as pradefovir,

MB07133 and MB07811. We continue to use this technology in our collaboration on hepatitis C and certain advanced discovery programs.

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Our Business Strategy

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

Advancing MB07811 and our second generation TRß agonist program. We are currently independently developing MB07811, which selectively targets a TRß agonist to the liver for treating hyperlipidemia. Our clinical development efforts, and the majority of our internal resources, are directed toward achieving key near-term clinical development milestones for MB07811. We also have on-going efforts focused on the discovery of a second generation TRß agonist. We believe that advancement of these programs will create significant value for our stockholders.

Establishing strategic collaborations that maximize the current and future value of our core assets while potentially allowing us to participate in their future worldwide clinical development and commercialization. Optimal clinical development and commercialization of metabolic disease product candidates can be complex, costly and time consuming. Therefore, we intend to collaborate with larger pharmaceutical and/or biotechnology companies to develop and commercialize our core metabolic disease assets. We are currently exploring strategic collaborations for one or more of our core assets with the intent to generate sufficient resources to execute on current and long-term business objectives while ensuring the continued development of these key discovery programs or product candidates. We intend to seek strategic collaborations for our core assets under terms that:

- maximize their current and future value to our stockholders, and/or
- allow us to enhance our internal capabilities by participating in the future worldwide clinical development and commercialization of any compounds subject to the collaboration.

Enhancing the value of our non-core assets by licensing them for future clinical development and commercialization or selling them to provide near-term resources to reinvest into our core asset pipeline. We currently retain rights to two non-core clinical development stage liver disease product candidates, pradefovir and MB07133, which we have developed as potential treatments for hepatitis B viral disease and primary liver cancer, respectively. In addition, we retain royalty-related interests in an advanced discovery program with Roche to develop a potential treatment for hepatitis C viral disease by applying our proprietary HepDirect technology to their compounds. Our interests in the advanced discovery program with Roche are the result of a collaboration that applies our proprietary HepDirect technology to their compounds. We may enter into additional technology-based collaborations in the future with others seeking access to our technology or intellectual property. These various programs are not core to our main metabolic disease focus. However, these non-core assets could provide significant value to our stockholders in the future if these products are successfully developed, generate milestone or royalty revenue or our interests in these products are sold. Therefore, we intend to further enhance the value of these non-core assets by licensing them, assisting current licensees in their development efforts or by selling these non-core assets to provide near-term resources to reinvest into our core assets.

Our Core Assets

Our metabolic disease product candidates focus on treating diseases such as type 2 diabetes and hyperlipidemia. These diseases 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 producing and/or metabolizing 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 60% 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. As a result, we believe more effective drugs are needed to treat these chronic diseases.

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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 accelerate 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. In addition, some plaque is unstable and can rupture and expose prothrombogenic (clotting) particles to the blood leading to reduced blood flow and acute cardiovascular events such as heart attacks and 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.

The number of patients diagnosed with hyperlipidemia is expected to increase from 301 million worldwide in 2006 to 330 million in 2015. In the U.S., the number of patients with hyperlipidemia is expected to increase from 111 million in 2006 to 124 million in 2015.

Current Treatments

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.

Major classes of hyperlipidemia drugs include, but are not limited to:

- statins, which reduce serum cholesterol levels by inhibiting a key enzyme involved in the biosynthesis of cholesterol,
- fibrates, which reduce the amount of cholesterol and triglycerides (fatty substances) in blood,
- nicotinic acid derivatives, which lower cholesterol, triglycerides and low density lipoproteins and increase high density lipoproteins,
- cholesterol absorption inhibitors, or CAIs, which inhibit the absorption of dietary and biliary cholesterol,
- bile acid sequestrants, which bind with cholesterol-containing bile acids in the intestines and remove them in bowel movements by excretion via the feces, and
- statin combination therapies, which combine statins with members of the above-mentioned classes.

Markets

Combined sales of products used to treat hyperlipidemia in the seven major pharmaceutical markets were $27 billion in 2007, with the U.S. accounting for $17.1 billion of that total. By 2016 combined sales in the seven major pharmaceutical markets are expected to decrease to $23 billion and sales in the U.S. are expected to decrease to $15 billion. Although total revenues driven by this market are decreasing, primarily driven by the impact of generic products, the overall need for therapies to treat hyperlipidemia is increasing.

Patients with mixed dyslipidemia (elevated LDL and elevated triglyceride levels) account for approximately 100 million patients in the seven major pharmaceutical markets, with the U.S. consisting of approximately 30% of this total. Approximately 45% are diagnosed and, of these patients, about 50% are treated for the disease. Hence, in the U.S. alone there are 25 million patients being treated for hyperlipidemia. Of this population, approximately 90%, or 22.5 million, of hyperlipidemia patients suffer from some form of increased low-density lipoprotein, or LDL. Our target patient population for MB07811 includes patients that are intolerant to statins or that do not meet target LDL-lowering levels with current therapies. Five percent of patients are intolerant to statins, whereas 60% of patients with dyslipidemia do not meet target LDL-lowering levels.

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MB07811: A liver-targeted thyroid hormone receptor agonist for treating hyperlipidemia

MB07811 is the result of our efforts to find a TRß agonist whose action is limited to the liver and thereby able to affect the levels of lipids, such as cholesterol, and triglycerides and lipoproteins, such as LDL, apolipoprotein B, or apoB, and Lp(a), that are associated with increased cardiovascular risk. MB07811 uses our HepDirect prodrug technology and other structural characteristics to target a TRß agonist to the liver. Thyroid hormone receptor agonists are known to reduce lipids 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 TRß receptor agonist that is designed to deliver the agonist to the site where lipids are 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 TRß agonists and thus unlock the therapeutic potential of this approach. In addition, MB07811, if approved, could be one of the first in an entirely new class of anti-hyperlipidemic agents which may help patients better reach targeted lipid levels either as first line therapy or in combination with statins.

Product Position

Although statins are first-line therapy for lowering high cholesterol levels, there are a number of treatment goals that may not be achieved by statins. These include patients who do not get adequate cholesterol lowering and need other therapies added to their treatment regimen either because they cannot tolerate higher doses of statins or high doses remain suboptimal in achieving cholesterol treatment targets, patients with a combination of high cholesterol and high triglyceride levels in which statins fail to adequately lower triglycerides, patients who remain at risk for cardiovascular events based on elevation of an emerging risk factor, Lp(a), and patients who cannot tolerate statins. Clinical and preclinical data suggest that MB07811 could be an effective approach for lowering cholesterol with the added benefit of reducing both serum and liver triglycerides as well as Lp(a). Importantly, MB07811 appears to have an additive effect in reducing cholesterol when used with statins based on preclinical studies. Thus, if MB07811 is ultimately approved, it may find broad acceptance among physicians as an add-on to statin therapy. In addition, while statins are generally considered to be first line agents for the majority of patients with hyperlipidemia, approximately 5%, or approximately 1.25 million, of patients with hyperlipidemia in the U.S. cannot use statins. For these statin-intolerant patients, MB07811 may be considered as an alternative therapy.

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 February 2000 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.

Clinical Trials

MB07811 has successfully completed a rising single-dose Phase 1 clinical trial and a rising multiple-dose Phase 1 clinical trial. MB07811 was well-tolerated in both clinical trials. In addition, although subjects in the Phase 1 trial had only modest elevations in LDL cholesterol, effective doses of MB07811 were associated with substantial decreases with each dose in LDL (15 41% difference from placebo), triglycerides (> 30% difference from placebo), apolipoprotein B (9 40% difference from placebo), and Lp(a) (28 -56% difference from placebo). No apparent cardiac effects were observed, including no differences in heart rate, heart rhythm or blood

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pressure between subjects treated with MB07811 and placebo. Mild increases in liver enzymes and dose related shifts in thyroid hormone levels were observed at the higher doses of MB07811. These changes in liver enzymes and thyroid hormone levels began to reverse during the one-week post-study observation period.

Based on the promising efficacy results seen in the Phase 1 clinical trials, we believe further study of MB07811 with longer duration of treatment in patients with higher cholesterol levels is warranted. Moreover, a longer study will elucidate the time course and possible adaptation by the liver and thyroid to treatment with MB07811. To evaluate these effects, three doses of MB07811 (plus placebo) will be tested in a 12-week Phase 2 clinical trial in subjects with high LDL levels, which we plan to initiate in the first half of 2009.

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 a decrease in the sensitivity of the body s tissues, such as muscle, liver and fat, to insulin action, increased glucose production and a relative underproduction of the hormone insulin by the pancreas. 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 observed 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 220 million people worldwide and over 21 million people in the U.S., and this number is projected to increase at an annual rate of 2.5% over the next 10 years.

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, or HbA1c, 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 HbA1c into the targeted range for a sustained period of time in the majority of patients with type 2 diabetes.

Drugs from each of the major classes of diabetes drugs exhibit side effects and tolerability issues, as well as decreased efficacy over time in many patients. These drug classes include:

- insulin secretion enhancers (e.g. sulfonylureas), 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 (e.g. thiazolidinediones), which lower glucose levels by enhancing insulin sensitivity. This drug class has been associated with fluid retention, weight gain and a risk of heart attacks and angina,

- hepatic glucose output inhibitors, which lower glucose levels by inhibiting liver glucose production. The only drug in this class is metformin, which, based on a study reported in the medical journal *Diabetes*, inhibits glucose production by the liver by only approximately 20-25%, even when administered at the maximum allowed dose. 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,

- incretin mimetics, which lower glucose by exhibiting many of the same glucose regulating actions of naturally occurring glucagon-like peptide-1, or GLP-1. GLP-1 is 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, and

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Dipeptidyl peptidase-4, or DPP-4, inhibitors, which inhibit an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-4 thus increases the half-life of endogenous GLP-1 by preventing cleavage and inactivation of GLP-1. The overall effect of drugs in this class is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion.

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 non-elderly obese patients who, according to a 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 HbA1c levels above the targeted range at three years. Progressively fewer patients were able to maintain baseline HbA1c levels at six years and nine years, respectively. Thus, there remain certain patient populations in whom high blood sugar is not adequately managed with currently available therapies.

One of the major underserved diabetic populations is patients who are ineligible for metformin therapy. These include patients not allowed to use metformin (particularly patients with impaired renal (kidney) function), patients intolerant to metformin (e.g. gastrointestinal side effects) and patients with severe diabetes who no longer respond to metformin, a problem that is prevalent with long-term use. The common alternative therapies to metformin, sulfonylureas and thiazolidinediones, have side effect profiles that are problematic, particularly in patients with renal impairment and severe diabetes. Moreover, the glucose-lowering effects of these medications also tend to wane over time, requiring the addition of other antidiabetic medications including insulin to achieve target HbA1c. We believe that because of these limitations in currently marketed drugs, the diabetes market is receptive to new drugs to address these unmet medical needs.

Markets

Combined sales of oral products used to treat type 2 diabetes in the seven major pharmaceutical markets, consisting of the U.S., Japan, United Kingdom, Germany, France, Italy and Spain, were $18 billion in 2007, with the U.S. accounting for $11.9 billion of that total. By 2016, combined sales of oral products used to treat type 2 diabetes, in the seven major pharmaceutical markets, are expected to increase to $25 billion, and sales in the U.S. are expected to increase to $16 billion.

We are initially targeting the use of MB07803 in the patient populations that are contraindicated or intolerant to metformin. In the U.S. alone, there are 1.4 million patients that are contraindicated to metformin (of which 1.1 million are renally impaired) and another 1.3 million patients that are intolerant and not on metformin. These two segments represent 17.1% of all diagnosed and treated patients. Additionally, we will be targeting MB07803 for use by those diabetic patients that eventually fail all oral therapies prior to being prescribed insulin. At any given time, approximately 30% of type 2 diabetes patients are on insulin. In the U.S. this patient population represents over 5 million of the total treated population.

MB07803: A second generation fructose-1, 6-bisphosphatase inhibitor for treating type 2 diabetes

MB07803 is an oral product candidate for treating type 2 diabetes that we discovered and is designed to inhibit FBPase. MB07803 is our second generation FBPase inhibitor to CS-917, our first product candidate designed for treating type 2 diabetes via this mechanism. CS-917 had demonstrated promising results in early clinical studies in patients with moderate to severe elevations in fasting plasma glucose. These studies were followed by a 12-week Phase 2 trial evaluating CS-917 predominately in a population of patients not previously treated with medication and exhibiting mild type 2 diabetes. While CS-917 failed to significantly lower the placebo-adjusted level of HbA1c at the doses tested, a subsequent analysis of the data from this trial showed that CS-917 significantly lowered both HbA1c and fasting plasma glucose in certain patient sub-populations over the three-month dosing period evaluated. These results, along with previous Phase 2 clinical trials, confirmed that FBPase inhibition is a promising mechanism for significantly improving glycemic control. The results from the

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CS-917 program have been utilized to guide our initial development plan for MB07803. We have designed MB07803 with certain improvements including improved oral bioavailability and metabolic stability, which we believe could lead to better tolerability and improved efficacy. Recent pre-clinical studies indicate that a metabolite present in humans at high levels following treatment with CS-917 appears to negatively impact mitochondrial function. MB07803 was designed to avoid this metabolism, and data from human studies on MB07803 show that the corresponding metabolite is formed at very low levels, such that effects on mitochondrial function are not expected. This difference may translate to an improved safety profile for MB07803.

Product Position

Our first generation FBPase inhibitor, CS-917, appeared to interact with metformin in a limited number of patients during a drug-drug interaction study, leading to serious adverse events in those patients. It is possible but not certain that MB07803 could also interact with metformin. Thus, initial clinical development of MB07803 will focus on diabetic populations that are underserved, the largest of which are patients ineligible for metformin therapy. Since MB07803 may lower glucose comparable to metformin, MB07803 could, if approved by regulatory authorities, initially be the drug of choice, alone or in combination with other oral therapies, for such patients.

Clinical Trials

We have completed five Phase 1 clinical trials of MB07803 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 supported the advancement of MB07803 into Phase 2 clinical trials. We have completed a Phase 2, 28-day initial proof-of-concept clinical trial for MB07803. This clinical trial was a randomized, double-blind, placebo-controlled trial in 105 patients with type 2 diabetes with moderately to severely elevated fasting plasma glucose, or FPG (average FPG of 187 mg/dL). Patients received either placebo or MB07803 at an oral dose of 10, 50, 100 or 200 mg once daily. Results indicate that the decrease in FPG by day 28 in patients treated with 200 mg was statistically and clinically significant (-28.9 mg/dL difference from placebo). In the subgroup of patients with FPG over 180 mg/dL treated with 200 mg, the decrease in FPG was also statistically and clinically significant (-49.7 mg/dL difference from placebo). MB07803 was safe and well tolerated with 94% of the patients completing the study and no patient withdrawals due to drug-related adverse events, or AEs. The frequency and nature of the AEs were similar to the AEs seen in the placebo group. There were two serious adverse events in the treatment group that were not drug-related. There were no cases of lactic acidosis, no significant gastrointestinal side effects and no drug-related hypoglycemia (low blood sugar).

The results of this Phase 2 clinical trial support the potential of MB07803 as an important new approach for treating patients with type 2 diabetes. Based on the favorable safety profile observed in the Phase 2 trial, another clinical trial was conducted to investigate whether administration of a newly developed MB07803 tablet formulation twice-daily would increase drug concentrations and whether higher drug concentrations would be safe and well-tolerated and result in better glucose lowering compared to placebo. This recently completed trial was a 14-day, ascending, multiple dose clinical trial in 42 poorly controlled type 2 diabetes patients (average FPG 221 mg/dL) in which 50, 200 and 400 mg tablets compared to matching placebo administered twice daily (every 12 hours) were evaluated. Results indicated that 200 mg and 400 mg doses taken twice a day resulted in higher drug concentrations than achieved in previous Phase 1 trials. The efficacy endpoint in the trial was the change from baseline at Day 14 in the glucose lowering response (determined by the area-under-the-curve, i.e. AUC) as measured after administration of the morning dose and during the last 6 hours of a prolonged 18 hour fast. The results showed that the 6-hour AUC was reduced from -93 (mg.hr/dL) for patients treated with placebo to -236 (p=0.17 vs. placebo), -442 (p=0.002 vs. placebo), and -532 (p=0.0002 vs. placebo) mg.hr/dL for patients treated with 50 mg, 200 mg and 400 mg twice daily, respectively. The top two doses also achieved statistical significance in the more clinically-relevant endpoint of a single point measure of FPG (-72 and -69 mg/dL change from baseline at the 200 and 400 mg twice daily dose compared to -14 mg/dL in placebo). In addition,

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all doses significantly reduced day long glycemia (24-hour glucose AUC). Dose-limiting vomiting was observed at the highest dose. In contrast, no patients in the 200 mg Q12h group experienced vomiting. Four of the 12 patients in this group experienced at least one episode of mild nausea, but none discontinued due to nausea. No patient in the 50 mg dose cohort experienced nausea or vomiting. One patient had glucose levels less than 60 mg/dL and exhibited symptoms consistent with hypoglycemia. This patient also had 3 nonconsecutive, asymptomatic elevations of lactate when glucose levels were less than 60 mg/dL. Other patients showed fasting glucose levels lower than 60 mg/dL, predominantly during the latter stages of the 18-hour fasting period, and were asymptomatic. No patient in the trial experienced lactic acidosis.

Metabolic Disease Advanced Discovery Programs

We are expanding our product pipeline by using our proprietary HepDirect technology, 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 HepDirect technology, which we use in several of our discovery 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 drug compounds. Our goal is to expand our pipeline by advancing new drug compounds from these programs into clinical development and continuing development of any product candidates with collaborative partners. We believe our advanced discovery programs have the potential to yield additional clinical development candidates in the near-term.

Our metabolic disease advanced discovery programs are:

A metabolic disease program focused on developing an AMPK activator for treating type 2 diabetes and potentially other metabolic diseases.

AMPK plays an important role in regulating carbohydrate and fat metabolism. Activation of AMPK switches cellular metabolism from an energy consuming state to an energy-sparing one. Accordingly, diseases manifested through overproduction of biochemical end products by energy-consuming pathways (e.g. glucose, cholesterol, fatty acids and triglycerides) are potential disease targets for AMPK activators. We have an advanced discovery program, being conducted in collaboration with Merck, that is focused on identifying drug candidates that activate AMPK to treat type 2 diabetes and potentially other metabolic diseases. This program may yield additional development candidates to expand our product pipeline.

A metabolic disease program focused on developing a glucagon receptor antagonist for treating type 2 diabetes.

Type 2 diabetes has long been considered a hormonal disorder with insulin deficiency and/or insensitivity and a relative glucagon excess. Glucagon opposes the actions of insulin leading to an inappropriate increase in glucose production by the liver and other metabolic disturbances. We have an advanced discovery program that is focused on identifying chemically novel, potent, orally bioavailable glucagon antagonists for treating type 2 diabetes. Our most advanced compound has shown significant and consistent lowering of blood glucose when dosed orally in numerous diabetic animal models. This program may yield additional development candidates to further expand our product pipeline.

A second generation TRß agonist program to identify drug candidates for treating hyperlipidemia.

We have an advanced discovery program to identify second-generation TRß agonists for treating hyperlipidemia. This program may yield additional development candidates that lower cholesterol and triglycerides by the same mechanism as MB07811 but with potential improvements.

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Non-Core Assets

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 often poorly treated with current drug therapies which can be associated with poor tolerability and/or inadequate efficacy. The use of existing drugs for treating 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.

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 or liver failure, resulting in death.

Hepatitis B is the most common serious liver infection in the world. Over 2 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.

Current Treatments

In the U.S., there are seven approved treatments for chronic hepatitis B that are either interferon or nucleoside analogue based therapies. All of these therapies have limitations in treating patients with hepatitis B. For example, the interferons are generally poorly tolerated. Other antivirals such as the nucleoside analogue are limited by high viral resistance rates. Adefovir dipivoxil, a nucleotide analogue, decreases virus levels, as measured by hepatitis B DNA in the blood serum, but 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 adefovir dipivoxil 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 adefovir dipivoxil (10 mg) may be suboptimal for reducing virus levels in patients with hepatitis B. In addition, although adefovir dipivoxil appears to show a low rate of virus resistance for the viral load reduction, the inability of adefovir dipivoxil to maximally suppress the virus at the marketed dose in the majority of patients increases the incidence of viral resistance in these patients.

Markets

In the seven major pharmaceutical markets combined, sales of oral hepatitis B anti-viral products were $661 million in 2007, with the U.S. accounting for $370 million of that total. By 2016, combined sales in the seven major pharmaceutical markets are expected to increase to $1.3 billion and sales in the U.S. are expected to increase to $488 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. Pradefovir, 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.

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

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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.

Pradefovir: A HepDirect prodrug of PMEA for treating hepatitis B

Pradefovir is an oral product candidate for treating hepatitis B, which is, like adefovir dipivoxil, a prodrug of 9-(2-phosphonylmethoxyethyl) adenine, or PMEA. Pradefovir is a HepDirect prodrug designed to deliver high concentrations of PMEA to the liver. Targeting PMEA production to the liver could significantly reduce the dose-related kidney toxicities reported for adefovir dipivoxil and thereby improve anti-viral activity. In preclinical studies, pradefovir increased delivery of PMEA to the liver while significantly decreasing levels of PMEA in the bloodstream or kidney. In a 48-week Phase 2 clinical trial, pradefovir reduced hepatitis B virus levels by ~ 1.5 log copies/mL compared to adefovir dipivoxil and improved efficacy with reduced PMEA levels in blood. In this clinical trial, pradefovir was also safe and well tolerated with no treatment-related trends in significant adverse events including evidence for adverse effects on the kidney and on the liver.

In October 2001, we entered into a development and license agreement with Valeant Pharmaceuticals North America, or 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 Corporation, or Schering, and further granted Schering a license to its intellectual property related to pradefovir. Concurrently, we and Schering 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 was granted exclusive worldwide rights to develop and commercialize pradefovir during the term of the agreement. In September 2007, we entered into an agreement with Schering and Valeant to terminate our agreements for the development and commercialization of pradefovir. In connection with this agreement, all rights to pradefovir were transferred back to us, subject to certain milestone and royalty payments due to Valeant should this product candidate be subsequently developed. These agreements were terminated as a result of numerous factors, including the results from the 24-month oral carcinogenicity studies of pradefovir in rats and mice.

In September 2008, we, Valeant and Schering entered into an agreement to amend certain terms of the assignment and assumption agreement and the termination agreement, each entered into by Valeant, Schering and us. The amendments to the assignment and assumption agreement provide for a reduction in the total number and value of milestone payments payable by us to Valeant upon the achievement of certain specified events to a single milestone payment due upon the first regulatory approval of pradefovir, and reduce certain royalty payments due from us to Valeant upon commercialization of pradefovir. In addition, the termination agreement was amended to transfer certain patient registry obligations, should they be required, to us from Valeant (excluding the cost thereof, up to a specified limit).

More recently, we convened a scientific advisory panel to provide an independent review of the results from the rat and mice carcinogenicity studies. The scientific advisory panel concluded that there was an acceptable margin of safety for the dose of pradefovir expected to be evaluated for a Phase 3 clinical trial. The results from the carcinogenicity studies were submitted to the FDA and were analyzed by the Executive Carcinogenicity Assessment Committee, or CAC. Based on advice from the CAC, the FDA concurred with the high multiple of human exposure at which any effects or potential effects occurred and requested that we submit protocols in order to resume clinical trials. Accordingly, we believe the results of the Phase 2 clinical trial support continued development and the evaluation of pradefovir in confirmatory Phase 3 clinical trials.

Product Position

Pradefovir, if approved by regulatory authorities, could be used as a first line therapy, either as a single agent or in combination with other marketed antiviral nucleosides or interferons, or as a second line therapy to provide better treatment for patients not responding well to current marketed treatments.

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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. In the U.S., the American Cancer Society reports that primary liver cancer is the ninth leading cause of cancer mortality in men and is the twelfth leading cause of cancer mortality in women. The American Cancer Society estimates that approximately 18,550 new cases of primary liver cancer were 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 terminal patients have an average life expectancy of less than one year. Treatment for inoperable and 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.

In late 2007, the FDA approved NEXAVAR® (sorafenib) as the first and only drug for the treatment of primary liver cancer. Sorafenib works by blocking certain kinases, or proteins, that trigger cancer cells to divide and control the growth of new blood vessels that feed cancer tumors. However, the survival benefit of sorafenib is modest and there is also growing evidence that sorafenib is poorly tolerated in primary liver cancer patients, especially those with advanced liver disease. Alternative therapies include chemotherapy injected through a catheter directly into the liver (known as Transcatheter Arterial Chemoembolization, or TACE), as well as regional tumor destruction and chemotherapy with unapproved agents that have shown limited efficacy.

Markets

In the seven major pharmaceutical markets approximately 125,000 patients were afflicted with primary liver cancer in 2007. By 2014, the prevalence rate in the seven major pharmaceutical markets is expected to increase to approximately 185,000 patients. The prevalence rate in the U.S. includes approximately 18,550 patients that were 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 350,000 patients as of 2007. This is greater than the rest of the world combined. The incidence rate in China is expected to rise to 600,000 by 2014.

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MB07133: A HepDirect prodrug of araC monophosphate for treating primary liver cancer

MB07133 is a product candidate for treating primary liver cancer, which is expected to be administered intravenously and continuously over a multiple-day period on an out-patient basis. 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 sufficient quantities of 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 sufficient quantities. 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 successfully completed a Phase 1/2 clinical trial designed to evaluate its safety and preliminary efficacy in non-terminal patients with inoperable primary liver cancer. In this study, MB07133 was well tolerated in this study population with reversible and manageable AE s and few significant AE s. A partial response and significant disease stabilization was observed as assessed by an independent radiology review.

MB07133 was granted Orphan Drug Designation by the FDA in September 2007 and Orphan Medicinal Product Designation by the European Commission in October 2007. Orphan drug designation is available for products designed to treat certain rare diseases and conditions, and provides several marketing incentives including a seven-year market exclusivity in the U.S. if approved.

Product Position

MB07133, if approved by regulatory authorities, could potentially be used as a chemotherapeutic treatment in combination with angiogenesis inhibitors, such as sorafenib, for patients with inoperable primary liver cancer. In addition, MB07133 could be used as second line therapy in patients that have failed or cannot tolerate sorafenib. 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 significant worldwide commercial opportunity.

Liver Disease-Related Programs

Viral enzyme inhibitor programs for treating 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.

We have entered into a non-exclusive collaboration with Roche to create liver-targeted prodrugs of certain viral enzyme inhibitors that Roche has supplied to us. All of our research activities under the collaboration are funded by Roche. Roche is solely responsible for conducting and funding all development work for compounds resulting from the collaboration and for commercializing any resulting products. If a product is successfully developed, we will receive milestone payments as well as receive a portion of the revenue from sales of a drug in the form of a royalty on net sales.

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HepDirect Technology

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 we are currently applying it in connection with our collaboration with Roche and may continue to use it in programs focused on the discovery of drugs for liver diseases such as hepatitis C as well as metabolic diseases.

Organ-specific drug targeting is a well recognized potential strategy for either increasing drug efficacy, improving drug safety, or both. However, despite several decades of research, few drugs that depend on tissue targeting to gain a therapeutic benefit have advanced into the clinic. We have extensive know-how in processes that reside in the liver that are important for drug uptake, metabolism and excretion. Using this knowledge and expertise, we have developed strategies for targeting certain drugs to the liver in order to affect proteins and pathways in the liver that represent potential drug targets for treating metabolic diseases and chronic liver diseases.

The HepDirect technology has been used with certain drugs to deliver high concentrations of the biologically active drug to the liver while keeping drug concentrations in peripheral tissues low. The technology entails 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 in 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 collaboration with Roche in which we are creating prodrugs of certain compounds to target the hepatitis C virus residing in the liver.

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Strategic Alliances

We use, and plan to continue to use, strategic alliances and collaborative partnerships with pharmaceutical and/or biotechnology companies to develop and commercialize our core metabolic disease products under terms designed to maximize their current and future value to our stockholders while balancing the resource needs of our company. 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 to enhance its value, and we intend to continue this practice in the future. Due to the need to fund our on-going operations, we are currently seeking potential partnerships for one or more of our core metabolic disease assets at an earlier stage in development than contemplated in the past. In addition to providing funding in the near-term, we intend to utilize these collaborations as a method of potentially participating in the future worldwide clinical development of our core metabolic disease products. In addition, we plan to license or sell our non-core liver disease assets to provide near-term resources to invest in MB07811 and our TRß agonist program.

Roche

In August 2008, we entered into a two-year collaboration agreement with Roche to discover new treatments for hepatitis C. Under the terms of the agreement, our HepDirect liver-targeted technology will be applied to proprietary Roche compounds to develop nucleoside analog drug candidates for treating hepatitis C virus. We received an upfront payment of $10.0 million from Roche in August 2008. Roche may also pay up to $2.1 million in sponsored research funding at the beginning of the second year of the research term, if applicable. In the event a development candidate is identified, Roche will assume development responsibility and we will be eligible to receive up to $193.0 million in additional payments upon achievement of predetermined preclinical and clinical development events as well as regulatory and commercialization events. Roche will retain full commercial rights for any marketed products resulting from the collaboration and will pay us a royalty on net sales of such products.

Merck

AMPK Collaboration

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 type 2 diabetes and potentially other metabolic diseases 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. In April 2008, the research term was extended for an additional year, through June 2009. We will receive $1.5 million over the course of the one year extension to support our research efforts. 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 U.S. 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 $7.8 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 terminated earlier. 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 upon 90 days advance written notice to us.

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Hepatitis C Collaboration

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. 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. Merck is 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. 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 terminated earlier. 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 upon 90 days advance written notice to us.

Idenix

In October 2006, we entered into a collaboration agreement with Idenix Pharmaceuticals Inc., or Idenix, to apply our HepDirect technology to certain Idenix lead compounds with the goal of improving the safety and efficacy of these compounds for treating hepatitis C. The agreement provided for up to two years of sponsored research. In addition, Idenix had 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. In October 2007, the sponsored research term of our collaboration agreement ended upon the first anniversary of the agreement and the collaboration agreement subsequently terminated in accordance with its terms.

Schering Corporation

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 and further granted Schering a license to Valeant s intellectual property related to pradefovir. Concurrently, we and Schering 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 was granted exclusive worldwide rights to develop and commercialize pradefovir during the term of the agreement. In September 2007, we, Schering and Valeant entered into an agreement to terminate the agreements for the development and commercialization of pradefovir. These agreements were terminated as a result of numerous factors, which may have included results from 24-month oral carcinogenicity studies of pradefovir in rats and mice. We received a non-refundable $1.8 million up-front license fee in the first quarter of 2007 when the agreements became effective. We will not receive any additional payments related to these agreements and all rights to pradefovir have been returned to us.

In September 2008, we, Valeant and Schering entered into an agreement to amend certain terms of the assignment and assumption agreement and the termination agreement, each entered into by Valeant, Schering and us. The amendments to the assignment and assumption agreement provide for a reduction in the total number and value of milestone payments payable by us to Valeant upon the achievement of certain specified events to a single milestone payment due upon the first regulatory approval of pradefovir, and reduce certain royalty payments due from us to Valeant upon commercialization of pradefovir. In addition, the termination agreement was amended to transfer certain patient registry obligations, should they be required, to us from Valeant (excluding the cost thereof, up to a specified limit).

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More recently, we convened a scientific advisory panel to provide an independent review of the results from the rat and mice carcinogenicity studies. The scientific advisory panel concluded that there was an acceptable margin of safety for the pradefovir dose projected for a Phase 3 clinical trial. The results from the carcinogenicity studies were submitted to the FDA and were analyzed by the CAC. Based on advice from the CAC, the FDA concurred with the high multiple of human exposure at which any effects or potential effects occurred and requested that we submit protocols in order to resume clinical trials.

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 HepDirect technology 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.

We believe we have a strong intellectual property position that relates to our HepDirect technology and compounds used in our current business. We own or hold exclusive rights to many issued U.S. patents and pending U.S. patent applications related to the development and commercialization of MB07811, MB07803, pradefovir, MB07133 and our other drug candidates and research programs. These patents and applications cover composition of matter, medical indications, methods of use, methods of manufacture, formulations and other inventive results. We also own or hold exclusive rights to various foreign patent applications that correspond to issued U.S. patents or pending U.S. patent applications.

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 pending, 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 HepDirect technology progress toward commercialization, the possibility of an infringement claim against us increases. While we attempt to be certain that our products and proprietary HepDirect technology do not infringe other parties patents and other proprietary rights, competitors or other parties may assert that we infringe on their proprietary rights.

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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 HepDirect technology, 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. At this time, we have not entered into collaborative partnerships for our core assets, MB07811 and MB07803. We plan to establish strategic collaborations for one or more of our core assets to secure additional financial resources, accelerate clinical development and access worldwide sales and marketing capabilities. We intend to license or sell pradefovir and MB07133 to ensure their further development and to fund the further development of our core assets.

We currently retain worldwide rights to all compounds from our internally discovered research programs, with the exception of any future metabolic disease and hepatitis C product candidates that are covered by our AMPK and hepatitis C collaborations with Merck and hepatitis C collaboration with Roche.

In the future, we intend to make decisions regarding commercialization of the product candidates for which we retain co-promotion rights based on our financial situation and the data derived from our development and research programs. If we proceed with commercialization 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 multinational and regional 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 MB07811 is ultimately determined safe and effective and approved for marketing, it may 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, which reduce serum cholesterol levels by inhibiting a key enzyme involved in the biosynthesis of cholesterol,
- fibrates, which reduce the amount of cholesterol and triglycerides (fatty substances) in blood,
- nicotinic acid derivatives, which lower cholesterol and triglycerides, decrease low density lipoproteins and increase high density lipoproteins,

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CAIs, which inhibit the absorption of dietary and biliary cholesterol,

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

statin combination therapies, which 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. Atorvastatin is currently the best selling prescription medicine. In addition, generic statins (cholesterol-reducers) have recently been approved in the major pharmaceutical markets and may also compete with MB07811.

If MB07803 is ultimately determined safe and effective and approved for marketing, it may face significant competition from various formulations of metformin and products containing metformin. Metformin is a drug that inhibits liver glucose production like MB07803, but does so through an unknown mechanism other than direct 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 MB07803 include, but are not limited to the following classes:

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

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

hepatic glucose output inhibitors, which lower glucose levels by inhibiting liver glucose production. The only drug in this class is metformin, which, based on a study reported in the medical journal *Diabetes*, inhibits glucose production by the liver by only approximately 20-25%, even when administered at the maximum allowed dose. 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,

incretin mimetics, which lower glucose by exhibiting many of the same glucose regulating actions of naturally occurring GLP-1. GLP-1 is 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, and

DPP-4 inhibitors, which inhibit an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-4 thus increases the half-life of endogenous GLP-1 by preventing cleavage and inactivation of GLP-1. The overall effect of drugs in this class is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion.

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, which mimic interferon, the naturally occurring infection-fighting immune substance produced by the body,

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

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nucleotide analogues, which chemically engineered nucleotide compounds structurally similar to the building blocks of DNA and RNA that interferes with the replication of hepatitis B.

A direct competitor to pradefovir would be adefovir dipivoxil which is a nucleotide analogue marketed in the U.S. Pradefovir and adefovir dipivoxil are prodrugs of the same active drug, and therefore may directly compete. Other competitors to pradefovir include the nucleotide analogue, tenofovir, which has been shown to be very effective in treating hepatitis B infection and has recently been approved for marketing in the U.S. and Europe.

Sorafenib, a chemotherapy approved for treating kidney cancer, is now the only approved drug for primary liver cancer in the U.S. or Europe. Sorafenib acts to inhibit a range of tyrosine kinases, including those involved in promoting tumor angiogenesis, the growth of new blood vessels, and cell proliferation. Even with the availability of sorafenib, 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.

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

We rely on several suppliers to manufacture sufficient quantities of MB07811 for use in clinical trials. We currently intend to continue this practice and/or rely on the resources of potential future pharmaceutical partners for the large-scale synthesis needed for any future clinical trials and commercialization of 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 core metabolic disease product candidates, MB07811 and MB07803; our non-core 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. Although our collaborations with Merck and Roche have not yet yielded product candidates, should they be successful, we will be dependent on Merck and/or Roche for clinical development and regulatory approval of any resulting product candidates. We are currently solely responsible for clinical development and regulatory approval of MB07811, MB07803, pradefovir and MB07133.

Product Regulation

Governmental authorities in the U.S. and foreign countries regulate, among other things, the preclinical and clinical testing, manufacturing, labeling, storage, recordkeeping, 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

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and clinical testing process, the New Drug Application, or 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 on-going 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 toxicology 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 Investigational New Drug, or 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,
- 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 GMP, requirements and other FDA regulations, and
- for some drugs, to manage known or potential serious risks of a drug, a risk management plan, or Risk Evaluation and Mitigation Strategy, or REMS, plan is required, which can include a Medication Guide, Patient Package Insert, a communication plan, elements to assure safe use, an implementation system and a timetable for assessment of the REMS.

Preclinical studies generally include animal studies to evaluate the product s mechanism of action, safety and efficacy. Compounds must be produced according to applicable GMP 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.

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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 2 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, and if required, a risk management plan, are submitted to the FDA as part of an NDA requesting approval for the marketing of the product. The FDA can also require a post- approval observational study or an outcomes study be submitted as part of the NDA for approval. The cost of preparing and submitting an NDA as well as costs associated with any required post-approval studies for on-going risk assessment are 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, a complete response letter is issued at the end of the review. A complete response letter takes the place of the prior approvable and not approvable letters issued by the FDA. A complete response letter will be issued to let a company know that the review period for a drug is complete and that the application is not yet ready for approval. The 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.

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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 substantially increase our operating 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 complete response letter. In this context, the complete response 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 current good manufacturing practices, or 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 the FDA of patents covering its listed

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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

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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 30, 2009, we employed 52 full-time employees, consisting of 33 employees in research, development and 19 in executive management, administration and facilities. As of the same date, 23 of our employees had a Ph.D. or M.D. degree. None of our employees are 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

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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 Finances and Capital Requirements

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 and affect our ability to continue as a going concern.

We believe we have adequate financial resources to fund our current operations into July 2009. However, in order to fund on-going cash requirements beyond that time, or to continue development or expand our programs, we will need to raise additional funds through achievement of milestones from existing collaboration agreements, the entry into new strategic collaborations with respect to one or more of our core assets or the license or monetization of our non-core assets, potential equity financings and/or other funding sources. In the event we are unable to generate sufficient capital through the attainment of contractual milestones, other business development activities, potential equity financings and/or other funding sources, we will be required to seek additional resources by pursuing other strategic alternatives including the merger with or sale of some or all of our assets to another company, or cease operations entirely, and our stockholders may lose all or part of their investments. If we raise additional funds by issuing equity securities, our stockholders will experience dilution of their ownership interests.

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

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

the costs and timing of regulatory approvals, and

the effect of competing technological and market developments.

Until we can generate significant continuing revenues, if ever, we expect to satisfy our future cash needs through corporate collaboration and licensing arrangements, public or private equity offerings and debt financings, 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 and we may be unable to continue our operations.

The recent changes in regulatory requirements for developing drugs for the treatment of metabolic disease have increased the cost of development of metabolic disease products and negatively impacted the economic potential of collaborative partnerships in the metabolic disease area, which may limit our ability to fund our near-term operational cash flow requirements through the licensing or sale of our non-core assets and the establishment of strategic collaborations with respect to one or more of our core assets.

We are seeking to fund our on-going cash requirements beyond July 2009 by establishing strategic collaborations with respect to one or more of our core assets and licensing or selling our non-core assets, among other means. Payments under our collaborations are generally made in the form of up-front license fees, milestone payments and downstream royalties. The amount of these payments are generally determined as a factor of the future estimated economic realizable return on the eventual commercialization of these products.

Our core assets consist of product candidates and advanced discovery programs being developed for the treatment of metabolic diseases. The clinical development, manufacturing and commercialization of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the U.S. 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. 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 and may be influenced by the results of other similar or competitive products. For example, in February 2008 the FDA released draft guidance regarding clinical trials for product candidates treating diabetes that may result in more stringent requirements for the clinical testing and regulatory approval of such product candidates. These and any future guidance that may result from recent FDA advisory panel discussions may make it more expensive to develop and commercialize such product candidates. Certain large pharmaceutical and/or biotechnology companies may elect to terminate development activities for diabetes products as a result of this draft guidance and possible increases in development costs and therefore become unavailable as potential licensing partners. Similarly, product candidates for treating hyperlipidemia may be subject to guidance in the future that limits the number of potential licensing partners.

The anticipated increases in the cost of development, complexity and time associated with expected additional regulatory requirements inherently increases the risk of delaying and/or not obtaining the FDA approvals necessary to develop, manufacture or commercialize products in metabolic diseases. Moreover, 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 on-going requirements for potentially costly post-approval studies. The increased costs associated with more stringent regulatory requirements may negatively impact the amount of up-front license fees, milestone payments or downstream royalties we may receive under any collaboration arrangements. If we are unsuccessful in establishing strategic collaborations for one or more of our core assets or generating sufficient up-front license fees from the collaborations we do establish, we may be required to delay, reduce the scope of or eliminate one or more of our research and development programs and we may be unable to continue our operations.

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Turmoil in the credit markets and the financial services industry may negatively impact our business, results of operations and financial condition.

Since our inception, we have funded our operations primarily with net proceeds from equity financings, our venture debt facility and strategic alliances and collaborative partnerships. Under our strategic plan we intend to fund our near-term and on-going cash requirements through equity financings or other means, including the achievement of milestones from existing collaboration agreements, the entry into new strategic collaborations with respect to one or more of our core assets or the license or monetization of our non-core assets. In the event we are not able to generate sufficient capital through equity financings or business development activities or we are not successful in attaining contractual milestones, we will be required to seek additional resources by pursuing other strategic alternatives. The credit markets and the financial services industry are currently experiencing a period of unprecedented turmoil and upheaval characterized by the bankruptcy, failure, collapse or sale of various financial institutions and an unprecedented level of intervention from the U.S. federal government. While the ultimate outcome of these events cannot be predicted, they may have a material adverse effect on our ability to obtain the capital necessary to carry out our strategic plan, which would negatively impact our business, results of operations and financial condition.

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

We have incurred net losses from our inception. As of December 31, 2008, we had an accumulated deficit of approximately $192.3 million. While we are unable at this time to determine whether our net losses will increase or decrease in the future, we expect to continue to incur net losses during the next several years as we conduct operations. Because of the numerous risks and uncertainties associated with our product development efforts, we are unable to predict when we will become profitable, if ever.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

In its audit opinion issued in connection with our balance sheets as of December 31, 2008 and 2007 and our statements of operations, stockholder s equity and cash flows for the years ended December 31, 2008, 2007 and 2006, our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern given our recurring net losses, negative cash flows from operations and our working capital not being sufficient to fund our operations through December 31, 2009. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The financial statements do not include any adjustments relating to reflect the possible future effects on the recoverability and classification of recorded assets or the amounts and classification of liabilities that might be necessary should we be unable to continue in existence.

Our independent registered public accounting firm s substantial doubt about our ability to continue as a going concern may negatively impact our ability to enter into new strategic alliances and collaborations. Traditional out-licensing arrangements may include participation from the licensor on the research and development of the program and in some cases co-promotion rights. If we are not able to demonstrate an ability to continue operations to participate in the development or commercialization of our proprietary products and discovery programs, we may be unsuccessful in entering into strategic alliances or collaborations under favorable terms, if at all. Although we do not maintain financial covenants on our existing debt facilities, our independent registered public accounting firm s opinion may be perceived by our existing creditors and investors as a risk of insolvency and potentially impair our ability to enter into new debt facilities or equity financings.

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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 up-front fees. Our ability to generate significant continuing revenues depends on a number of factors, including:

- successful completion of on-going development activities for our product candidates,
- achievement of regulatory approval for our product candidates, and
- successful completion of our current and future strategic collaborations.

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 may not have sufficient authorized and available shares of common stock to raise additional funds by issuing securities.

We had 54,012,415 authorized shares of common stock available for future issuance as of March 25, 2009. If we are unable to obtain shareholder approval to increase our authorized shares, then our ability to raise additional funds through public or private equity offerings may be limited due to our having insufficient authorized and available shares of common stock. If we are unable to raise additional funds through the issuance of securities and no alternative source of funds is available, we may be required to delay, reduce the scope of or eliminate one or more of our research and development programs and we may be unable to continue our operations.

Certain provisions of our financing facilities may require us to pay any outstanding balance of indebtedness and could limit our ability to fund on-going operations or obtain additional financing.

Our outstanding debt and equipment loan agreements with Oxford contain events of default that may be triggered by a material adverse change, which is defined in the agreements as any material change in the general affairs, senior management, results of operations, or financial condition of the Company, whether or not arising from transactions in the ordinary course of business, that is likely to impair the ability of the Company to repay any portion of the obligations or a material impairment in the value or priority of the lender s security interest in the collateral. We currently do not have sufficient working capital to fund our operations through December 31, 2009 without additional sources of cash. While the determination of the occurrence of a material adverse event is subjective, Oxford has confirmed that we are not in default under the outstanding debt and equipment loan agreements as of December 31, 2008. In the event we are not successful in securing additional sources of cash in the near-term, Oxford may claim that a material adverse change has occurred under the debt or equipment loan agreements, and Oxford could demand immediate repayment of the balances outstanding under the agreements.

If we are required to pay any outstanding balance of indebtedness immediately, we may be faced with the following negative consequences:

- we will need a substantial portion of our cash flow to pay the principal and interest on our indebtedness,
- payments of our indebtedness will reduce the funds that would otherwise be available for our operations and future strategic initiatives, and
- there would be a material adverse effect on our business and financial condition if we were unable to service our indebtedness or obtain additional financing.

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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 establishment of strategic collaborative, licensing or other arrangements, and the timing of payments we may receive under these arrangements,
- the development status of our product candidates, including results of our clinical trials and other studies,
- 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,
- impact of restructuring costs, and
- changes in the use assumptions in the application of Statement of Financial Accounting Standard, or SFAS, No. 123R, *Share-Based Payment*, 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.

Raising additional funds by issuing securities or through collaboration and licensing arrangements may 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, corporate collaboration and licensing arrangements, debt financings, grants or our Committed Equity Financing Facility, or CEFF, if available. We currently do not have access to additional capital through the CEFF. 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 in the future for an aggregate initial offering price of up to $75 million, subject to substantial limitations relating to the aggregate market value of our common stock held by non-affiliates. 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 resale 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 statements 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 HepDirect technology, or grant licenses on terms that are not favorable to us.

Given the on-going financial crisis in the U.S. and other current negative macroeconomic indicators, such as the recession in the U.S. or other economic downturns in the global markets, our ability to issue securities or obtain debt financing in the future may not be available or attainable on favorable terms, if at all.

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Our CEFF 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 an institutional investor and may result in dilution to our stockholders.

We have entered into a CEFF with an institutional investor that entitles us to sell and obligates the investor to purchase, from time to time over a period of up to 36 months which commenced in December 2006, shares of our common stock at a discount of up to 10% for cash consideration up to an aggregate of $50.0 million, or 6,046,701 shares, of common stock, subject to specified conditions and restrictions. Our current market capitalization does not meet the CEFF minimum threshold of $53 million, and therefore, we do not currently have access to this capital.

The investor will not be obligated to purchase shares under the CEFF unless specified conditions are met, which include a minimum price for our common stock; a minimum amount of our market capitalization; the accuracy of representations and warranties made to the investor; 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, the investor 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 the investor 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 the investor to suspend the use of the prospectus covering the shares of common stock issued in connection with the CEFF and prohibit the investor from selling shares under that 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 covering the resale of the shares of common stock to be issued in connection with the CEFF is not effective in circumstances not permitted by our registration rights agreement with the investor, then we must make a payment to the investor, or issue the investor additional shares in lieu of this payment, calculated on the basis of a specified number of shares held by the investor 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 resale 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 the investor 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.

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

As of December 31, 2008 we fail to meet one of the Nasdaq Global Market s continued listing requirements and our common stock could be delisted from the Nasdaq Global Market, which could negatively impact the price of our common stock and our ability to access the capital markets.

As of December 31, 2008, our stockholders equity totaled $3.4 million which does not meet the minimum stockholders equity requirement for continued listing on the Nasdaq Global Market and while we are currently seeking to transfer to the Nasdaq Capital Market, we may not be successful in doing so. In order to maintain our listing on the Nasdaq Global or Capital Market, we will need to continue meeting certain minimum listing standards that include, or may include, our stockholders equity, the market value of our listed or publicly-held securities, the number of publicly-held shares, our net income, a minimum bid price for our common stock, the number of stockholders, the number of market makers and compliance with certain of our corporate governance policies. If we fail to maintain the standards required now or in the future, our common stock could be delisted from the Nasdaq Global or Capital Market. The delisting of our common stock would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common

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stock. In addition, the delisting of our common stock could materially adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from the Nasdaq Global or Capital Market could also have other negative results, including the potential loss of confidence by suppliers and employees and the loss of institutional investor interest.

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 is not necessarily consistent with the interests of other stockholders.

Our executive officers, directors and holders of 5% or more of our outstanding common stock, beneficially owned approximately 74% of our common stock as of December 31, 2008. 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 is not necessarily consistent with the interests of other stockholders.

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 development activities,

establishment of new collaborative arrangements,

events affecting Merck, Roche 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 statements 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,

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

changes in industry and general market conditions, including the recent economic crisis.

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

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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 incur costs associated with regulatory compliance, and these costs could be significant.

There are numerous regulatory requirements for 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. Section 404 requires management to report on, and our independent registered public accounting firm to attest to, our internal controls over financial reporting. 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 laws and regulations 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. Compliance with these rules could also result in continued diversion of management s time and attention, which could be disruptive to normal business operations. If we do not satisfactorily or timely comply with these requirements, possible consequences could include sanction or investigation by regulatory authorities such as the Securities and Exchange Commission or the Nasdaq Stock Market; fines and penalties; incomplete or late filing of our periodic reports, including our annual report on Form 10-K; or civil or criminal liability. Our stock price and business could also be adversely affected.

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 2,363,556 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, an institutional investor is committed to purchase up to $50 million or 6,046,471 shares of our common stock over a 36 month period which commenced in December 2006, subject to certain conditions. Our current market capitalization does not meet the CEFF minimum threshold of $53 million, and therefore, we do not currently have access to this capital. 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.

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 core metabolic disease assets, MB07811 and MB07803, and our non-core liver disease assets, pradefovir and MB07133. Early clinical trials conducted to date have provided initial evidence of safety and therapeutic effect with all of our product candidates. However, to date, 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

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been completed with any of our product candidates. All of our product candidates will require additional development, including clinical trials as well as further animal studies to evaluate their toxicology, carcinogenicity and pharmacokinetics and optimize their formulation, and regulatory clearances before they can be commercialized. Positive results obtained during early development do not necessarily mean later development will succeed or that regulatory clearances will be obtained. Our product development efforts may not lead to commercial drugs, either because our product candidates fail to be safe and effective or because we have inadequate financial or other resources to pursue our product candidates through the clinical development 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 potential future 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 development of our product candidates does not produce favorable results, we and our collaborators, as applicable, may be unable to commercialize these products.

To receive regulatory approval for the commercialization of our core metabolic disease assets, MB07811 and MB07803, our non-core liver disease assets, 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. In addition, regulatory approval of our product candidates may be affected by adverse results in animal studies conducted during clinical development to, among other things, evaluate their toxicology, carcinogenicity and pharmacokinetics and optimize their formulation.

The development process is expensive, can take many years and has an uncertain outcome. Failure can occur at any stage of the process. We may experience numerous unforeseen events during, or as a result of, the development 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,
- animal studies conducted on product candidates during clinical development to, among other things, evaluate their toxicology and pharmacokinetics and optimize their formulation may produce unfavorable results,
- patient recruitment and enrollment in clinical trials may be slower than we anticipate,
- costs of development 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 development of our product candidates may not devote sufficient resources to these clinical trials or other studies of these candidates or conduct them in a timely manner, or

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

Success in early development does not mean that later development will be successful because, for example, product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy despite having progressed through initial clinical testing. For example, in July 2007, we were informed by Daiichi Sankyo, our former collaborative partner on CS-917, that results from a completed Phase 2 clinical trial showed that this product candidate failed to achieve the primary endpoint of the clinical trial despite having successfully achieved the primary endpoints of other earlier clinical trials. In January 2008, we and Daiichi Sankyo agreed to terminate our strategic collaboration on CS-917 and return the rights to this product candidate to us. We do not intend to further develop this product candidate.

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. In addition, the requirements for regulatory approval of our product candidates may change, making it more difficult for us to achieve such approval in a timely manner or at all. For example, in February 2008 the FDA released draft guidance regarding clinical trials for product candidates treating diabetes that may result in more stringent requirements for the clinical testing and regulatory approval of such product candidates. This and any future guidance that may result from recent FDA advisory panel discussions may make it more expensive to develop and commercialize such product candidates. Such increased expense could make it more difficult to obtain favorable terms in the collaborative arrangements we require to maximize the value of our programs seeking to develop new product candidates for diabetes.

We currently do not have strategic collaborations in place for any of our current product candidates in clinical development. Therefore, in the future, we and/or any potential future collaborative partner will be responsible for establishing the targeted endpoints and goals for development of our product candidates. These targeted endpoints and goals may be inadequate to demonstrate the safety and efficacy levels required for regulatory approvals. Even if we believe data collected during the development 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, data generated during development 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.

We may not be able to enter into collaborations with respect to our core assets, MB07811, MB07803 and our glucagon antagonist program and our non-core assets, pradefovir and MB07133, on acceptable terms, if at all, which would lead to development and commercialization delays.

Since we do not currently possess the resources necessary to independently develop and commercialize the potential product candidates that may be based upon our technologies, including MB07811, MB07803, our glucagon antagonist program, pradefovir and MB07133, we plan to enter into additional collaborative agreements to assist in the development and assume the future commercialization of some or all of these assets as a component of our strategic plan. 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, which would adversely affect our business.

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 observed in human clinical trials or in supportive animal studies with our product candidates could interrupt, delay or halt their development and could

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result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications or adversely affect the marketability of any such product candidates that receive regulatory approval. In turn, this could eliminate or limit our ability to commercialize our product candidates and generate revenues from their sale.

Our product candidate may exhibit adverse effects in animal toxicology studies. For example, data from 24-month oral carcinogenicity studies of pradefovir in rats and mice showed that the incidence of rats or mice with tumors was increased in the animals dosed with the highest dose levels tested. As a result of numerous factors which may have included these findings, we entered into an agreement with Schering and Valeant to terminate our agreements for the development and commercialization of pradefovir, and all commercial rights to pradefovir have been returned to us, subject to certain milestone and royalty payments we may be required to make to Valeant should pradefovir be subsequently developed.

Our product candidates could also exhibit adverse interactions with other drugs. For example, in earlier clinical trials conducted by Daiichi Sankyo, CS-917, our first generation product candidate for type 2 diabetes which we are no longer developing, was associated with incidents of lactic acidosis in two patients when it was combined with metformin in a Phase 1 clinical trial. After extensive analysis, Daiichi Sankyo concluded that these incidents were likely due to significant interactions with metformin. CS-917 was also associated in a limited number of patients with episodes of hypoglycemia, asymptomatic lactate elevation as well as lactate elevation with clinical symptoms that could be considered signs of lactic acidosis. We are currently conducting 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 as CS-917.

The unique nature of our proprietary HepDirect technology may cause undesirable side effects in future clinical trials or supportive animal studies. In addition, our product candidates may have greater or lesser degrees of potential risk of undesirable side effects relative to other product candidates based on the nature of their molecular targets and the various physiological responses associated with those targets. For example, MB07811 is a product candidate designed to exploit the beneficial hepatic effects of thyroid hormone agonists while avoiding toxicities related to systemic exposure to these types of compounds. If MB07811 is not successful in this regard, it could be associated with undesirable side effects.

There are also risks associated with additional requirements FDA may impose for marketing approval in a particular disease. For example, MB07803 is a product candidate to treat patients with type 2 diabetes. FDA has recently issued guidance for companies developing anti-diabetic compounds that require companies to demonstrate that the product will not result in an unacceptable increased risk of cardiovascular effects. There is a risk that our product will not show an acceptable risk level and FDA may require we study more patients for approval, following approval, or even prevent our product from receiving a marketing approval.

Our products may require a risk management program that could include but not be limited to patient and healthcare provider education, usage guidelines, appropriate promotional activities, a post-marketing observational study, and on-going safety and reporting mechanisms. Prescribing could be limited to physician specialists or physicians trained in the use of the product or prescribing could be limited to a more restrictive patient population. Any risk management program required for approval of our product candidates could potentially have an adverse impact on our business.

Undesirable side effects involving 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,

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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 development 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 or our partners 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 studies, 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 Merck and Roche for the development and commercialization of product candidates related to those collaborations, and we may be dependent on future collaborators for the development of our current and future product candidates. Events involving our collaborations with Merck and Roche, or any future collaborations could prevent us from developing and commercializing our product candidates and achieving or sustaining profitability.

We have entered into two collaborations with Merck and a collaboration with Roche. The first collaboration with Merck sought to develop and commercialize new products for treating hepatitis C infection and the second seeks to develop and commercialize new products to treat type 2 diabetes and potentially other metabolic diseases. Our collaboration with Roche seeks to develop new products for treating hepatitis C. The sponsored research term of our hepatitis C collaboration with Merck has ended. The sponsored research term of our AMPK collaboration with Merck continues through June 2009, and the research term of our collaboration with Roche continues through July 2010. Although our collaborations with Merck and Roche have not yet yielded any product candidates, should they ultimately be successful, we will be dependent on Merck and/or Roche, as applicable, for further development and commercialization of any resulting product candidates.

We have limited control over the amount and timing of resources that Merck or Roche or any future collaborators devote to our programs or potential product candidates. These collaborations with us may end or may be terminated or our collaborators may otherwise fail to conduct their collaborative activities successfully and in a timely manner. Further, our collaborators may not develop product candidates 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 do 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

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would be forced to discontinue its development or commercialization. For example, at this time, we do not intend to independently develop pradefovir or MB07133 and intend to license or sell these 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,
- our product candidates do not meet the primary endpoints of any clinical trials conducted on them or exhibit undesirable side effects,
- we are unable to obtain patent protection for the product candidates or our proprietary HepDirect technology 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 and Roche may involve Merck s or Roche s proprietary compounds, if Merck or Roche terminates development of product candidates containing these compounds, 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 was 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. 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 type 2 diabetes and potentially other metabolic diseases 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. Our agreement with Roche to develop new products to treat hepatitis C infection may include the development of compounds owned or controlled by Roche. If our collaboration with Roche is terminated, we may not have any right to develop product candidates developed in connection with the collaboration.

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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 Merck or Roche 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 HepDirect technology and our knowledge and expertise to develop novel drugs to address some of the world s most widespread and costly chronic diseases. We intend to expand our existing pipeline of core assets by advancing drug compounds from current on-going discovery programs into clinical development. However, the process of researching and discovering drug compounds is expensive, time-consuming and unpredictable. Data from our current discovery 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. For example, we recently implemented a restructuring plan that resulted in the suspension of certain discovery programs in order to preserve our cash and focus our resources on the clinical development of our core assets, MB07811 and our TRß agonist discovery program.

Delays in the commencement or completion of clinical trials could result in increased costs to us and delay our ability to establish strategic collaborations.

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, but not limited to, 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,

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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 establish strategic collaborations 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. In addition, given our limited financial resources, a delay in our 12-week Phase 2 clinical trial for MB07811 would negatively impact our business, including our ability to complete the study.

We rely on third parties in connection with the development of our product candidates. 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.

We rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories, to assist in the development of MB07811 and intend to rely on similar organizations to assist in the development of any other future product candidates that we may develop for which a collaborator is not responsible for development. At this time, we do not intend to independently develop MB07803, our glucagon antagonist program, pradefovir or MB07133 and intend to establish strategic collaborations, license or, as in the case of our non-core assets, sell these product candidates. We may rely on strategic collaborators for the development of our other core metabolic disease assets, MB07811 and our TRß agonist program, in the future. If successful in entering into these future collaborations and license agreements, we will be dependent upon our collaborative partners and licensees for the further development and commercialization of these product candidates. Although our collaborations with Merck and Roche have not yet yielded product candidates, should they do so, we will be dependent on Merck and/or Roche, as applicable, to conduct the development of any resulting product candidates. If Merck or Roche or these other third parties do not successfully meet their obligations under our agreements, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to applicable protocols or for other reasons, clinical trials or other studies may be extended, delayed or terminated, and these product candidates may not receive regulatory approval or be successfully commercialized.

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

We applied our HepDirect technology to pradefovir, MB07811 and MB07133, and have applied it in certain other programs as well. We intend to use this and future proprietary technologies to expand our product pipeline in the future. We may also leverage our HepDirect and other liver-targeting technology through strategic alliances and collaborations with other companies, such as our hepatitis C collaboration with Roche in which we applied our technology to certain Roche compounds. Our proprietary HepDirect technology is subject to many of the same risks as our product candidates, including risks related to:

- obtaining and maintaining patent and trade secret protection,
- avoiding infringement of the proprietary rights of third parties,
- the development of competing technologies by others, and
- the safety and effectiveness of this technology in humans.

Because certain of our product candidates and research programs are dependent on our proprietary HepDirect technology, adverse events affecting our proprietary HepDirect technology 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 and may be influenced by the results of other similar or competitive products. For example, in February 2008 the FDA released draft guidance regarding clinical trials for product candidates treating diabetes that may result in more stringent requirements for the clinical testing and regulatory approval of such product candidates. This and any future guidance that may result from recent FDA advisory panel discussions may make it more expensive to develop and commercialize such product candidates. Such increased expense could make it more difficult to obtain favorable terms in the collaborative arrangements we require to maximize the value of our programs seeking to develop new product candidates for diabetes. 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 generated during development 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.

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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 on-going 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 on-going 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 on-going 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

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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 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, which reduce serum cholesterol levels by inhibiting a key enzyme involved in the biosynthesis of cholesterol,
- fibrates, which reduce the amount of cholesterol and triglycerides (fatty substances) in blood,
- nicotinic acid derivatives, which lower cholesterol, triglycerides and low density lipoproteins and increase high density lipoproteins,
- CAIs, which inhibit the absorption of dietary and biliary cholesterol,
- bile acid sequestrants, which bind with cholesterol-containing bile acids in the intestines and remove them in bowel movements, and
- statin combination therapies, which 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. Atorvastatin is currently one of the best selling prescription medicines. In addition, generic statins (cholesterol-reducers) have recently been approved in the major pharmaceutical markets and would also compete with MB07811.

If MB07803 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:

- sulfonylureas, which lower glucose levels by inducing insulin secretion from the pancreas. This drug class has been associated with a significant risk of hypoglycemia,
- thiazolidinediones, which lower glucose levels by enhancing insulin sensitivity. This drug class has been associated with fluid retention, weight gain and a risk of heart attacks and angina,
- hepatic glucose output inhibitors, which lower glucose levels by inhibiting liver glucose production. The only drug in this class is metformin, which, based on a study reported in the medical journal *Diabetes*, inhibits glucose production by the liver by only approximately 20-25%, even when administered at the maximum allowed dose. 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,

incretin mimetics, which lower glucose by exhibiting many of the same glucose regulating actions of naturally occurring GLP-1. GLP-1 is 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. Exenatide injection is currently the only marketed drug in this class, and

DPP-4 inhibitors, which inhibit an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-4 thus increases the half-life of endogenous GLP-1 by preventing cleavage and

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inactivation of GLP-1. The overall effect of drugs in this class is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion.

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, which mimic interferon, the naturally occurring infection-fighting immune substance produced by the body,

nucleoside analogues, which are 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 hepatitis B, and

nucleotide analogues, which are 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 hepatitis B.

A competitor to pradefovir would be adefovir dipivoxil, which is a nucleotide analogue currently marketed in the U.S. and Europe. Pradefovir and adefovir dipivoxil are prodrugs of the same active drug, PMEA, and therefore may directly compete. In order to effectively compete with adefovir dipivoxil, pradefovir may have to be significantly more beneficial or less expensive than adefovir dipivoxil. Other competitors to pradefovir include the nucleotide analogue, tenofovir, which has been shown to be very effective in treating hepatitis B infection and has recently been approved for marketing in the U.S. and Europe.

A competitor to MB07133 would be sorafenib, which is a chemotherapy agent approved in the U.S., Europe and most of Asia for the treatment of primary liver cancer. In addition, companies are developing therapies for other solid tumors which may be efficacious in treating primary liver cancer. These companies may develop and introduce products competitive with or superior to MB07133.

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 our products.

Our ability to develop 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 development and eventual commercialization. We have relied on a number of suppliers to manufacture sufficient quantities of MB07811 for use in clinical trials during development. 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 current and potential future collaborators and third-party manufacturers may encounter difficulties with the small- and large-scale formulation and manufacturing processes required to manufacture our product candidates,

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resulting in delays in our clinical trials development 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 development activities related to 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 MB07811 may impede the development of this compound.

In addition, we, our collaborators or other third-party manufacturers of our products must comply with CGMP requirements enforced by the FDA and other foreign regulatory agencies through their facilities inspection programs. These requirements include quality control, quality assurance and the maintenance of records and documentation. In addition, product manufacturing facilities in California are subject to licensing requirements of the California Department of Health Services and may be inspected by the California Department of Health Services, and other applicable regulatory authorities, at any time. We, our collaborators or other third-party manufacturers of our products may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. We have little control over third-party manufacturers compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval.

If we are unable to 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. Although our hepatitis C and metabolic disease collaborations with Merck have not yet yielded a product candidate, should they be successful, Merck will be responsible for worldwide marketing and commercialization of any resulting product candidate subject to, our option to co-promote the product in the U.S. with certain financial assistance from Merck. Similarly, should our hepatitis C collaboration with Roche yield a product candidate, Roche will be responsible for worldwide marketing and commercialization of a resulting product candidate. In order to commercialize MB07811, MB07803, pradefovir, MB07133 or any future product candidates for which we retain commercialization rights, we may be required to 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 our 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.

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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 assuming either competitive or potential premium pricing requirements, based on the profile of our product candidates and target markets,
- effectiveness of our or our partners sales and marketing strategy, and
- our ability to obtain sufficient third-party coverage or reimbursement.

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,
- our ability to distribute our products due to constraints imposed by a risk management plan,
- 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, in January 2007, the House of Representatives passed the Medicare Prescription Drug Price Negotiation Act of 2007. The bill requires the federal government (specifically the Department of Health and Human Services) to negotiate with drug companies over the price of drugs for Medicare participants. In addition, 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 these legislations, it is possible that the new Medicare prescription drug benefit, which is 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

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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. Restrictions imposed by a risk management plan could limit accessibility and distribution of our products.

We may need to further decrease the size of our organization, and we may experience difficulties in managing those organizational changes.

In November 2008 and January 2009 we committed to two separate restructuring plans that resulted in the aggregate reduction of approximately 60% of our workforce. We are highly dependent on principal members of our management team and scientific staff to operate our business and have become even more dependent on existing personnel since the significant workforce reductions. We are more susceptible to remaining team members voluntarily leaving employment with us given the uncertainty of our ability to continue to fund our on-going operations. We are located in southern California, which is headquarters to many other biotechnology and biopharmaceutical companies and many academic and research institutions. As a result, there remains competition for certain skilled personnel in our market. Former employees may seek employment with competitors. Also, when recruiting new personnel, the occurrence of our recent restructurings may make it more difficult to attract new personnel and we may not have the ability to respond rapidly to new growth, if necessary.

We may need to further decrease the number of our full-time employees in the event we are unsuccessful in generating sufficient resources to fund our on-going operations or in the event of other adverse business events. Further reducing our workforce may lead to additional unanticipated attrition. None of our employees have employment commitments for any fixed period of time and may leave our employment at will. If our future staffing is inadequate because of additional unanticipated attrition or because we failed to retain or replace the staffing level required to accomplish our business objectives we may be delayed or unable to continue the development of our product candidates, which could impede our ability to generate revenues and achieve profitability.

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 development 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 severance agreements.

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

Risks Related to our Intellectual Property

Our success depends upon our ability to protect our intellectual property, including the proprietary HepDirect technology 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, our proprietary HepDirect technology and their uses, as well as successfully

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defending any patents that issue against third-party challenges. We may only be able to protect our product candidates, proprietary HepDirect technology and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

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

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

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

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

- we might not have been the first to make the inventions covered by each of our pending patent applications and issued patents,
- we might not have been the first to file patent applications for these inventions,
- others may independently develop similar or alternative technologies or duplicate any of our technologies,
- it is possible that none of our pending patent applications will result in issued patents,
- our issued patents may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or may be challenged by third parties,
- our issued patents may not be valid or enforceable,
- we may not develop additional proprietary HepDirect technology that is 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

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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 HepDirect technology 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 HepDirect technology may infringe. We have not conducted a complete search of existing patents to identify existing patents that our product candidates or proprietary HepDirect technology 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 HepDirect technology infringe their intellectual property rights. If one of these patents was found to cover our product candidates, proprietary HepDirect technology 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 HepDirect technology 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 HepDirect technology 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.

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

Our product candidate pradefovir is a prodrug of PMEA. A third party, Gilead, has rights to another product called adefovir dipivoxil that is a non-liver specific prodrug of PMEA. 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 PMEA. 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 adefovir dipivoxil thereby extending protection of adefovir dipivoxil in those countries to September 2016. Additional third party patents covering adefovir dipivoxil or PMEA 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. 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.

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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.

Item 2. Properties

We believe that our currently leased and occupied facilities are well maintained, in good operating condition and are sufficient for our current needs. The following table is a summary of our currently leased and occupied facilities:

Leased Property Location	Square Feet	Use	Lease Expiration Date
La Jolla, California	82,000	Research, development and administrative	October 2015(1)
Ann Arbor, Michigan	2,900	Development	December 2008(2)

(1) We have options to extend the lease for two renewal periods of five years each.

(2) We are currently operating under a monthly lease and expect to vacate these facilities by March 31, 2009.

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.

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PART II

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

Market Information

Our common stock is traded on the Nasdaq Stock Market under the symbol MBRX. 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, 2008		
Fourth Quarter	$ 1.33	$ 0.27
Third Quarter	$ 1.86	$ 0.66
Second Quarter	$ 2.80	$ 1.40
First Quarter	$ 2.98	$ 1.40

	High	Low
Year Ended December 31, 2007		
Fourth Quarter	$ 3.33	$ 2.35
Third Quarter	$ 7.15	$ 2.65
Second Quarter	$ 8.64	$ 6.94
First Quarter	$ 8.10	$ 6.57

The last sale price for our common stock as reported on the Nasdaq Stock Market on March 25, 2009 was $0.77 per share. As of March 25, 2009, there were 100 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

Information about our equity compensation plans is included in Item 12 of Part III of this annual report.

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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 54-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.

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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,				
	2008	2007	2006	2005	2004
	(In thousands, except per share amounts)				
Statements of Operations Data:					
Revenue	$ 4,810	$ 9,019	$ 4,386	$ 3,771	$ 6,837
Total operating expenses	47,107	53,357	41,195	28,438	22,112
Loss from operations	(42,297)	(44,338)	(36,809)	(24,667)	(15,275)
Other income (expense), net	(17)	2,539	3,541	1,087	303
Net loss(1)	$ (42,314)	$ (41,799)	$ (33,268)	$ (23,580)	$ (14,972)
Basic and diluted net loss per share(1)					
Historical	$ (1.25)	$ (1.37)	$ (1.15)	$ (1.20)	$ (1.49)
Proforma					$ (0.98)
Shares used to compute basic and diluted net loss per share					
Historical	33,779	30,587	29,019	19,706	10,034
Proforma					15,254

(1) The shares used to compute pro forma basic net loss per share represent the historical weighted average common shares outstanding adjusted for weighted average unvested common shares subject to repurchase totaling 418,000 for the year ended December 31, 2004. The shares used to compute pro forma diluted net loss per share represent the historical weighted average common shares outstanding adjusted for the effect of conversion of preferred stock totaling 5,220,000 for the year ended December 31, 2004.

	As of December 31,				
	2008	2007	2006	2005	2004
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents and securities available-for-sale	$ 21,599	$ 42,438	$ 77,923	$ 66,893	$ 43,855
Working capital	8,792	32,068	68,877	60,146	40,906
Total assets	27,742	50,123	85,855	73,878	47,860
Long-term obligations (including current portion)	11,680	8,586	7,332	3,504	2,230
Accumulated deficit	(192,326)	(150,012)	(108,213)	(74,945)	(51,365)
Total stockholders equity (deficit)	3,381	32,101	68,138	59,582	41,864

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

You should read the following discussion and analysis 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 committed to the discovery, development and commercialization of novel drugs for metabolic diseases using our proprietary technology and our knowledge of processes and pathways within the liver that are useful for liver-selective drug targeting and treatment of metabolic diseases. We have established a broad pipeline of product candidates and advanced discovery programs targeting large markets with significant unmet needs. Our product pipeline includes product candidates and advanced discovery programs for the treatment of metabolic diseases such as diabetes and hyperlipidemia, which we refer to as our core assets, as well as product candidates and advanced discovery programs for the treatment of liver diseases such as hepatitis and primary liver cancer, which we refer to as our non-core assets. All of our product candidates were developed internally using our proprietary HepDirect technology.

We currently have four product candidates at the clinical stage of development. These product candidates include our core metabolic disease proprietary product candidates, MB07811 and MB07803, which are being developed as potential treatments for type 2 diabetes and hyperlipidemia, respectively, and our non-core liver disease proprietary product candidates, pradefovir and MB07133, which have been developed as potential treatments for hepatitis B and primary liver cancer, respectively.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern given our recurring net losses, negative cash flows from operations and our working capital not being sufficient to fund our operations through December 31, 2009. Our current financial resources will support our on-going planned operating expenses into July 2009.

In January 2009, we announced a plan to restructure our organization which followed the initiation of a separate restructuring plan that we announced in November 2008. The two restructuring plans resulted in an approximately 60% reduction of our workforce. As part of the January 2009 plan, we narrowed our research and development efforts and intend to utilize a significant portion of our existing resources on the planned Phase 2 clinical trial for MB07811, which we believe will provide significant value for stockholders. In addition, we continue to support our on-going sponsored research programs in collaboration with Merck and Roche.

To a lesser extent, we have committed resources towards the advancement of our second generation TRß agonist and our glucagon antagonist discovery programs to the preparatory stage of preclinical development. We believe the second generation TRß agonist discovery program could result in one or more compounds that could enhance the overall value of our hyperlipidemia program to potential strategic partners. Additionally, we believe the advancement of the glucagon antagonist program will improve our ability to secure additional financial resources under a collaborative arrangement.

Our pipeline of clinical-stage product candidates also consists of our core asset, MB07803, and our non-core assets, pradefovir and MB07133. As part of our near-term strategic focus, we have not committed resources for the further development of these product candidates as we intend to establish a strategic partnership with respect to MB07803 and, in the case of our non-core assets, license or monetize these product candidates to secure additional financial resources. In addition, we have suspended all activities related to various other metabolic disease advanced discovery programs.

Completion of the MB07811 Phase 2 clinical trial, currently anticipated by the end of 2009, is dependent upon our ability to raise significant additional capital to continue operations beyond July 2009 through the achievement of milestones from existing collaboration agreements, the entry into new strategic collaborations

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with respect to one or more of our core assets or the license or monetization of our non-core assets, potential equity financing and/or other funding sources. In the event we are not able to generate sufficient capital through the attainment of contractual milestones, other business development activities, potential equity financing and/or other funding sources, we will be required to seek additional resources by pursuing other strategic alternatives including the merger with or sale of some or all of our assets to another company, or cease our operations entirely. If we raise additional funds by issuing securities, our stockholders will experience dilution of their ownership interests.

Recent Events

In March 2009, we announced the results of a 14-day trial, ascending, multiple dose clinical trial in type 2 diabetes to assess whether administration of a newly developed MB07803 tablet formulation twice-daily would increase drug concentrations and whether higher drug concentrations would be safe and well-tolerated and result in better glucose lowering compared to placebo. Forty two poorly controlled type 2 diabetes patients (average FPG 221 mg/dL) in which 50, 200 and 400 mg tablets compared to matching placebo administered twice daily (every 12 hours) were evaluated. Results indicated that 200 mg and 400 mg doses taken twice a day resulted in higher drug concentrations than achieved in previous Phase 1 trials. The efficacy endpoint in the trial was the change from baseline at Day 14 in the glucose lowering response (determined by the area-under-the-curve, i.e. AUC) as measured after administration of the morning dose and during the last 6 hours of a prolonged 18 hour fast. The results showed that the 6-hour AUC was reduced from -93 (mg.hr/dL) for patients treated with placebo to -236 (p=0.17 vs. placebo), -442 (p=0.002 vs. placebo), and -532 (p=0.0002 vs. placebo) mg.hr/dL for patients treated with 50 mg, 200 mg and 400 mg Q12h, respectively. The top two doses also achieved statistical significance in the more clinically-relevant endpoint of a single point measure of FPG (-72 and -69 mg/dL change from baseline at the 200 and 400 mg twice daily dose compared to -14 mg/dL in placebo). In addition, all doses significantly reduced day long glycemia (24-hour glucose AUC). Dose-limiting vomiting was observed at the highest dose. In contrast, no patients in the 200 mg Q12h group experienced vomiting. Four of the 12 patients in this group experienced at least one episode of mild nausea, but none discontinued due to nausea. No patient in the 50 mg dose cohort experienced nausea or vomiting. One patient had glucose levels less than 60 mg/dL and exhibited symptoms consistent with hypoglycemia. This patient also had 3 nonconsecutive, asymptomatic elevations of lactate when glucose levels were less than 60 mg/dL. Other patients showed fasting glucose levels lower than 60 mg/dL, predominantly during the latter stages of the 18-hour fasting period, and were asymptomatic. No patient in the trial experienced lactic acidosis.

In January 2009, we completed an offer to exchange certain outstanding options to purchase shares of our common stock, that were originally granted under our 2001 Equity Incentive Plan and that had an exercise price that is equal to or greater than $1.50 per share, for replacement options to purchase shares of our common stock,. Eligible option holders included employees and scientific advisory board members. Subject to the participant s continued service with us, 25% of the shares underlying the replacement options will vest six months after the date the replacement options are granted and the remaining 75% of the shares will vest in equal monthly installments beginning on the date of grant of the replacement options so that the replacement options will be vested in full three years from the grant date of the replacement options.

Upon expiration of the offer, we accepted elections to replace eligible stock options to purchase 1,831,887 shares of common stock, representing 64.3% of the shares subject to options that were eligible to be exchanged in the Offer. As a result, options to purchase 1,831,887 shares of common stock were immediately granted to the participants at an exercise price of $1.00 per share, in accordance with the terms of the offer. The closing sales price of our common stock on January 29, 2009 was $0.47.

Other Events

In September 2008, we, Valeant and Schering entered into an agreement to amend certain terms of the assignment and assumption agreement and the termination agreement, each entered into by Valeant, Schering

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and us and relating to the development and commercialization of pradefovir. The amendments to the assignment and assumption agreement provide for a reduction in the total number and value of milestone payments payable by us to Valeant upon the achievement of certain specified events to a single milestone payment due upon the first regulatory approval of pradefovir, and reduce certain royalty payments due from us to Valeant upon commercialization of pradefovir. In addition, the termination agreement was amended to transfer certain patient registry obligations, should they be required, to us from Valeant (excluding the cost thereof, up to a specified limit).

More recently, we convened a scientific advisory panel to provide an independent review of the results from the rat and mice carcinogenicity studies, the result of which may have contributed to the prior termination of the agreements for the development and commercialization of pradefovir. The scientific advisory panel concluded that there was an acceptable margin of safety for the pradefovir dose projected for a Phase 3 clinical trial. The results from the carcinogenicity studies were submitted to the FDA and were analyzed by the CAC. Based on advice from the CAC, the FDA concurred with the high multiple of human exposure at which any effects or potential effects occurred and requested that we submit protocols in order to resume clinical trials.

In August 2008, we entered into a two-year collaboration agreement with Roche to discover new treatments for hepatitis C. Under the terms of the agreement, our HepDirect liver-targeted technology will be applied to proprietary Roche compounds to develop second-generation nucleoside analog drug candidates for treating hepatitis C virus. We received an upfront payment of $10.0 million from Roche in August 2008. Roche may also pay up to $2.1 million in sponsored research funding at the beginning of the second year of the research term, if applicable. In the event a development candidate is identified, Roche will assume development responsibility and we will be eligible to receive up to $193.0 million in additional payments upon achievement of predetermined preclinical and clinical development events as well as regulatory and commercialization events. Roche will retain full commercial rights for any marketed products resulting from the collaboration and will pay us a royalty on net sales of such products.

History of Losses, Prior Funding

We have incurred annual net losses since inception. As of December 31, 2008, our accumulated deficit was approximately $192.3 million. We expect to incur losses for the next several years as we:

- continue to develop our current and future core metabolic disease clinical product candidates, and
- continue and potentially expand our research and development programs.

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, our registered direct offering of common stock in March 2006, our warrant exchange and concurrent private placement in April 2008, 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 collaborative partners and, to a lesser extent, the sale of common stock through our stockholder approved equity incentive plans.

Commercial, Manufacturing Rights, Risks

We currently do not have strategic collaborations in place related to MB07811 or MB07803 and we intend to seek strategic collaborations for one or more of our core assets and license or sell our non-core assets. We retain worldwide commercialization rights to all of the compounds that we have generated from our past and current discovery programs, with the exception of any potential future product candidates that may result from our collaborations with Merck and Roche. Our potential future agreements with strategic collaborators may include joint marketing or promotion arrangements which may allow us to eventually co-market one or more of our product candidates through our own sales force or with a co-promotion partner. Alternatively, we may grant

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exclusive rights to our collaborators in exchange for upfront fees, milestones and royalties on future sales, if any, or directly sell certain of our assets.

We will rely on our collaborators or third-party manufacturers to produce sufficient quantities of our product candidates for clinical studies and large-scale commercialization upon their approval. Since we do not currently possess the resources necessary to independently develop and commercialize all of the potential product candidates that may be based upon our HepDirect technology, we plan to enter into additional collaborative agreements to assist in the development and commercialization of some or all of our 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.

Our business is subject to significant risks, including the risks inherent in our on-going 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 salaries, stock-based compensation and other expenses for research and development personnel, costs associated with the 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. Beginning January 1, 2008, we revised our estimate of the rate we use to allocate occupancy and information systems costs between research and development expenses and general and administrative expenses. We believe the current allocation is more reflective of the actual consumption of these expenses in these operational functions for fiscal 2008.

Our development activities are focused on the development of our core metabolic disease assets, MB07811, our glucagon antagonist program and our second-generation TRß agonist discovery program. Our activities related to MB07803 and our non-core liver disease assets, pradefovir and MB07133, are currently limited to planning, consultation, design and other efforts preparatory to their potential future clinical development by licensees. We are responsible for all costs incurred for our product candidates and our advanced discovery programs with the exception of the AMPK and hepatitis C programs partnered with Merck and the hepatitis C program partnered with Roche.

Our AMPK collaboration with Merck seeks to develop and commercialize new products to treat type 2 diabetes and potentially other metabolic diseases. Under the terms of our AMPK collaboration agreement with Merck, we have received approximately $12.4 million in cumulative sponsored research and license fees funding through December 31, 2008, which includes funding for sponsored research efforts through March 2009.

Our other collaboration with Merck sought to develop and commercialize new products for treating hepatitis C infection. Our efforts and internal costs related to the hepatitis C collaboration with Merck ceased upon completion of its research term in December 2005. Under the terms of the Merck agreement, we have received approximately $3.2 million in cumulative license fees and sponsored research funding through December 31, 2005. Merck is solely responsible for conducting and funding all development work for any compounds resulting from these collaborations and for commercializing any resulting products.

Our two-year collaboration with Roche seeks to develop and commercialize new products for treating hepatitis C infection. Under the terms of the Roche agreement, we received an upfront payment of $10.0 million in August 2008. We are entitled to receive payments on the achievement of certain milestones and during the second year of the agreement, we are entitled to additional sponsored research funding.

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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 discovery 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 and other 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 as we continue the development of our core assets, as well as continue to expand our discovery 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 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 on-going basis in response to the scientific and clinical success of each product candidate, our on-going assessment of its market potential and consideration of 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. Additionally, under our strategic plan, we intend to establish strategic collaborations for one or more of our core assets and our non-core assets to secure additional resources, accelerate progress and ensure their continued development. However, delays in finding appropriate partnerships could also have a material unfavorable effect on our ability to continue 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, 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. Beginning January 1, 2008, we revised our estimate of the rate we use to allocate occupancy and information systems costs between research and development expenses and general and administrative expenses. We believe the current allocation is more reflective of the actual consumption of these expenses in these operational functions for fiscal 2008.

Other Income (Expense)

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

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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 access to our proprietary HepDirect technology and research and development services. Payments under our collaborations are generally made in the form of up-front license fees, milestone payments and downstream royalties. All fees are nonrefundable. Revenue from milestones is recognized when earned, provided that:

- the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, and
- collaborator funding, if any, of our performance obligations after the milestone achievement will continue at a level comparable to before the milestone achievement.

If both of these criteria are not met, the milestone payment is recognized over the remaining minimum period of our performance obligations under the agreement. Up-front, 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 SFAS No. 123R which we adopted effective January 1, 2006. As of December 31, 2008, we had approximately $5.5 million of unrecognized compensation expense which we expect to recognize over a weighted average period of 2.5 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 SAB No. 107.

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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.

Restructuring Charges. In accounting for restructuring charges we consider the primary elements to our restructuring plans: one-time termination benefits and the discontinued use or abandonment of any assets. We recognize the fair value of one-time termination benefits when we have taken actions or have the appropriate approval for taking action, and when a liability is incurred (when the plan has been communicated to employees). If employees are required to render service beyond a 60-day minimum retention period, the fair value of the obligation is determined on the date of the communication to the employee and recognized over the service period. We recognize charges for the abandonment of assets in the period we cease to use the assets. We recognize the cumulative effect of any changes to the plan subsequent to the communication date and cease-use date in the period of the change.

Recently Issued Accounting Pronouncements

In November 2007, the EITF issued EITF Issue No. 07-1, *Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property.* Companies may enter into arrangements with other companies to jointly develop, manufacture, distribute, and market a product. Often the activities associated with these arrangements are conducted by the collaborators without the creation of a separate legal entity (that is, the arrangement is operated as a virtual joint venture). The arrangements generally provide that the collaborators will share, based on contractually defined calculations, the profits or losses from the associated activities. Periodically, the collaborators share financial information related to product revenues generated (if any) and costs incurred that may trigger a sharing payment for the combined profits or losses. The consensus requires collaborators in such an arrangement to present the result of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 is effective for collaborative arrangements in place at the beginning of the annual period beginning after December 15, 2008. We are in the process of determining the effect, if any, the adoption of EITF Issue No. 07-1 will have on our financial statements.

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations*. SFAS No. 141(R) replaces SFAS No. 141. SFAS No. 141(R) requires the acquirer of a business to recognize and measure the identifiable assets acquired, the liabilities assumed and any non-controlling interest in the acquiree at fair value. SFAS No. 141(R) also requires transaction costs related to the business combination to be expensed as incurred. SFAS No. 141(R) applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008 (our 2009 fiscal year). The adoption of SFAS No. 141(R) is not expected to have a material impact on our financial statements.

In May 2008, the FASB issued SFAS No. 162, *The Hierarchy of Generally Accepted Accounting Principles*. SFAS No. 162 identifies the sources of accounting principles and provides entities with a framework for selecting the principles used in preparation of financial statements that are presented in conformity with GAAP. The current GAAP hierarchy has been criticized because it is directed to the auditor rather than the entity, it is complex and it ranks FASB Statements of Financial Accounting Concepts, which are subject to the same level of due process as FASB SFAS, below industry practices that are widely recognized as generally accepted but that are not subject to due process. The FASB believes the GAAP hierarchy should be directed to entities because it is the entity (not its auditors) that is responsible for selecting accounting principles for financial statements that are presented in conformity with GAAP. SFAS No. 162 is effective 60 days following the Securities and Exchange Commissions approval of the Public Company Accounting Oversight Board amendments to AU Section 411, *The*

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Meaning of Present Fairly in Conformity With Generally Accepted Accounting Principles. We adopted SFAS No. 162, and it did not have a material impact on our financial statements.

In June 2008, the EITF issued EITF No. 08-3, *Accounting by Lessees for Maintenance Deposits under Lease Agreements*. Under certain lease arrangements, the lessee is contractually responsible for repair and maintenance of the leased asset, and the lessee is required to make deposits with the lessor to fund that maintenance. The deposit is refunded to the lessee only to the extent that the lessee incurs qualified maintenance costs. Questions have arisen as to the proper accounting for these deposits as some companies account for the maintenance deposits as deposits, while other companies account for them as contingent rental expense. EITF No. 08-3 concludes that maintenance deposits should be considered deposits when paid to the lessor if it is probable that the deposits will be refunded to the lessee. If it is not probable, then the deposits are recognized as rental expense. If it is determined at the inception of the lease that a portion of the deposits is not probable of being refunded to the lessee, then the lessee should recognize as expense a pro-rata portion of the deposits as they are paid. The cost of maintenance activities should be expensed or capitalized, as appropriate. The definition of probable will fall under the guidance of FASB Concept Statement No. 6, *Elements of Financial Statements.* EITF No. 08-3 is effective for fiscal years beginning after December 15, 2008 (beginning with our 2009 fiscal year). Early application is not permitted. The adoption of EITF No. 08-3 is not expected to have a material impact on our financial statements.

In December 2008, the FASB issued FSP FAS 140-4 and FIN 46(R)-8, *Disclosures by Public Entities about Transfers of Financial Assets and Interests in Variable Interest Entities.* The purpose of this FSP is to promptly increase disclosures by public entities and enterprises until the pending amendments to SFAS No. 140, *Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities* and FASB Interpretation No., or FIN 46R, *Consolidation of Variable Interest Entities,* or FIN 46(R), are finalized and approved by the FASB. The FSP is effective for reporting periods (interim and annual) ending after December 15, 2008 (our 2008 fiscal year).

This FSP amends SFAS No. 140 to require public entities to provide additional disclosures about transferors continuing involvement with transferred financial assets. This FSP also amends FIN 46(R) to require public enterprises, including sponsors that have a variable interest in a variable interest entity, to provide additional disclosures about their involvement with variable interest entities. This FSP also requires disclosures by a public enterprise that is (a) a sponsor of a qualifying special-purpose entity, or SPE, that holds a variable interest in the qualifying SPE but was not the transferor of financial assets to the qualifying SPE and (b) a servicer of a qualifying SPE that holds a significant variable interest in the qualifying SPE but was not the transferor of financial assets to the qualifying SPE. The adoption of this FSP did not have a material impact on our financial statements.

Results of Operations

Comparison of the Years Ended December 31, 2008 and 2007

Revenues. Revenues were $4.8 million for the year ended December 31, 2008, compared with $9.0 million for the year ended December 31, 2007. The $4.2 million decrease was mainly due to lower license fee and sponsored research revenues of $3.1 million from Idenix as a result of the completion of the sponsored research term of our collaboration in October 2007 and a decrease of $1.3 million in the Merck AMPK license fee and sponsored research revenue. The decrease in the AMPK license fee revenue relates to a reduction in the rate of revenue recognized as a result of the extension of the research term (amortization period) through June 2009. The decrease was also due to the absence of $1.8 million in license fees due to the termination of our collaboration with Schering in September 2007. These reductions were partially offset by an increase of $2.3 million in license fees and sponsored research revenues recognized in connection with the Roche agreement we entered into in August 2008. Absent any changes to our existing collaborations with Merck or Roche and if we are unable to generate significant or additional revenues from new strategic collaborations with respect to one or more of our core assets and our non-core assets, we expect a decrease in sponsored research and license revenues in 2009

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compared to 2008 as the sponsored research portion of our AMPK collaboration with Merck is scheduled to be completed in June 2009.

Research and Development Expenses. Research and development expenses were $36.4 million for the year ended December 31, 2008, compared with $40.9 million for the year ended December 31, 2007. The $4.5 million decrease was mainly due to decreases of $6.0 million in clinical and development expenses for the MB07803, MB07811 and MB07133 programs, $0.7 million in non-cash stock-based compensation expense and a net decrease of $0.5 million in personnel-related costs due to the absence of performance-based compensation benefits in 2008. These decreases were partially offset by an increase of approximately $1.6 million of non-cash depreciation and occupancy costs as a result of a change in the allocation rate of these costs, as discussed above, and $1.1 million in severance and other termination benefits associated with our November 2008 restructuring plan. We expect costs in research and development in 2009 to significantly decrease compared to 2008 as we begin to realize the impact of scaling back our research and development efforts.

General and Administrative Expenses. General and administrative expenses were $10.8 million for the year ended December 31, 2008, compared with $12.4 million for the year ended December 31, 2007. The $1.6 million decrease primarily relates to a decrease of $1.2 million in occupancy and non-cash depreciation expenses due to a change in the allocation rate of these costs, as discussed above, a decrease of $0.6 million related to the absence of incentive compensation and lower personnel-related costs, a decrease of $0.6 million of non-cash stock-based compensation expense and other miscellaneous expenses. These decreases were offset by an increase of $0.5 million related to separation benefits provided to our former chief executive officer and an increase of approximately $0.3 million in severance and other termination benefits associated with our November 2008 restructuring plan. We do not expect a significant change in general and administration costs in 2009 compared to 2008.

Other Income (Expense). Net interest expense was $17,000 for the year ended December 31, 2008, compared to net interest income of $2.5 million for the year ended December 31, 2007. The $2.5 million decrease was due to lower interest income as a result of decreasing average cash balances for the twelve months ended December 31, 2008 as compared to the same period in 2007 as well as interest expense incurred in 2008 as a result of the long-term debt acquired in March 2008.

Comparison of the Years Ended December 31, 2007 and 2006

Revenues. Revenues were $9.0 million for the year ended December 31, 2007, compared with $4.4 million for the year ended December 31, 2006. The $4.6 million increase was mainly due to increased license fee and sponsored research revenues as a result of a $2.8 million increase in revenues from our hepatitis C collaboration with Idenix and the $1.8 million up-front license fee received from Schering in connection with the collaboration agreement for the development of pradefovir.

Research and Development Expenses. Research and development expenses were $40.9 million for the year ended December 31, 2007, compared with $29.9 million for the year ended December 31, 2006. The $11.0 million increase was mainly due to increased spending of $6.0 million in clinical development expense for MB07803, MB07811 and MB07133, an increase of $3.5 million in payroll and related benefits as a result of a higher average number of employees in 2007, a $1.2 million increase in stock-based compensation costs and $0.3 million in increased occupancy costs and depreciation expense.

General and Administrative Expenses. General and administrative expenses were $12.4 million for the year ended December 31, 2007, compared with $11.3 million for the year ended December 31, 2006. The $1.1 million increase primarily relates to an increase of $0.8 million in increased payroll and related benefits as a result of a higher average number of employees in 2007, an increase of $0.2 million in occupancy related costs and depreciation expense, and increased stock-based compensation expense of $0.1 million as a result of additional grants made during fiscal 2007.

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Net Interest Income. Net interest income was $2.5 million for the year ended December 31, 2007, compared to net interest income of $3.5 million for the year ended December 31, 2006. The $1.0 million decrease was due to lower interest income as a result of decreasing average cash balances for the twelve months ended December 31, 2007 as compared to the same period in 2006. Our average cash balances were higher in 2006 as compared to 2007 due to the net proceeds from our March 2006 stock offering.

Liquidity and Capital Resources

Since our inception, we have funded our operations primarily with $55.8 million in net proceeds from equity financings prior to becoming a public company and $117.4 million in aggregate net proceeds from our initial public offering in June 2004, a private placement of common stock and warrants in October 2005, a registered direct offering of common stock in March 2006 and our warrant exchange and concurrent private placement in April 2008.

In August 2008, we entered into a two-year collaboration with Roche to develop new products for treating hepatitis C infection. Under the terms of the Roche agreement, we received an upfront payment of $10.0 million in August 2008. We are entitled to receive payments on the achievement of certain milestones and during the second year of the agreement, we are entitled to additional sponsored research funding.

In April 2008, we entered into a warrant exchange and concurrent private placement, referred to together as the Transaction, which raised $9.9 million in cash. The investors in the Transaction were certain current investors who held existing warrants for the purchase of our common stock issued previously by us in our October 2001 and October 2005 private placements.

In connection with the Transaction, we entered into a Warrant Exercise Agreement pursuant to which we reduced the exercise prices of the investors warrants to purchase our common stock acquired in our October 2001 and October 2005 private placements to an exercise price of $2.34 per share, in exchange for an irrevocable commitment by the investors to exercise such warrants at the closing. As a result of the Warrant Exercise Agreement, warrants for the purchase of 1,685,836 shares of our common stock were exercised at $2.34 per share. Additionally, in connection with the Transaction, we entered into a Securities Purchase Agreement pursuant to which we issued and sold to the investors 2,485,103 shares of our common stock at an exercise price of $2.34 per share, and warrants to purchase up to 1,057,196 shares of our common stock at an exercise price of $2.69 per share.

In March 2008, we entered into a venture debt facility with a lender, pursuant to which the lender provided us with a three-year, $5.0 million term loan. We are using the proceeds from the loan for general working capital purposes. Interest accrues at an annual rate of 9.83%, with six interest-only monthly payments, made in arrears, beginning in May 2008, followed by 30 equal monthly payments of principal and interest beginning in November 2008. We paid a facility fee of $50,000 upon signing of the term sheet and are required to pay an additional fee of 4% of the term loan amount, or $200,000, at the end of the three year term. We have the option to prepay the outstanding balance of the term loan in full, subject to a prepayment fee. The loan is collateralized by our general assets, excluding intellectual property. There are no financial covenants associated with the venture debt facility. In the event we become in default of the loan agreement, the lender has the right under a control agreement to assume control over our bank accounts, which include our operating and short-term investment accounts. In connection with the venture debt facility, we issued to the lender a warrant to purchase up to 154,639 shares of our common stock at an exercise price of $1.94 per share. The warrant is currently exercisable and expires in March 2018.

Our outstanding debt and equipment loan agreements with Oxford contain events of default that may be triggered by a material adverse change, which is defined in the agreements as any material change in the general affairs, senior management, results of operations, or financial condition of the Company, whether or not arising from transactions in the ordinary course of business, that is likely to impair the ability of the Company to repay

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any portion of the obligations or a material impairment in the value or priority of the lender s security interest in the collateral. We currently do not have sufficient working capital to fund our operations through December 31, 2009 without additional sources of cash. While the determination of the occurrence of a material adverse event is subjective, Oxford has confirmed that we are not in default under the outstanding debt and equipment loan agreements as of December 31, 2008. In the event we are not successful in securing additional sources of cash in the near-term, Oxford may claim that a material adverse change has occurred under the debt or equipment loan agreements, and Oxford could demand immediate repayment of the balances outstanding under the agreements.

In April 2007, we filed an additional shelf registration statement to increase the amount of common stock and warrants available for issuance under our existing shelf registration statement by approximately $40 million to a total of $75 million, subject to substantial limitations relating to the aggregate market value of our common stock held by non-affiliates. The additional shelf registration statement was declared effective in May 2007.

We have entered into a CEFF with an institutional investor, under the terms of which, the investor is committed to providing us up to $50 million or 6,046,471 shares of common stock, based on certain market capitalization levels, in funding from time to time for a period up to 36 months that commenced in December 2006 through the purchase of newly-issued shares of our common stock. In February 2008, the CEFF was amended to reduce the minimum market capitalization required to permit a draw down and to eliminate certain termination rights maintained by the investor, among other things. Our market capitalization currently does not meet the minimum threshold of $53 million, and therefore, we currently do not have access to this capital.

Additionally, we have received cumulative proceeds from collaborative arrangements with strategic partners for the development of certain core assets, non-core assets, for the application of our HepDirect technology on third-party programs and to a lessor extent from Small Business Innovation Research, or SBIR, grant funding totaling approximately $34.1 million through December 31, 2008.

As of December 31, 2008, we had $21.6 million in cash and cash equivalents and securities available-for-sale as compared to $42.4 million as of December 31, 2007, a decrease of $20.8 million. The decrease is primarily a result of net cash used in operations of $33.1 million offset by $12.3 million of net cash flows provided by financing activities.

As of December 31, 2008, we have financed through leases and loans the purchase of equipment and leasehold improvements totaling approximately $12.4 million, of which $3.9 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. Until additional funding sources are available, we plan to limit the use of our cash reserves for leasehold improvements and capital equipment necessary to support our clinical development efforts and research programs for 2009. We no longer have available funds through this financing facility, however we intend to seek financing for our equipment and leasehold improvements through 2009 under a separate facility.

We believe we have adequate financial resources to fund our current operations into July 2009. However, in order to fund on-going cash requirements beyond that point, or to continue development or expand our programs, we will need to raise additional funds through equity financings or other means, including the achievement of milestones from existing collaboration agreements, the entry into new strategic collaborations with respect to one or more of our core assets or the license or monetization of our non-core assets. We may not be successful in entering into additional collaboration agreements, or in receiving milestone or royalty payments under current or future agreements. Additionally, we may be required 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. Also, based on recent FDA draft guidelines and advisory panel discussions, the cost to develop and commercialize our diabetes programs may increase beyond current expectations and such increases may make it more difficult to obtain favorable terms in the collaborative arrangements we require to maximize the value of these programs.

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In January 2009, we announced a plan to restructure our organization which followed the initiation of a separate restructuring plan that we announced in November 2008. The two restructuring plans resulted in an approximately 60% reduction of our workforce. As part of the January 2009 plan, we scaled back efforts on certain research and development programs. Having insufficient funds may require us to delay, scale back or eliminate some or all of our research or development programs even further. No assurances can be made that additional funding, through any resources, including our CEFF, will be available when needed or that, if available, financing will be obtained on terms favorable to us or our stockholders. 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 or sales of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. The global financial crisis and the deterioration of the U.S. capital markets may negatively impact our ability to issue securities or obtain debt financing. In the event we are not able to generate sufficient capital through equity financings, business development activities or we are not successful in attaining contractual milestones, we will be required to seek additional resources by pursuing other strategic alternatives such as, merge with or sell some or all of our assets to another company, or cease operations entirely.

The following summarizes our long-term contractual obligations as of December 31, 2008 (in thousands):

	Total	Less than 1 Year	1 to 3 Years	4 to 5 Years	After 5 Years
Operating lease	$ 22,214	$ 2,820	$ 9,576	$ 6,848	$ 2,970
Equipment financing	3,845	2,005	1,730	75	35
Term loan	4,703	1,885	2,818		
Interest on long-term debt	1,247	677	557	12	1
Purchase commitments	968	968			
Capital leases	53	26	27		
Interest on capital leases	6	4	2		
	$ 33,036	$ 8,385	$ 14,710	$ 6,935	$ 3,006

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 we have met our obligations under these agreements. As of December 31, 2008, $0.6 million in severance and other separation benefit costs were accrued in connection with the separation of our former chief executive officer in December 2008.

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 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,

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the costs and timing of regulatory approvals,

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

the effect of competing technological and market developments.

Environmental Risk

Our research and development activities involve the use of biological and hazardous materials. We incurred approximately $578,000, $516,000 and $435,000 for the years ended December 31, 2008, 2007 and 2006, respectively, of costs associated with managing hazardous substances and pollution in on-going operations.

Off-Balance Sheet Arrangements

As of December 31, 2008, 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. We do not invest in auction rate securities. A 100 basis point increase or decrease in interest rates would increase or decrease our current investment balance by approximately $13,000 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.

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Item 9A. Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, 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, 2008, 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, 2008 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, 2008.

The effectiveness of our internal control over financial reporting as of December 31, 2008 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

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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 Metabasis Therapeutics, Inc. s internal control over financial reporting as of December 31, 2008 based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Metabasis Therapeutics, Inc. s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the company s internal control over financial reporting based on our audit.

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

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

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

In our opinion, Metabasis Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets as of December 31, 2008 and 2007, and the related statements of operations, stockholders equity and cash flows for each of the three years in the period ended December 31, 2008 of Metabasis Therapeutics, Inc. and our report dated March 27, 2009 expressed an unqualified opinion thereon that included an explanatory paragraph regarding Metabasis Therapeutic s ability to continue as a going concern.

/s/ Ernst & Young LLP

San Diego, California

March 27, 2009

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Item 9B. Other Information
Not applicable.

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, 2008, 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

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.

The following table provides certain information as of December 31, 2008, 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)	7,770,890	$ 4.06	1,535,104

Equity compensation plans not approved by stockholders(2)				
Total	7,770,890	$	4.06	1,535,104

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(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. 1,005,533 shares under column (c) are attributable to our 2004 Employee Stock Purchase Plan.

(2) As of December 31, 2008, we did not have any equity compensation plans that were not approved by our stockholders.

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.

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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, 2008 and 2007

Statements of operations for the years ended December 31, 2008, 2007 and 2006

Statements of stockholders equity for the years ended December 31, 2008, 2007 and 2006

Statements of cash flows for the years ended December 31, 2008, 2007 and 2006

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(12)	Amended and Restated Bylaws of the Company.
4.1(1)	Form of Common Stock Certificate.
4.2(1)	

	Amended and Restated Investors Rights Agreement dated October 28, 2003 between the Company and certain of its stockholders.
4.3(6)	Form of Warrant issued pursuant to the Securities Purchase Agreement dated September 30, 2005.
4.4(11)	Common Stock Purchase Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited.
4.5(16)	Amendment to Common Stock Purchase Agreement dated February 15, 2008 by and between the Company and Kingsbridge Capital Limited.
4.6(11)	Registration Rights Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited.
4.7(16)	Amended and Restated Warrant dated February 15, 2008 issued by the Company to Kingsbridge Capital Limited.
4.8(17)	Warrant to Purchase Shares of Common Stock dated March 14, 2008 issued by the Company to Oxford Finance Corporation.
4.9(19)	Form of Registration Rights Agreement dated April 14, 2008 by and among the Company and the individuals and entities identified on the signature page thereto.

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Exhibit Number	Description
4.10(19)	Form of Warrant issued pursuant to Securities Purchase Agreement dated April 14 2008 by and among the Company and the individuals and entities identified on the signature page thereto.
10.1(1)	Form of Indemnity Agreement.
10.2(13)	Amended and Restated 2001 Equity Incentive Plan and Form of Stock Option Agreement thereunder.
10.3(14)	2004 Non-Employee Directors Stock Option Plan and Form of Stock Option Agreement thereunder.
10.4(13)	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.
10.7	Employment offer letter dated September 15, 2005 between the Company and Howard Foyt.
10.8	Addendum to Employment offer letter dated November 7, 2005 between the Company and Howard Foyt.
10.9(1)	Stock Restriction Agreement dated June 30, 2003 between the Company and Paul K. Laikind.
10.10(1)	Stock Restriction Agreement dated June 30, 2003 between the Company and Mark D. Erion.
10.11(1)	Stock Restriction Agreement dated June 30, 2003 between the Company and John W. Beck.
10.12	Amended and Restated Severance Agreement dated December 31, 2008 between the Company and Edgardo Baracchini.
10.13(7)	Amended and Restated Severance Agreement dated July 19, 2006 between the Company and Paul K. Laikind.
10.14(15)	First Amendment dated April 27, 2007 to Amended and Restated Severance Agreement dated July 19, 2006 between the Company and Paul K. Laikind.
10.15	Amended and Restated Severance Agreement dated December 31, 2008 between the Company and Mark D. Erion.
10.16(15)	Severance Agreement dated April 27, 2007 between the Company and John W. Beck.
10.17(15)	Severance Agreement dated April 27, 2007 between the Company and Howard Foyt.
10.18	Employment offer letter dated September 19, 2006 between the Company and Barry Gumbiner.
10.19	Addendum to Employment offer letter dated September 19, 2006 between the Company and Barry Gumbiner.
10.20	Severance Agreement dated June 18, 2007 between the Company and Barry Gumbiner.
10.21(1)	License Agreement dated June 30, 1999 between the Company and Sicor Inc.
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.
10.24(3)	Lease Agreement dated December 21, 2004 between the Company and CarrAmerica Realty, L.P.
10.25(4)*	Amendment dated January 18, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.

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Exhibit Number	Description
10.26(5)*	License and Collaboration Agreement dated June 22, 2005 between the Company and Merck & Co., Inc.
10.27(8)*	Amendment dated August 29, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.28(8)*	Amendment dated November 2, 2005 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.29(9)*	Amendment dated May 1, 2006 to Exclusive License and Research Collaboration Agreement dated December 23, 2003 between the Company and Merck & Co., Inc.
10.30(19)	Amendment dated May 16, 2006 to Lease Agreement dated December 21, 2004 between the Company and CarrAmerica Realty, L.P.
10.31(10)	Offer Letter dated September 12, 2006 between the Company and David F. Hale.
10.32(2)	Assignment and Assumption Agreement dated December 13, 2006 by and among the Company, Valeant Research & Development and Schering Corporation.
10.33(7)	Termination Agreement among Valeant Pharmaceuticals North America, Schering Corporation and the Company dated September 19, 2007.
10.34(7)	Loan and Security Agreement dated March 14, 2008 between the Company and Oxford Finance Corporation.
10.35(18)*	Collaboration Agreement Extension Letter dated April 16, 2008 between the Company and Merck & Co., Inc.
10.36(19)	2008 Employee Incentive Compensation Plan.
10.37(20)*	Collaboration and License Agreement dated August 7, 2008 between the Company and Hoffman-La Roche Inc., F. Hoffman-La Roche LTD and Roche Palo Alto LLC.
10.38(20)*	Amendment Agreement dated September 24, 2008 among the Company, Schering Corporation and Valeant Pharmaceuticals North American.
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 requested or granted 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 Company s Registration Statement on Form S-1 (No. 333-112437), originally filed on February 3, 2004.

(2) Incorporated by reference to the Valeant Pharmaceuticals International Annual Report on Form 10-K for the fiscal year ended December 31, 2006.

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

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

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

(6) Incorporated by reference to the Company s Current Report on Form 8-K filed on October 5, 2005.

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

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

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

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

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

(12) Incorporated by reference to the Company s Current Report on Form 8-K filed on October 2, 2007.

(13) Incorporated by reference to the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2006.

(14) Incorporated by reference to the Company s Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2007.

(15) Incorporated by reference to the Company s Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2007.

(16) Incorporated by reference to the Company s Current Report on Form 8-K filed on February 15, 2008.

(17) Incorporated by reference to the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2007.

(18) Incorporated by reference to the Company s Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2008.

(19) Incorporated by reference to the Company s Current Report on Form 8-K filed on April 22, 2008.

(20) Incorporated by reference to the Company s Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2008.

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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.

METABASIS THERAPEUTICS, INC.

By: /s/ MARK D. ERION
Mark D. Erion, Ph.D.

President, Chief Executive Officer and Chief Scientific Officer

Dated: March 31, 2009

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/ MARK D. ERION **Mark D. Erion, Ph.D.**	President, Chief Executive Officer, Chief Scientific Officer and Director	March 31, 2009
/s/ TRAN B. NGUYEN **Tran B. Nguyen, M.B.A.**	Vice President, Chief Financial Officer, Treasurer and Corporate Secretary (Principal Financial Officer)	March 31, 2009
/s/ TRISHA M. MILLICAN **Trisha M. Millican, C.P.A.**	Controller (Principal Accounting Officer)	March 31, 2009
/s/ DAVID F. HALE **David F. Hale**	Chairman of the Board of Directors	March 31, 2009
/s/ DANIEL D. BURGESS **Daniel D. Burgess, M.B.A.**	Director	March 31, 2009
/s/ LUKE B. EVNIN **Luke B. Evnin, Ph.D.**	Director	March 31, 2009
/s/ PAUL K. LAIKIND **Paul K. Laikind, Ph.D.**	Director	March 31, 2009
/s/ ARNOLD L. ORONSKY **Arnold L. Oronsky, Ph.D.**	Director	March 31, 2009
/s/ WILLIAM R. ROHN **William R. Rohn**	Director	March 31, 2009
/s/ GEORGE F. SCHREINER **George F. Schreiner, M.D., Ph.D.**	Director	March 31, 2009

/s/ Elizabeth Stoner	Director	March 31, 2009

Elizabeth Stoner, M.D.

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METABASIS THERAPEUTICS, INC.

INDEX TO FINANCIAL STATEMENTS

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

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Metabasis Therapeutics, Inc. at December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that Metabasis Therapeutics, Inc. will continue as a going concern. As more fully described in Note 2, the Company s existing working capital is not sufficient to meet its cash requirements to fund planned operating expenses and working capital requirements through December 31, 2009 without additional sources of cash. This condition raises substantial doubt about the Company s ability to continue as a going concern. Management s plans in regard to this matter is also described in Note 2. The most recent year financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Metabasis Therapeutics, Inc. s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 24, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California

March 27, 2009

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METABASIS THERAPEUTICS, INC.

BALANCE SHEETS

(in thousands, except par value data)

	December 31, 2008	December 31, 2007
Assets		
Current assets:		
Cash and cash equivalents	$ 12,599	$ 14,141
Securities available-for-sale	9,000	28,297
Prepaids and other current assets	1,091	1,157
Total current assets	22,690	43,595
Property and equipment, net	4,779	6,356
Other assets	273	172
Total assets	$ 27,742	$ 50,123
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 93	$ 802
Accrued compensation	2,439	3,181
Accrued liabilities	1,798	4,132
Deferred revenue, current portion	5,652	1,321
Current portion of long-term debt	3,890	2,068
Current portion of capital lease obligations	26	23
Total current liabilities	13,898	11,527
Deferred revenue, net of current portion	2,499	
Deferred rent	3,079	2,595
Long-term debt	4,658	3,845
Capital lease obligations, net of current portion	27	55
Other Long Term Liabilities	200	
Total liabilities	24,361	18,022
Stockholders equity:		
Preferred stock, $0.001 par value; 5,000 shares authorized at December 31, 2008 and December 31, 2007, no shares issued or outstanding		
Common stock, $0.001 par value; 100,000 shares authorized at December 31, 2008 and December 31, 2007; 35,152 and 30,754 shares issued and outstanding at December 31, 2008 and December 31, 2007, respectively	35	31
Additional paid-in capital	195,640	182,003
Accumulated deficit	(192,326)	(150,012)
Accumulated other comprehensive loss	32	79
Total stockholders equity	3,381	32,101
Total liabilities and stockholders equity	$ 27,742	$ 50,123

See accompanying notes.

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METABASIS THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS

(in thousands, except per share data)

	Years Ended December 31,		
	2008	**2007**	**2006**
Revenues:			
License fees	$ 2,344	$ 5,301	$ 1,984
Sponsored research	2,466	3,398	2,210
Other revenue		320	192
Total revenues	4,810	9,019	4,386
Operating expenses:			
Research and development	36,356	40,915	29,945
General and administrative	10,751	12,442	11,250
Total operating expenses	47,107	53,357	41,195
Loss from operations	(42,297)	(44,338)	(36,809)
Other income (expense):			
Interest income	916	3,095	3,932
Interest expense	(933)	(556)	(391)
Total other (expense) income	(17)	2,539	3,541
Net loss	$ (42,314)	$ (41,799)	$ (33,268)
Basic and diluted net loss per share	$ (1.25)	$ (1.37)	$ (1.15)
Shares used to compute basic and diluted net loss per share	33,779	30,587	29,019

See accompanying notes.

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METABASIS THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS EQUITY

(in thousands)

	Common Stock		Additional Paid-In Capital	Deferred Compensation	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders Equity
	Shares	Amount					
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 offering costs of $2,696	4,938	5	37,299				37,304
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
Net loss					(41,799)		(41,799)
Unrealized gain on short-term investments						56	56
Net comprehensive loss							(41,743)
Issuance of common stock for option exercises	48		71				71
Issuance of common stock pursuant to the Employee Stock Purchase Plan	206	1	599				600
Exercise of series C preferred warrants	7						
Stock-based compensation			5,035				5,035
Balance at December 31, 2007	30,754	$ 31	$ 182,003	$	$ (150,012)	$ 79	$ 32,101
Net loss					(42,314)		(42,314)
Unrealized loss on short-term investments						(47)	(47)
Net comprehensive loss							(42,361)
Issuance of common stock for option exercises	12		10				10
Issuance of common stock pursuant to the Employee Stock Purchase Plan	215		169				169
Exercise of warrants pursuant to warrant exchange	1,686	2	3,613				3,615
Issuance of common stock pursuant to private placement	2,485	2	5,906				5,908
Stock-based compensation			3,939				3,939
Balance at December 31, 2008	35,152	$ 35	$ 195,640	$	$ (192,326)	$ 32	$ 3,381

See accompanying notes.

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METABASIS THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS

(in thousands)

	Years Ended December 31,		
	2008	2007	2006
Operating activities			
Net loss	$ (42,314)	$ (41,799)	$ (33,268)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	3,939	5,035	3,745
Depreciation and amortization	2,073	2,028	1,602
Deferred rent	484	1,029	1,236
Amortization of discount and premium on securities available-for-sale	(494)	(2,220)	(925)
Loss on disposal of assets	29	153	29
Change in operating assets and liabilities:			
Other current assets	66	333	679
Other assets	99	7	(27)
Deferred revenue	6,830	(3,501)	167
Accounts payable	(709)	(251)	(692)
Accrued compensation and other liabilities	(3,076)	2,803	118
Net cash flows used in operating activities	(33,073)	(36,383)	(27,336)
Investing activities			
Purchases of securities available-for-sale	(24,498)	(78,358)	(134,752)
Sales/maturities of securities available-for-sale	44,242	118,208	104,179
Purchases of property and equipment	(525)	(2,274)	(3,230)
Net cash flows provided by (used in) investing activities	19,219	37,576	(33,803)
Financing activities			
Issuance of common stock, net	9,702	671	38,002
Principal payments on debt and capital lease obligations	(2,390)	(1,965)	(1,486)
Proceeds received from debt and capital lease obligations	5,000	2,190	4,078
Net cash flows provided by financing activities	12,312	896	40,594
(Decrease) increase in cash and cash equivalents	(1,542)	2,089	(20,545)
Cash and cash equivalents at beginning of year	14,141	12,052	32,597
Cash and cash equivalents at end of period	$ 12,599	$ 14,141	$ 12,052
Supplemental disclosure of cash flow information:			
Interest paid	$ 933	$ 556	$ 405
Supplemental schedule of noncash investing and financing activities:			
Disposal of assets	$ 26	$ 4,563	$
Net-share settlement of warrant	$	$ 56	$
Unrealized (loss) gain on short-term investments	$ (47)	$ 56	$ 77

Debt issuance costs	$ 200	$	$
Reclass of deferred compensation	$	$	$ 3,266
Fair value of warrant issued in connection with the Committed Equity Financing Facility	$	$	$ 1,098

See accompanying notes.

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METABASIS THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Basis of Presentation

Metabasis Therapeutics, Inc. (Metabasis or the Company) is a biopharmaceutical company focused on the discovery development of novel drugs by applying our proprietary technologies, scientific expertise and unique capabilities for targeting the liver and liver pathways.

2. Going Concern

The Company has incurred significant net losses since inception and has relied on its ability to fund its operations through private equity financings, an initial public offering, private placements of common stock, a registered direct offering of common stock, proceeds from business collaborations and other traditional debt financings. Management expects operating losses and negative cash flows to continue for the foreseeable future as the Company incurs additional costs and expenses related to the continued development of its products. The Company s working capital will not be sufficient to fund its operations through December 31, 2009 without additional sources of cash. The funding of on-going operating expenses is dependent upon the Company s ability to generate significant additional funding through equity financings, attainment of milestones from existing collaboration agreements, entering into new strategic collaborations with respect to one or more of its metabolic disease assets and licensing or otherwise monetizing its hepatitis B or primary liver cancer programs. If the Company is unable to generate sufficient additional funding in a timely manner, it will be required to seek additional resources by pursuing other strategic alternatives including the merger with or sale of some or all of its assets to another company, or cease operations entirely. These conditions raise substantial doubt about the Company s ability to continue as a going concern. The accompanying financial statements have been prepared on a going concern basis that contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The financial statements do not include adjustments to reflect the possible future effects on the recoverability and classification of recorded assets or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

3. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles (GAAP) 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.

Fair Value of Financial Instruments

In September 2006, the Financial Accounting Standards Board (the FASB) issued Statement of Financial Accounting Standards (SFAS) No. 157, *Fair Value Measurements* (SFAS No. 157). This statement provides a definition of fair value, establishes a hierarchy for measuring fair value in GAAP, and requires certain disclosures about fair values used in financial statements. This statement does not extend the use of fair value beyond what is currently required by other pronouncements, and it does not pertain to stock-based compensation under SFAS No. 123(R), *Share-Based Payment,* or to leases under SFAS No. 13, *Accounting for Leases.*

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This statement was effective for financial statements issued for fiscal years beginning after November 15, 2007 (beginning with the Company s 2008 fiscal year).

On February 14, 2008, FASB Staff Position (FSP) FAS 157-2, *Effective Date of FASB Statement No. 157* (FSP FAS 157-2), was issued. FSP FAS 157-2 defers application of SFAS No. 157 for non-financial assets and liabilities to years beginning after November 15, 2008 (beginning with the Company s 2009 fiscal year). As a result, the Company partially adopted SFAS No. 157 as it relates to the Company s financial assets and liabilities until it is required to apply this pronouncement to its non-financial assets and liabilities beginning with fiscal year 2009. The adoption did not have any effect on the Company s results of operations or financial condition.

The Company applies fair value accounting to its securities available-for-sale in accordance with SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities* (SFAS No. 115). These securities consist of treasury backed money market funds, corporate bonds and commercial paper. Due to the current market conditions, the Company no longer invests in asset backed securities. The following table shows the fair value measurement for its financial assets at December 31, 2008 and the fair value hierarchy level, as defined in SFAS No. 157.

		Fair Value Measurements (in thousands)		
Description	**Asset Total**	**Quoted Prices in Active Markets for Identical Assets (Level 1)**	**Significant Other Observable Inputs (Level 2)**	**Significant Unobservable Inputs (Level 3)**
Securities available-for-sale	$ 9,000	$ 9,000	$	$

Asset classes that fall within the Level 1 fair value hierarchy are those assets whose fair value assumptions are based on market data obtained from sources independent of the Company (observable inputs). Level 1 observable inputs are quoted prices for identical items in active markets that the Company has access to at the measurement date.

Asset classes that fall within the Level 2 fair value hierarchy are those assets whose fair value assumptions are also based on independent market data. Level 2 observable inputs are quoted prices for similar items in active markets or quoted prices for identical or similar items in inactive markets. An inactive market is one where there are few transactions, the prices are not current, price quotations vary substantially over time or among market makers or where little information is released publicly.

Asset classes that fall within the Level 3 fair value hierarchy are those assets whose fair value assumptions are based on the Company s own information.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities, including an amendment of SFAS No. 115* (SFAS No. 159). SFAS No. 159 expands the use of fair value accounting but does not affect existing standards that require assets or liabilities to be carried at fair value. Under SFAS No. 159, a company may elect to use fair value to measure accounts and loans receivable, available-for-sale and held-to-maturity securities, equity method investments, accounts payable, guarantees and issued debt. Other eligible items include firm commitments for financial instruments that otherwise would not be recognized at inception and non-cash warranty obligations where a warrantor is permitted to pay a third party to provide the warranty goods or services. If the use of fair value is elected, any upfront costs and fees related to the item must be recognized in earnings and cannot be deferred, such as debt issuance costs. The fair value election is irrevocable and generally made on an instrument-by-instrument basis, even if a company has similar instruments that it elects not to measure based on fair value. At the adoption date, unrealized gains and losses on existing items for which fair value has been elected are reported as a cumulative adjustment to beginning retained earnings. Subsequent to the adoption of SFAS No. 159, changes in fair value are recognized in earnings. SFAS No. 159 was effective for fiscal years beginning after November 15, 2007 (beginning with the Company s 2008 fiscal year).

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The Company considers the carrying amount of cash and cash equivalents, prepaid expenses and other current assets, securities available-for-sale, accounts receivable, accounts payable, accrued liabilities and deferred revenue 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. Therefore, the Company has elected not to apply the fair value option to these financial assets and liabilities under SFAS No. 159. However, the Company does apply fair value accounting to its securities available-for-sale in accordance with SFAS No. 115.

Short-term investments are classified as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders equity. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income. The cost of securities sold is based on the specific-identification method. Interest and dividends on securities classified as available-for-sale are included in interest income. Total realized gains from fair value changes included in earnings for the fiscal years ended December 31, 2008, 2007 and 2006 were immaterial. There were no cumulative adjustments to beginning retained earnings as a result of adopting SFAS No. 159.

Concentration of Credit Risks

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 treasury backed money market funds, corporate bonds and commercial paper. Due to the current market conditions, the Company no longer invests in asset backed securities. In accordance with its investment policy, the Company does not invest in auction rate securities. 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.

Property and Equipment

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

Impairment of Long-Lived Assets

The Company assesses potential impairment to its long-lived 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. In connection with a corporate restructuring in November 2008 (Note 6), the Company evaluated its long-lived assets for impairment. The impact of the restructuring to long-lived assets was deemed immaterial.

Revenue Recognition

The Company s revenue recognition policies are in accordance with the Staff Accounting Bulletin (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 access to proprietary technologies and research and development services. Payments under collaborations are generally made in the form of up-front license fees, milestone payments and downstream royalties. All fees are

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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 March 2005, the Securities and Exchange Commission (SEC) 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 Amended and Restated 2001 Equity Incentive Plan (Equity Incentive Plan) and the 2004 Non-Employee Directors Stock Option Plan (Directors Stock Option Plan) are 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 is recognized based on the grant date fair value as estimated in accordance with SFAS No. 123. Compensation expense is recognized over the requisite service period which is typically the period over which the stock-based compensation awards vest. Compensation expense under the 2004 Employee Stock Purchase Plan (Employee Stock Purchase Plan) is 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. Compensation expense is reduced for estimated forfeitures. Forfeitures are estimated at the time of grant for option awards and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

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,

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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 2008, 2007 and 2006 was immaterial.

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 option-pricing 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.

Comprehensive Income (Loss)

SFAS No. 130, *Reporting Comprehensive Income*, requires that all components of comprehensive income (loss), including net loss, be reported in the financial statements in the period in which they are recognized. Comprehensive income (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 income (loss) for 2008, 2007 and 2006 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 7,609,266, 7,236,732 and 6,694,740 in 2008, 2007 and 2006, respectively.

	Years Ended December 31,		
	2008	2007	2006
	(in thousands, except per share amounts)		
Actual:			
Numerator:			
Net loss	$ (42,314)	$ (41,799)	$ (33,268)
Denominator:			
Weighted average common shares	33,779	30,587	29,152
Weighted average unvested common shares subject to repurchase			(133)
Denominator for basic and diluted net loss per share	33,779	30,587	29,019
Basic and diluted net loss per share	$ (1.25)	$ (1.37)	$ (1.15)

Warrants

The Company has issued warrants to purchase its shares of common stock in connection with financing or debt arrangements. Generally, the warrants have been provided as additional consideration to an investor for the purchase of the Company s common stock, or the commitment to purchase common stock in the future, through a structured offering. The terms of the warrants vary, but generally include an exercise price equal to a specific premium over the value of the common stock at the time of the warrant issuance. The warrant holder may elect to exercise the warrants by physical settlement or net-share settlement.

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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 if and when applicable, 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, 2008, all warrants issued were classified as equity.

Recent Accounting Pronouncements

In November 2007, the EITF issued EITF Issue No. 07-1, *Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property.* Companies may enter into arrangements with other companies to jointly develop, manufacture, distribute, and market a product. Often the activities associated with these arrangements are conducted by the collaborators without the creation of a separate legal entity (that is, the arrangement is operated as a virtual joint venture). The arrangements generally provide that the collaborators will share, based on contractually defined calculations, the profits or losses from the associated activities. Periodically, the collaborators share financial information related to product revenues generated (if any) and costs incurred that may trigger a sharing payment for the combined profits or losses. The consensus requires collaborators in such an arrangement to present the result of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. EITF Issue No. 07-1 is effective for collaborative arrangements in place at the beginning of the annual period beginning after December 15, 2008. The Company does not expect the adoption of EITF Issue No. 07-1 to have a material impact on its financial statements.

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* (SFAS No. 141(R)). SFAS No. 141(R) replaces SFAS No. 141. SFAS No. 141(R) requires the acquirer of a business to recognize and measure the identifiable assets acquired, the liabilities assumed and any non-controlling interest in the acquiree at fair value. SFAS No. 141(R) also requires transaction costs related to the business combination to be expensed as incurred. SFAS No. 141(R) applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008 (the Company s 2009 fiscal year). The adoption of SFAS No. 141(R) is not expected to have a material impact on the Company s financial statements.

In May 2008, the FASB issued SFAS No. 162, *The Hierarchy of Generally Accepted Accounting Principles* (SFAS No. 162). SFAS No. 162 identifies the sources of accounting principles and provides entities with a framework for selecting the principles used in preparation of financial statements that are presented in conformity with GAAP. The current GAAP hierarchy has been criticized because it is directed to the auditor rather than the entity, it is complex and it ranks FASB Statements of Financial Accounting Concepts, which are subject to the same level of due process as FASB SFAS, below industry practices that are widely recognized as generally accepted but that are not subject to due process. The FASB believes the GAAP hierarchy should be directed to entities because it is the entity (not its auditors) that is responsible for selecting accounting principles for financial statements that are presented in conformity with GAAP. SFAS No. 162 is effective 60 days following the SEC s approval of the Public Company Accounting Oversight Board amendments to AU Section 411, *The Meaning of Present Fairly in Conformity With Generally Accepted Accounting Principles*. The Company adopted SFAS No. 162, and it did not have a material impact on the Company s financial statements.

In June 2008, the EITF issued EITF No. 08-3, *Accounting by Lessees for Maintenance Deposits under Lease Agreements* (EITF No. 08-3). Under certain lease arrangements, the lessee is contractually responsible for repair and maintenance of the leased asset, and the lessee is required to make deposits with the lessor to fund that maintenance. The deposit is refunded to the lessee only to the extent that the lessee incurs qualified maintenance

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costs. Questions have arisen as to the proper accounting for these deposits as some companies account for the maintenance deposits as deposits, while other companies account for them as contingent rental expense. EITF No. 08-3 concludes that maintenance deposits should be considered deposits when paid to the lessor if it is probable that the deposits will be refunded to the lessee. If it is not probable, then the deposits are recognized as rental expense. If it is determined at the inception of the lease that a portion of the deposits is not probable of being refunded to the lessee, then the lessee should recognize as expense a pro-rata portion of the deposits as they are paid. The cost of maintenance activities should be expensed or capitalized, as appropriate. The definition of probable will fall under the guidance of FASB Concept Statement No. 6, *Elements of Financial Statements.* EITF No. 08-3 is effective for fiscal years beginning after December 15, 2008 (beginning with the Company s 2009 fiscal year). Early application is not permitted. The adoption of EITF No. 08-3 is not expected to have a material impact on the Company s financial statements.

In December 2008, the FASB issued FSP FAS 140-4 and FIN 46(R)-8, *Disclosures by Public Entities about Transfers of Financial Assets and Interests in Variable Interest Entities.* The purpose of this FSP is to promptly increase disclosures by public entities and enterprises until the pending amendments to FASB Statement No. 140, *Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities,* (SFAS No. 140) and FASB Interpretation No. 46 (revised December 2003), *Consolidation of Variable Interest Entities,* (FIN 46(R)) are finalized and approved by the FASB. The FSP is effective for reporting periods (interim and annual) ending after December 15, 2008 (the Company s 2008 fiscal year).

This FSP amends SFAS No. 140 to require public entities to provide additional disclosures about transferors continuing involvement with transferred financial assets. This FSP also amends FIN 46(R) to require public enterprises, including sponsors that have a variable interest in a variable interest entity, to provide additional disclosures about their involvement with variable interest entities. This FSP also requires disclosures by a public enterprise that is (a) a sponsor of a qualifying special-purpose entity (SPE) that holds a variable interest in the qualifying SPE but was not the transferor of financial assets to the qualifying SPE and (b) a servicer of a qualifying SPE that holds a significant variable interest in the qualifying SPE but was not the transferor of financial assets to the qualifying SPE. The adoption of this FSP did not have a material impact on the Company s financial statements.

4. Stock-Based Compensation

Equity Plans

The Company maintains three shareholder-approved share-based compensation plans that are subject to the requirements of SFAS No. 123R. 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. The Directors Stock Option Plan provides for the grant of non-statutory stock options to non-employee directors. The 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 (IRC).

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 may be either incentive stock option grants or non-qualified stock option grants if they are granted to employees and are 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 three years, and expire ten years

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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.

SFAS No. 123R Compensation Expense

In accordance with SFAS No. 123R, the Company recognized share-based compensation expense for all three plans as follows (in thousands, except per share data):

	December 31,		
	2008	2007	2006
Stock-based compensation expense:			
Research and development	$ 2,381	$ 3,118	$ 1,936
General and administrative	1,558	1,917	1,809
Total stock-based compensation expense	$ 3,939	$ 5,035	$ 3,745
Effect on loss per share:			
Basic and diluted	$ 0.12	$ 0.16	$ 0.13

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, 2008 was recognized on a straight-line basis over the vesting period of each grant, net of estimated forfeitures.

The estimated fair value of the options and share purchase rights granted during 2006 and in subsequent years was calculated using a Black-Scholes model. The following summarizes the assumptions used in the Black-Scholes model:

	December 31, 2008	
	Equity Incentive Plan and Directors Stock Option Plan	Employee Stock Purchase Plan
Risk-free interest rate(1)	3.1%	3.2%
Volatility(2)	81.3%	79.8%
Dividend yield(3)	0.0%	0.0%
Expected Life(4)	5.8 years	1.3 years
Weighted average fair value at date of grant	$ 1.23	$ 1.12

	December 31, 2007	
	Equity Incentive Plan and Directors Stock Option Plan	Employee Stock Purchase Plan
Risk-free interest rate(1)	4.5%	4.7%
Volatility(2)	72.1%	69.7%
Dividend yield(3)	0.0%	0.0%
Expected Life(4)	5.8 years	1.3 years
Weighted average fair value at date of grant	$ 4.51	$ 3.03

	December 31, 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

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(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.

As of December 31, 2008, the Company had approximately $5.5 million of unrecognized stock-based compensation expense under the Equity Incentive Plan and the Directors Stock Option Plan The expense is expected to be recognized on a straight-line basis over a weighted average period of approximately 2.5 years.

During the year ended December 31, 2008, the Company recognized approximately $245,000 of additional stock-based compensation expense associated with the modification of vesting terms on stock options held by former officers of the Company. These modifications were made pursuant to existing severance agreements the Company.

Equity Plan Activity

The following is a summary of stock option activity under the Equity Incentive Plan and the Directors Stock Option Plan as of December 31, 2007, and changes during the twelve months ended December 31, 2008 (in thousands, except per share data):

	Outstanding Options	
	Number of Options	Weighted Average Exercise Price Per Share
Outstanding at December 31, 2007	3,558	$ 5.97
Granted	2,923	$ 1.73
Exercised	(13)	$ 0.83
Canceled	(1,061)	$ 4.84
Outstanding at December 31, 2008	5,407	$ 3.91
Exercisable at December 31, 2008	2,519	$ 5.00

The total intrinsic value of options exercised in 2008, 2007 and 2006 was $10,722, $220,000 and $254,000, respectively.

The aggregate intrinsic values of stock options exercisable and outstanding as of December 31, 2008 were immaterial. The weighted average remaining contractual terms of options outstanding and exercisable as of December 31, 2008 were 4.8 years and 4.1 years, respectively.

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5. Balance Sheet Details

Securities Available-For-Sale

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

	December 31, 2008			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate debt securities	$ 4,330	$ 20	$	$ 4,350
Government securities	4,638	12		4,650
Total	$ 8,968	$ 32	$	$ 9,000

	December 31, 2007			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate debt securities	$ 21,268	$ 73	$	$ 21,341
Asset-backed securities	6,950	6		6,956
Total	$ 28,218	$ 79	$	$ 28,297

Gross realized gains and losses on available-for-sale securities were immaterial during the years ended December 31, 2008, 2007 and 2006. All realized gains and losses are reclassified out of other comprehensive income (loss) in the period recognized based on the specific identification method. Proceeds from the sale of short-term investments totaled $44.2 million, $118.2 million and $104.2 million for the years ended December 31, 2008, 2007 and 2006, respectively. All available-for-sale securities at December 31, 2008 have a contractual maturity of one year or less.

Investments considered to be temporarily impaired at December 31, 2008 are immaterial. There are no investments held at December 31, 2008, which are considered to be temporarily impaired with maturities 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.

Property and Equipment

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

	December 31,	
	2008	2007
Laboratory equipment	$ 9,250	$ 8,972
Computers and electronics	2,186	1,903
Leasehold improvements	1,401	1,356
Office furniture and fixtures	624	600
Construction in progress		160
	13,461	12,991
Less: accumulated depreciation and amortization	(8,682)	(6,635)

	$ 4,779	$ 6,356

Depreciation and amortization expense, which include assets held under capital leases, was $2.1 million, $2.0 million and $1.6 million for the years ended December 31, 2008, 2007 and 2006, respectively. Assets held

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under capital leases were approximately $98,000 at December 31, 2008 and 2007, and accumulated depreciation was approximately $83,000 and $60,000 at December 31, 2008 and 2007, respectively. The balance of capital leases and equipment loans totaled approximately $3.9 million and $6.0 million at December 31, 2008 and 2007, respectively.

The Company recorded $55,000 of asset disposals resulting in a loss of $29,000 for the twelve months ended December 31, 2008. The Company recorded $153,000 in loss on disposals for the twelve months ended December 31, 2007 and $29,000 for the twelve months ended December 31, 2006.

Accrued Liabilities and Accrued Compensation

Accrued liabilities and accrued compensation consisted of the following (in thousands):

	December 31,	
	2008	**2007**
Accrued development expenses	$ 1,244	$ 3,241
Accrued legal and patent fees	73	216
Other accrued liabilities	481	675
	$ 1,798	$ 4,132
Accrued employee benefits	$ 1,849	$ 1,914
Accrued restructuring expenses	582	
Accrued bonuses	8	1,267
	$ 2,439	$ 3,181

6. Corporate Restructuring

In November 2008, the Company committed to a restructuring plan that resulted in the reduction of approximately 30% of the Company s workforce. The restructuring was a result of a strategic realignment of the Company to preserve cash and reduce on-going operating expenses. Employees directly affected by the restructuring plan received notification and were provided with severance payments, retention bonuses, where applicable, continued benefits for a specified period of time and outplacement assistance. The Company expects to complete the restructuring plan by the end of the first quarter of 2009.

The Company anticipates incurring restructuring charges of approximately $1.7 million, primarily associated with personnel-related termination costs. The Company does not expect to incur any expense related to contractual or lease obligation or other exit costs. However, this expectation is subject to a number of assumptions, and actual results may materially differ. Pursuant to SFAS No. 146, *Accounting for Costs Associated with Exit or Disposal Activities,* the Company recorded a charge of approximately $1.5 million for the twelve month period ending December 31, 2008, of which approximately $1.2 million was included in research and development expense and approximately $334,000 was included in general and administrative expense. The remaining $229,000 of anticipated costs associated with this restructuring relates to employees who were retained and will be recognized as earned over the retention period, which is expected to be completed by the end of the first quarter of 2009.

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As of December 31, 2008, the Company had a remaining balance of $582,000 of accrued restructuring expenses included in the balance sheet. The changes to the accrued liability during 2008 are as follows (in thousands):

	Termination Costs for Involuntary Employee Terminations
Accrual balance at December 31, 2007	$
Accruals	1,483
Payments	(901)
Accrual balance as of December 31, 2008	$ 582

7. 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 September 2007, the Company entered into an operating lease agreement pursuant to which the Company leased approximately 2,900 square feet of office space in Ann Arbor, Michigan. The lease expired on December 31, 2008, and the Company continues to pay for the office space on a month-to-month basis. As a result of a corporate restructuring that occurred in November 2008, the Company does not anticipate occupying this office space after the first quarter of 2009.

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 terminated sooner. 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 $24.2 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.

Rent expense was approximately $2.9 million for the year ended December 31, 2008 and approximately $2.8 million for the years ended December 31, 2007 and 2006.

Debt

In March 2008, the Company entered into a Loan and Security Agreement (Agreement) with Oxford Corporation (Oxford), pursuant to which Oxford provided the Company with a three-year, $5.0 million term loan. The Company is using the proceeds from the loan for general working capital purposes. Interest accrues at an annual rate of 9.83%, with six interest-only monthly payments, made in arrears, beginning in May 2008, followed by 30 equal monthly payments of principal and interest beginning in November 2008. The Company paid a facility fee of $50,000 upon signing of the term sheet and is required to pay an additional fee of 4% of the term loan amount, or $200,000, at the end of the three year term. The Company has the option to prepay the outstanding balance of the term loan in full, subject to a prepayment fee. The loan is collateralized by the general assets of the Company, excluding intellectual property. There are no financial covenants under the terms of this Agreement. In the event the Company becomes in default of the loan agreement, the lender has the right under a control agreement, to assume control over the Company s bank accounts, which include its operating and short-term investment accounts.

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In connection with the Agreement, the Company issued to Oxford a warrant to purchase up to 154,639 shares of the Company s common stock at an exercise price of $1.94 per share, which represents the closing price of the Company s common stock on the date of the Agreement. The warrant is immediately exercisable and expires in March 2018. The warrant holder may elect to exercise the warrant by physical settlement or net-share settlement. 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 $220,000 at March 14, 2008, was determined using the Black-Scholes model with the following assumptions: risk free interest rate of 3.05%, dividend yield of 0%, expected volatility of 81.63%, and an expected term of 5 years.

In August 2003, the Company entered into a $1.4 million equipment loan agreement with a financing company. This agreement was subsequently amended two times to increase the amount available to $7.6 million. The proceeds were used to finance lab equipment, computer and electronic equipment and furniture, which serve as collateral under the loan. The Company utilized the total amount available under the equipment loan agreement by December 31. 2007. 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 is 10.46%. The outstanding balance of this loan is $3.6 million and $5.7 million at December 31, 2008 and 2007, respectively.

The Company s outstanding debt and equipment loan agreements with Oxford contain events of default that may be triggered by a material adverse change, which is defined in the agreements as any material change in the general affairs, senior management, results of operations, or financial condition of the Company, whether or not arising from transactions in the ordinary course of business, that is likely to impair the ability of the Company to repay any portion of the obligations or a material impairment in the value or priority of the lender s security interest in the collateral. As described in Note 2, the Company currently does not have sufficient working capital to fund its operations through December 31, 2009 without additional sources of cash. While the determination of the occurrence of a material adverse event is subjective, Oxford has confirmed that the Company was not in default under the outstanding debt and equipment loan agreements as of December 31, 2008. In the event the Company is not successful in securing additional sources of cash in the near-term, Oxford may claim that a material adverse change has occurred under the debt or equipment loan agreements, and Oxford could demand immediate repayment of the balances outstanding under the agreements.

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 was $229,000 and $254,000 at December 31, 2008 and 2007, respectively. Payment schedules for commitment and contractual obligations at December 31, 2008, are as follows (in thousands):

	Capital Leases	Long-term Debt	Operating Leases
2009	$ 31	$ 4,567	$ 2,820
2010	24	3,640	3,112
2011	4	1,422	3,185
2012		44	3,279
2013		44	3,374
Thereafter		78	6,444
Total minimum payments	59	9,795	$ 22,214
Less amount representing interest	(6)	(1,247)	
Present value of net minimum payments	53	8,548	
Less current portion	(26)	(3,890)	
Long-term debt and capital lease obligations	$ 27	$ 4,658	

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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 $967,000 million at December 31, 2008. These purchase commitments expire at varying dates through December 31, 2009.

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 part of the Company s restructuring and reduction in workforce described in Note 6 above, the employment of Howard Foyt, Ph.D., M.D., Vice President of Clinical Development, was terminated. In connection with his termination, the Company recognized $352,000 of severance costs for the year ended December 31, 2008.

In December, Paul K. Laikind, Ph.D. resigned as the Company s President, Chief Executive Officer and Interim Chief Financial Officer, effective December 9, 2008. Dr. Laikind continues to serve as a member of our board of directors. In connection with his resignation, the Company recognized $554,000 of separation costs for the year ended December 31, 2008.

Clinical Development Agreements

The Company has entered into agreements with various vendors for the research 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.

8. Collaborative Research and Development Agreements

Roche

In August 2008, the Company entered into a two-year Research Collaboration and License Agreement with Hoffmann-La Roche Inc., F. Hoffmann-La Roche LTD and Roche Palo Alto LLC (collectively, Roche). Under the terms of the Roche agreement, the Company s HepDirect liver-targeted technology will be applied to proprietary Roche compounds to develop second-generation nucleoside analog drug candidates for treating hepatitis C virus. The Company received an upfront payment of $10.0 million from Roche in August 2008, of which $8.3 million will be recognized as license fees revenue and $1.7 million will be recognized as sponsored research revenue. Roche may also pay up to $2.1 million in sponsored research funding at the beginning of the second year of the research term, if applicable. In the event a development candidate is identified, Roche will assume development responsibility and the Company will be eligible to receive up to $193.0 million in additional payments upon achievement of predetermined preclinical and clinical development events as well as regulatory and commercialization events. Roche will retain full commercial rights for any marketed products resulting from the collaboration and will pay the Company a royalty on net sales of such products. The Company recognized revenue of $2.3 million for the year ended December 31, 2008 related to this collaboration. Deferred revenue of approximately $7.7 million is reflected on the balance sheet as of December 31, 2008, relating to this agreement.

Merck

In June 2005, the Company entered into a collaboration agreement with Merck & Co. (Merck), to research, develop and commercialize novel small molecule therapeutics with the potential to treat type 2 diabetes, and potentially other metabolic diseases, by activating an enzyme in the liver called AMP-activated

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Protein Kinase. As part of this collaboration, Merck paid an initial non-refundable license fee of $5.0 million in July 2005 and provided research support funding of approximately $6.3 million over the three year research term. The three-year research term is subject to renewal for one additional year upon the parties mutual agreement. In April 2008, the research term was extended for an additional year, through June 2009. The Company will receive $1.5 million over the course of the one year extension to support continued research efforts. 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, 2008, 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.

The Company recognized revenue of $2.5 million for the year ended December 31, 2008 and $3.8 million for the years ended December 31, 2007 and 2006 related to this collaboration. Deferred revenue of approximately $478,000 is reflected on the balance sheet as of December 31, 2008, relating to this agreement.

In December 2003, the Company entered into a non-exclusive collaboration agreement with Merck to discover new treatments for hepatitis C. The research term of the collaboration was initially for one year and in January 2005, was extended for an additional year through December 2005. 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 zero for the years ended December 31, 2008, 2007 and 2006. 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, the Company may be entitled to payments which total up to $25.3 million, plus royalties. Merck is solely responsible for conducting and funding all development work for compounds resulting from the collaboration and for commercializing any resulting products.

Idenix

In October 2006, the Company entered into a non-exclusive collaboration agreement with Idenix Pharmaceuticals, 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 agreement provided for up to two years of sponsored research. In addition, Idenix had the option to terminate the research term upon the first anniversary of the effective date of the agreement or upon the achievement of certain research 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 November 2006 and agreed to provide research funding of up to $1.7 million per year during the research term. In October 2007, the sponsored research term of the collaboration agreement ended upon the first anniversary of the agreement and the collaboration agreement subsequently terminated in accordance with its terms.

Daiichi Sankyo

In April 1997, the Company entered into a multi-year 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 was responsible for funding the clinical development of compounds selected for development under the agreement. Daiichi Sankyo had the right to select compounds discovered during the discovery period and was responsible for conducting and funding the clinical development of any compound selected for development. Daiichi Sankyo selected CS-917 as a clinical candidate in 1999 and completed the clinical trials through Phase 2b in the third quarter of 2007. The results of

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the Phase 2b clinical trial indicated CS-917 failed to achieve the trial s primary endpoint. As a result, the Company and Daiichi Sankyo agreed to terminate the collaboration agreement and return all rights and data related to this product candidate to the Company in January 2008. During the term of the collaboration agreement, the Company achieved three developmental milestones triggering a total of $6.5 million in payments, none of which were received in 2008, 2007 or 2006.

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, 2008, 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 Corporation

In January 2007, Valeant entered into an Assignment and Assumption Agreement (the Assignment Agreement) with Schering Corporation (Schering), under which Valeant assigned its rights, interests and obligations under the development and license agreement to Schering, and further granted Schering a license to its intellectual property related to pradefovir. Concurrently, the Company and Schering 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 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.

In September 2007, the Company, Schering and Valeant entered into a Termination Agreement (the Termination Agreement) to terminate the agreements for the development and commercialization of pradefovir. These agreements were terminated as a result of numerous factors, which may include the results of the 24-month oral carcinogenicity studies of pradefovir in rats and mice. The Company will not receive any additional payments related to these agreements and all rights to pradefovir have been returned to the Company, subject to certain milestone and royalty payments the Company may be required to make to Valeant should this product candidate be subsequently developed.

In September 2008, the Company, Schering and Valeant entered into an Amendment Agreement (the Amendment Agreement) to amend certain terms of the Assignment Agreement and the Termination Agreement. Pursuant to the Amendment Agreement, among other things, the Assignment Agreement was amended to provide for a reduction in the total number and value of milestone payments payable by the Company to Valeant upon the achievement of certain specified events to a single milestone payment due upon the first regulatory approval of pradefovir, and to reduce certain royalty payments due from the Company to Valeant upon commercialization of pradefovir. In addition, the Termination Agreement was amended to transfer certain patient registry obligations, should they be required, to the Company from Valeant (excluding the cost thereof, up to a specified limit).

9. Committed Equity Financing Facility

In November 2006, the Company entered into a Committed Equity Financing Facility (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 shares of common stock, over a three-year term through the purchase of newly-issued shares of the Company s common stock. In February 2008, the CEFF was amended to reduce the minimum market capitalization required to permit a draw down and to eliminate certain

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termination rights maintained by the investor, among other things. The Company may access capital under the CEFF in tranches of up to the lesser of $10 million or from between 1.0% to 1.5% of the Company s market capitalization at the time of the draw down of such tranche, subject to certain conditions. Currently, the Company does not meet these conditions and, therefore, does not have access to the CEFF. 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 $1.75 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.

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 per share 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. In connection with the amendment of the CEFF, the warrant was cancelled and replaced with a new warrant for 260,000 shares of common stock at an exercise price of $4.76 per share. The warrant is exercisable 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, 2008 and 2007.

The Company filed a registration statement with the SEC 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 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 No. 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. In 2007, an effective registration statement was filed with the SEC and the Company had not utilized this financial instrument.

10. Stockholders Equity

Common Stock

In April 2008, the Company raised $9.9 million in cash through a warrant exchange and concurrent private placement of common stock (together, the Transaction). The investors in the Transaction were certain current investors who held existing warrants for the purchase of the Company s common stock issued previously in its October 2001 and October 2005 private placements. Investment banking fees and other offering expenses were approximately $369,000.

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 SEC.

Warrants

Warrants were issued in connection with the Company s CEFF (see Note 9).

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In connection with the April 2008 Transaction discussed above, the Company entered into a warrant exercise agreement (the Warrant Exercise Agreement) pursuant to which the Company reduced the exercise prices of the investors warrants to purchase the Company s common stock acquired in its October 2001 and October 2005 private placements to an exercise price of $2.34 per share, in exchange for an irrevocable commitment by the investors to exercise such warrants at the closing. As a result of the Warrant Exercise Agreement, warrants for the purchase of 127,557 shares of the Company s common stock with a prior exercise price of $8.70 per share and warrants for the purchase of 1,558,279 shares of the Company s common stock with a prior exercise price of $6.74 per share were exercised at $2.34 per share.

Additionally, in connection with the Transaction, the Company entered into a securities purchase agreement (the Securities Purchase Agreement) pursuant to which the Company issued and sold to the investors 2,485,103 shares of its common stock at an exercise price of $2.34 per share, and warrants to purchase up to 1,057,196 shares of its common stock at an exercise price of $2.69 per share (the Warrants). The Warrants are exercisable commencing six months after the Transaction date until April 16, 2013. At the closing, the investors paid an additional purchase price for the Warrants equal to $0.125 per whole share issuable upon exercise of the Warrants. In connection with the Securities Purchase Agreement, the Company also entered into a registration rights agreement (the Registration Rights Agreement) pursuant to which the Company granted to the investors certain registration rights relating to the securities issued and sold in the Securities Purchase Agreement. The Company filed a registration statement pursuant to the Registration Rights Agreement on May 9, 2008 and the SEC declared the registration statement effective on May 30, 2008.

Certain of the Company s existing stockholders, including entities affiliated with MPM Capital, Hale BioPharma Ventures and InterWest Partners, invested in the Transaction. Certain of such investors and/or their affiliates are parties to the Company s amended and restated investors rights agreement dated October 28, 2003. Luke B. Evnin, Ph.D., David F. Hale and Arnold L. Oronsky, Ph.D., members of the Company s board of directors, are associated with MPM Capital, Hale BioPharma Ventures and InterWest Partners, respectively.

The Company accounted for the Warrants issued under the Securities Purchase Agreement in accordance with EITF Issue No. 00-19. According to EITF Issue No. 00-19, the Warrants met all criteria within the guidance providing for the classification of these financial instruments as equity. The fair values of the Warrants were approximately $1.5 million in aggregate and was determined using the Black-Scholes model using the following assumptions: risk-free interest rates of 3.02%; dividend yield of 0%; expected volatility of 81.9%; and a term of 5 years.

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. As discussed above, certain investors who held warrants issued in the 2005 private placement participated in the Transaction and exercised such warrants covering approximately 1,558,000 shares. At December 31, 2008, warrants issued in the 2005 private placement covering approximately 892,000 shares remained outstanding.

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 had an exercise price of $8.69 per share. As discussed above, certain investors who held the 2001 Series D warrants participated in the Transaction and exercised such warrants covering approximately 128,000 shares. The remaining warrants issued in the 2001 offering expired in accordance with their terms on October 18, 2008.

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 had an exercise price of $6.08 per share and expired on December 31, 2007 with 7,406 shares issued as a result of exercises during 2007.

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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 1,000,000, 1,000,000 and 915,000 shares were added to the Equity Incentive Plan on January 1, 2008, 2007 and 2006, 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, 2008 and 2007 were approximately 2,240,000 and 1,483,000, respectively.

There were no shares of common stock, originally issued pursuant to option exercises, outstanding at December 31, 2008 and 2007, respectively, that were subject to repurchase by the Company.

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 each of January 1, 2008, 2007 and 2006, 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, 2008 and 2007 were approximately 279,000 and 213,000, respectively.

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 375,000, 375,000 and 305,000 shares were added to the plan on January 1, 2008, 2007 and 2006, 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
2008	214,761	$ 0.79	$ 168,685
2007	205,941	$ 2.91	599,366
2006	198,158	$ 3.04	602,961
	618,860		$ 1,371,012

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Shares Reserved For Future Issuance

The following shares of common stock were reserved for future issuance at December 31, 2008:

Warrants to purchase shares in conjunction with the 2005 private placement	891,721
Warrants to purchase shares in conjunction with the CEFF	260,000
Warrants to purchase shares in conjunction with the venture debt	154,639
Warrants to purchase shares in conjunction with the 2008 private placement	1,057,196
Common stock options:	
Granted and outstanding	5,407,334
Reserved for future issuance	529,571
Employee stock purchase plan	1,005,533
	9,305,994

11. Income Taxes

On July 13, 2006, the FASB issued FIN No. 48 an interpretation of SFAS No. 109, *Accounting for Income Taxes*, to create a single model to address accounting for uncertainty in tax positions. FIN No. 48 clarifies the accounting for income taxes by prescribing a minimum recognition threshold in which a tax position be reached before financial statement recognition. FIN No. 48 also provides guidance on derecognition, measurement, classification, interest and penalties, accounting in interim periods, disclosure and transition. FIN No. 48 is effective for fiscal years beginning after December 15, 2006. The Company adopted FIN No. 48 as of January 1, 2007, as required. The adoption of this guidance did not have a material impact on the Company s results of operations or financial position.

At December 31, 2008, the Company had net deferred tax assets of $81.5 million. These deferred tax assets are primarily comprised of net operating loss (NOL) and research and development (R&D) credit carryforwards, capitalized research and development costs, deferred revenue, deferred rent and stock-based compensation expense. Due to uncertainties surrounding the Company s ability to generate future taxable income to realize these assets, a full valuation has been established to offset the net deferred tax asset. Additionally, the future utilization of the Company s NOL and R&D Credit carryforwards to offset future taxable income may be subject to an annual limitation as a result of ownership changes pursuant to IRC Sections 382 and 383. For the year ended December 31, 2007, the Company removed the NOL and R&D Credit carryforwards from the deferred tax asset table because the Section 382 and 383 analysis had not been completed. For the year ended December 31, 2008, the Company completed a Section 382 and 383 analysis for the period from inception through December 31, 2008 and determined that, although multiple ownership changes have occurred, the Company will be able to utilize the total NOL and R&D Credit carryforwards that existed as of December 31, 2008, provided it generates sufficient future earnings. Accordingly, the Company re-established the deferred tax assets associated with the NOL and R&D Credit carryforwards and recorded a corresponding increase to the valuation allowance. Future ownership changes under Section 382 and 383 may limit the Company s ability to fully utilize these tax benefits.

Due to the existence of the valuation allowance, future changes in our unrecognized tax benefits will not impact the Company s effective tax rate. The Company is subject to taxation in the U.S. and state jurisdictions. The Company s tax years for 2000 and forward are subject to examination by the U.S. and California tax authorities due to the carryforward of unutilized NOL s and R&D credits. The Company is currently not under examination by any taxing authorities.

The Company s practice is to recognize interest and/or penalties related to income tax matters in income tax expense. During the year ended December 31, 2008, the Company did not recognize any interest or penalties. Upon adoption of FIN No. 48 on January 1, 2007, the Company did not record any interest or penalties.

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Significant components of the Company s deferred tax assets as of December 31, 2008 and 2007 are shown below (in thousands). A valuation allowance of $81.5 million and $11.7 million has been established at December 31, 2008 and 2007 respectively, to offset the net deferred tax assets as realization is uncertain.

	December 31,	
	2008	2007
Deferred tax assets:		
Capitalized R&D	$ 32,904	$ 8,654
Deferred revenue	3,321	538
Net operating loss carryforwards	33,287	
Research and development credits	9,472	
Other, net	2,532	2,498
Total deferred tax assets	81,516	11,690
Deferred tax liabilities:		
Deferred compensation		9
Valuation allowance for deferred tax assets	(81,516)	(11,699)
Net deferred assets	$	$

At December 31, 2008, the Company had federal and California NOL carryforwards of $82.5 million and $79.4 million, respectively, which begin to expire in 2019 and 2011, respectively, unless previously utilized, and federal and state R&D Credit carryforwards of $6.0 million and $5.2 million, respectively. The federal R&D Credit carryforwards begin to expire in 2019 and the state R&D Credit carryforwards do not expire. Pursuant to IRC Sections 382 and 383, use of our NOL and R&D credit carry forwards may be limited because of a cumulative change in ownership of more than 50%, which may occur in the future. The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2008, 2007 and 2006, due to the following (in thousands):

	2008	2007	2006
Federal income taxes at 35%	$ (14,810)	$ (14,630)	$ (11,644)
State income tax, net of Federal benefit	(2,172)	(2,156)	(1,751)
Tax effect on non-deductible expenses and credits	(276)	1,195	(305)
Increase in valuation allowance(1)	17,258	15,591	13,700
	$	$	$

(1) The removal and re-establishment of the valuation allowance related to the NOL s and R&D credits is not included in the increase in the valuation allowance. See above for explanation.

12. 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 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. In 2007, the Board of Directors authorized a matching contribution up to 25% of employee contributions, subject to certain limitations, totaling approximately $330,000 and $255,000 for the years ended December 31, 2008 and 2007, respectively. Plan administration costs totaled $6,525, $6,875 and $6,850 for the years ended December 31, 2008, 2007 and 2006, respectively.

13. Related Party Transactions

In April 2008, the Company raised $9.9 million in cash through the Transaction, as described in Note 10. Certain of the Company s existing stockholders, including entities affiliated with MPM Capital, Hale BioPharma

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Ventures and InterWest Partners, invested in the Transaction. Certain of such investors and/or their affiliates are parties to the Company s amended and restated investors rights agreement dated October 28, 2003. Luke B. Evnin, Ph.D., David F. Hale and Arnold L. Oronsky, Ph.D., members of the Company s board of directors, are associated with MPM Capital, Hale BioPharma Ventures and InterWest Partners, respectively. See Note 10 for further information.

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 spin-off from Sicor, 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 spin-off from Sicor 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.

14. Subsequent Events

Offer to Exchange Stock Options

On January 29, 2009, the Company completed an Offer to Exchange certain outstanding options to purchase shares of the Company s common stock, that were originally granted under the Company s Equity Incentive Plan and that had an exercise price that is equal to or greater than $1.50 per share, for replacement options to purchase shares of the Company s common stock (the Offer). Eligible option holders included employees and scientific advisory board members. Subject to the participant s continued service with the Company, 25% of the shares underlying the replacement options will vest six months after the date the replacement options are granted and the remaining 75% of the shares will vest in equal monthly installments beginning on the date of grant of the replacement options so that the replacement options will be vested in full three years from the grant date of the replacement options.

Upon expiration of the Offer, the Company accepted elections to replace eligible stock options to purchase 1,831,887 shares of common stock, representing 64.3% of the shares subject to options that were eligible to be exchanged in the Offer. As a result, options to purchase 1,831,887 shares of common stock were immediately granted to the participants at an exercise price of $1.00 per share, in accordance with the terms of the Offer. The closing sales price of the Company s common stock on January 29, 2009 was $0.47 per share.

Restructuring Plan

On January 15, 2009, the Company committed to a restructuring plan that will result in the reduction of approximately 43% of the Company s workforce as of that date. In connection with the restructuring plan, the Company will focus on its clinical-stage product candidate, MB07811 for the treatment of hyperlipidemia , as well as on advancing its glucagon antagonist program and its second-generation TRß agonist program. Employees directly affected by the restructuring plan have received notification and will be provided with severance payments, continued benefits for a specified period of time and outplacement assistance. The Company expects to complete the restructuring plan by the end of the second quarter of 2009.

The Company anticipates incurring restructuring charges of approximately $1.4 million, primarily associated with personnel-related termination costs. The majority of these costs will be recognized during the first quarter of 2009.

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The severance-related charge that the Company expects to incur in connection with the restructuring is subject to a number of assumptions, and actual results may materially differ. The Company may also incur other material charges not currently contemplated due to events that may occur as a result of, or associated with, the restructuring plan.

15. Summary of Quarterly Financial Data (Unaudited)

The following is a summary of the quarterly results of operations for the years ended December 31, 2008 and 2007 (in thousands, except for net loss per share data):

	Quarters Ended				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Year Ended Dec 31(1)
2008					
Revenue	$ 942	$ 687	$ 1,402	$ 1,779	$ 4,810
Research and development	9,745	9,667	8,480	8,464	36,356
General and administrative	2,519	2,569	2,659	3,004	10,751
Total operating expenses	12,264	12,236	11,139	11,468	47,107
Net loss	(11,100)	(11,542)	(9,834)	(9,838)	(42,314)
Basic and diluted net loss per share:	$ (0.36)	$ (0.34)	$ (0.28)	$ (0.28)	$ (1.25)
2007					
Revenue	$ 3,426	$ 1,604	$ 2,653	$ 1,336	$ 9,019
Research and development	9,506	11,065	10,866	9,478	40,915
General and administrative	3,264	3,186	2,834	3,158	12,442
Total operating expenses	12,770	14,251	13,700	12,636	53,357
Net loss	(8,505)	(11,935)	(10,480)	(10,879)	(41,799)
Basic and diluted net loss per share:	$ (0.28)	$ (0.40)	$ (0.34)	$ (0.35)	$ (1.37)

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