METABASIS THERAPEUTICS INC
Form 424B3
December 22, 2006

Pursuant to Rule 424(b)(3)
File No. 333-138720

The information in this prospectus is not complete and may be changed. The selling stockholder may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

PROSPECTUS

6,046,471 Shares of Common Stock

This prospectus relates to the resale from time to time of up to 6,046,471 shares of our common stock that we may issue to the selling stockholder listed in the section entitled Selling Stockholder on page 30 of this prospectus. The shares of common stock offered under this prospectus by the selling stockholder are issuable to Kingsbridge Capital Limited, or Kingsbridge, pursuant to a common stock purchase agreement between us and Kingsbridge dated November 2, 2006, and a warrant we issued to Kingsbridge on that date. We are not selling any shares under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholder.

The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section entitled Plan of Distribution on page 31 of this prospectus. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is currently traded on the Nasdaq Global Market under the symbol MBRX . On December 21, 2006, the last reported sales price for our common stock was $7.45 per share.

Investment in our common stock involves a high degree of risk.

See the section entitled Risk Factors on page 5 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 22, 2006

TABLE OF CONTENTS

You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. We have not, and the selling stockholder has not, authorized anyone to provide you with different information. The selling stockholder is not making an offer of the common stock to be sold under this prospectus in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus or any applicable prospectus supplement is accurate as of any date other than the date on the front cover of this prospectus or the prospectus supplement, or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of our common stock.

PROSPECTUS SUMMARY

This prospectus contains forward-looking statements which involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors referred to in Risk Factors and elsewhere in this prospectus.

The following summary does not contain all the information that may be important to you. You should read the entire prospectus, including the financial statements and other information incorporated by reference in this prospectus, before making an investment decision.

Metabasis Therapeutics, Inc.

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

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

Product Candidate	**Disease Indication**
pradefovir	hepatitis B
CS-917	type 2 diabetes
MB07133	primary liver cancer
MB07803	type 2 diabetes
MB07811	hyperlipidemia

Our agreements with collaborators may include joint marketing or promotion arrangements of our products. For example, we have retained co-promotion rights for CS-917 in North America with Daiichi Sankyo, Co. Ltd. Alternatively, we may grant exclusive marketing rights to our collaborators in exchange for up-front fees, milestones and royalties on future sales, if any. We have licensed worldwide commercialization rights for pradefovir to Valeant Pharmaceuticals International, which recently assigned those rights to Schering Corporation subject to customary closing conditions, including the expiration or early termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or the HSR Act, applicable to the transaction. We have retained rights to MB07133, MB07803, MB07811 and all of the compounds generated from our current research programs, with the exception of product candidates covered by our collaborations with Merck & Co., Inc. and Idenix Pharmaceuticals, Inc. We intend to eventually market one or more of the product candidates for which we retain commercialization rights through our own sales force or with a co-promotion partner in the U.S. and through strategic collaborations abroad.

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

Our principal offices are located at 11119 North Torrey Pines Road, La Jolla, California 92037, and our telephone number is (858) 587-2770. Our website address is http://www.mbasis.com. The information contained in, or that can be accessed through, our website is not part of this prospectus. Unless the context indicates otherwise, as used in this prospectus, the terms Metabasis, we, us and our refer to Metabasis Therapeutics, Inc., a Delaware corporation, and the terms selling stockholder and Kingsbridge refer to Kingsbridge Capital Limited. We use Metabasis, NuMimetic and HepDirect as trademarks in the U.S. and other countries. This prospectus also contains trademarks and tradenames of other companies.

1

Equity Financing Facility With Kingsbridge

On November 2, 2006, we entered into a committed equity financing facility, or CEFF, with Kingsbridge, pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to $50.0 million of our common stock. In connection with the CEFF, we entered into a common stock purchase agreement and registration rights agreement with Kingsbridge, both dated November 2, 2006, and on that date we also issued a warrant to Kingsbridge to purchase 260,000 shares of our common stock at an exercise price of $9.26 per share. This warrant is exercisable beginning on May 2, 2007 and for a period of five years thereafter, subject to earlier termination in specified circumstances.

The common stock purchase agreement entitles us to sell and obligates Kingsbridge to purchase, from time to time over the 36-month period described below, shares of our common stock for cash consideration up to an aggregate of $50.0 million, subject to specified conditions and restrictions. The shares of common stock that may be issued to Kingsbridge under the common stock purchase agreement and the warrant will be issued pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act. Pursuant to the registration rights agreement, we have filed a registration statement of which this prospectus is a part, covering the possible resale by Kingsbridge of any shares that we may issue to Kingsbridge under the common stock purchase agreement or upon exercise of the warrant. Through this prospectus, the selling stockholder may from time to time offer to the public for resale shares of our common stock that we may issue to Kingsbridge pursuant to the common stock purchase agreement, or that Kingsbridge may acquire upon exercise of the warrant.

For a period of 36 months from the first trading day following the effectiveness of the registration statement of which this prospectus is a part, we may, from time to time, at our discretion, and subject to specified conditions that we must satisfy, draw down funds under the CEFF by selling shares of our common stock to Kingsbridge. The purchase price of these shares will be at a discount of up to ten percent from the volume weighted average price of our common stock for each of the eight trading days following our election to sell shares, or draw down under the CEFF. The discount on each of these eight trading days will be determined as follows:

VWAP*	PERCENT OF VWAP	(APPLICABLE DISCOUNT)
Greater than $9.50 per share	94 %	(6)%
Greater than $5.75 per share but less than or equal to $9.50 per share	92 %	(8)%
Equal to or greater than $2.25 per share but less than or equal to $5.75 per share	90 %	(10)%

* As set forth in the common stock purchase agreement, VWAP means the volume weighted average price (the aggregate sales price of all trades of our common stock during each trading day divided by the total number of shares of common stock traded during that trading day) of our common stock during any trading day as reported by Bloomberg, L.P. using the AQR function. Except as described below, the VWAP and corresponding discount will be determined for each of the eight trading days during a draw down pricing period.

During the eight trading day pricing period for a draw down, if the VWAP for any one trading day is less than the greater of (i) $2.25 or (ii) 90% of the closing price of our common stock on the trading day immediately preceding the beginning of the draw down period, the VWAP for that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one-eighth of the draw down amount initially specified. In addition, if trading in our common stock is suspended for any reason for more than three consecutive or non-consecutive hours during any trading day during a draw down pricing period, that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one-eighth of the draw down amount initially specified.

The maximum number of shares of common stock that we can issue pursuant to the CEFF is 6,046,471 shares, including 260,000 shares of common stock issuable upon exercise of the warrant that we issued to Kingsbridge in

connection with Kingsbridge s entry into the CEFF. We may exercise our right to draw down amounts under the CEFF, if and to the extent available, at such times as we have a need for additional capital and when we believe that sales of stock under the CEFF provide an appropriate means of raising capital.

Our ability to require Kingsbridge to purchase our common stock is subject to various limitations. The maximum dollar amount of shares that we may require Kingsbridge to purchase in any draw down pricing period under the CEFF is equal to the lesser of $10 million or a specified percentage of our market capitalization at the time of a draw down under the CEFF. The specified percentage will be 1.5% if our market capitalization is equal to or exceeds $175 million, 1% if our market capitalization is equal to or exceeds $100 million but is less than $175 million, or 0.75% if our market capitalization is equal to or exceeds $65 million but is less than $100 million.

Unless we and Kingsbridge agree otherwise, a minimum of three trading days must elapse between the expiration of any draw down pricing period and the beginning of the next succeeding draw down pricing period.

During the term of the CEFF, without the prior written consent of Kingsbridge, we may not (i) issue any rights, warrants or options to subscribe for or purchase our common stock, or any other securities directly or indirectly convertible into or exchangeable or exercisable into shares of our common stock, at an effective conversion, exchange or exercise price that varies or may vary with or is otherwise issuable in relation to the market price of our common stock, including by way of one or more resets to any fixed price; (ii) make any at-the-market offering (as defined in Rule 415(a)(4) under the Securities Act or any successor rule thereto) of our securities; and (iii) enter into any equity line or other form of financing that is substantially similar to the arrangement provided for in the CEFF. Except for the foregoing restrictions, the CEFF does not prohibit us from conducting additional debt or equity financings, other than during the eight trading day pricing period for a draw down. For the avoidance of confusion, except during the eight trading day pricing period for a draw down, the CEFF does not prohibit us from undertaking (i) a customary, firm-commitment underwritten public offering of our securities or (ii) a registered direct public offering or an unregistered private placement of our securities where the price per share of such securities is fixed concurrently with the execution of definitive documentation relating to the offering or placement, as applicable.

The issuance of our common stock under the CEFF or upon exercise of the Kingsbridge warrant will have no effect on the rights or privileges of existing holders of common stock except that the voting interests and potentially the economic interests of existing stockholders will be diluted as a result of the issuance. Although the number of shares of common stock that stockholders presently own will not decrease, these shares will represent a smaller percentage of our total shares that will be outstanding after any issuances of shares of common stock to Kingsbridge. If we draw down amounts under the CEFF when our stock price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Such issuances will have a dilutive effect and may further decrease our stock price.

Kingsbridge agreed in the common stock purchase agreement that during the term of the CEFF, neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will enter into or execute, or cause any person or entity to enter into or execute, any short sale of any shares of our common stock.

Before Kingsbridge is obligated to buy any shares of our common stock pursuant to a draw down, the following conditions, none of which is in the control of Kingsbridge, must be met as of the draw down exercise date and the date upon which each settlement of the purchase and sale of our common stock occurs:

- Each of our representations and warranties in the common stock purchase agreement must be true and correct in all material respects as of the date when made as though made at that time, except for representations and warranties that are expressly made as of a particular date.

- We must have performed, satisfied and complied in all material respects with all covenants, agreements and conditions required by the common stock purchase agreement, the registration rights agreement and the warrant to be performed, satisfied or complied with by us.

- We must have complied in all respects with all applicable federal, state and local governmental laws, rules, regulations and ordinances in connection with the execution, delivery and performance of the common stock purchase agreement and the consummation of the transactions contemplated by it, except for any noncompliance that generally would not have a material adverse effect on our business.

- The registration statement, which includes this prospectus, shall have previously become effective and shall remain effective, and neither we nor Kingsbridge shall have received notice that the Securities and Exchange Commission, or SEC, has issued or intends to issue a stop order with respect to the registration statement or otherwise has suspended or withdrawn its effectiveness or intends or has threatened to do so, and no other suspension of the use of or withdrawal of the effectiveness of the registration statement or this prospectus shall exist.

- We shall not have knowledge of any event that could reasonably be expected to have the effect of causing the registration statement applicable to the resale of shares of our common stock by Kingsbridge to be suspended or otherwise ineffective.

- Trading in our common stock shall not have been suspended by the SEC, the Nasdaq Global Market or the National Association of Securities Dealers and trading in securities generally on the Nasdaq Global Market shall not have been suspended or limited.

- No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority which prohibits the consummation of any of the transactions contemplated by the common stock purchase agreement.

- No action, suit or proceeding before any arbitrator or any governmental authority shall have been commenced, and no investigation by any governmental authority shall have been threatened, against us or any of our officers, directors or affiliates seeking to enjoin, prevent or change the transactions contemplated by the common stock purchase agreement.

- We shall have sufficient shares of common stock, calculated using the closing price of our common stock as of the trading day immediately preceding a draw down, registered under the registration statement to issue and sell such shares in accordance with such draw down.

- We shall not be in default in any material respect under the warrant to purchase 260,000 shares of our common stock issued to Kingsbridge in connection with the CEFF.

There is no guarantee that we will be able to meet the foregoing conditions or any other conditions under the common stock purchase agreement or that we will be able to draw down any portion of the amounts available under the CEFF.

Pursuant to our registration rights agreement with Kingsbridge, we have filed a registration statement, which includes this prospectus, with the SEC relating to the resale by Kingsbridge of any shares of common stock purchased by Kingsbridge under the common stock purchase agreement or issued to Kingsbridge as a result of the exercise of the Kingsbridge warrant. As described more fully above, the effectiveness of this registration statement is a condition precedent to our ability to sell common stock to Kingsbridge under the common stock purchase agreement. We are entitled in certain circumstances, including the existence of certain kinds of nonpublic information, to deliver a blackout notice to Kingsbridge to suspend the use of this prospectus and prohibit Kingsbridge from selling shares under this prospectus. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement of which this prospectus is a part is not effective in circumstances not permitted by the registration rights agreement, then we must pay specified amounts to Kingsbridge (or issue Kingsbridge additional shares in lieu of payment) as liquidated damages.

The foregoing summary of the CEFF does not purport to be complete and is qualified by reference to the common stock purchase agreement, the registration rights agreement and the warrant, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risk factors described below, as well as in our subsequent filings with the SEC. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

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 five current product candidates, pradefovir, CS-917, MB07133, MB07803, and MB07811. Clinical trials conducted to date in patients treated with pradefovir have provided evidence of efficacy as measured by various parameters that we believe to be clinically and statistically significant. However, no pivotal, adequate and well-controlled clinical trials designed to provide clinical and statistically significant proof of efficacy, or to provide sufficient evidence of safety to justify approval, have been completed with any of our products. All of our product candidates will require additional development, clinical trials and regulatory clearances before they can be commercialized. Positive results from preclinical studies and early clinical trials do not necessarily mean later clinical trials will succeed. Our product development efforts may not lead to commercial drugs, either because our product candidates fail to be safe and effective in clinical trials or because we have inadequate financial or other resources to pursue our product candidates through the clinical trial and approval processes. If any of our product candidates fail to demonstrate safety or efficacy at any time or during any phase of development, we would experience potentially significant delays in, or be required to abandon, development of the product candidate.

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

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

To receive regulatory approval for the commercialization of pradefovir, CS-917, MB07133, MB07803, MB07811 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 U.S. Food and Drug Administration, or FDA, in the U.S. and other regulatory agencies elsewhere in the world. In order to support marketing approval, these agencies typically require successful results in one or more Phase 3 clinical trials, which our current product candidates have not yet reached and may never reach. Clinical testing is expensive, can take many years and has an uncertain outcome. Failure can occur at any stage of the testing. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent commercialization of our current or future product candidates, including the following:

- clinical trials may produce negative or inconclusive results,
- patient recruitment and enrollment in clinical trials may be slower than we anticipate,
- costs of clinical trials may be greater than we anticipate,

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

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

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

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

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

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

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

For example, the inhibition of gluconeogenesis can cause elevated levels of lactic acid, or lactate, which, if high and sustained under certain conditions, could lead to lactic acidosis, a serious and potentially fatal condition. Certain preclinical animal studies have shown that CS-917 raises lactate levels two- to three-fold in some but not all animal models. Elevated lactate levels have also been observed in certain human clinical trials of CS-917. For example, in a 28-day Phase 2 clinical trial of CS-917, isolated instances of lactate elevation significantly above the normal range were seen in some patients in both CS-917 and placebo treated groups over the course of the 28 days. No patient exhibited sustained lactate levels significantly above the normal range over a period of consecutive days during the clinical trial. However, one patient who received 200 milligrams of CS-917 twice a day was withdrawn from the clinical trial by the investigator on day 15 due to concerns over consistently elevated lactate levels measured the previous day. Other incidences of elevated lactate levels have been observed and will likely occur in the future.

Our product candidates could also exhibit adverse interactions with other drugs. For instance, in March 2005, we were notified by Daiichi Sankyo that two serious adverse events involving lactic acidosis had occurred in two patients in a Phase 1 clinical trial evaluating the interaction of CS-917 with metformin. The serious adverse events were resolved after medical intervention. The two patients were administered CS-917 in combination with metformin. At high blood levels, metformin is believed to cause mitochondrial toxicity, a cellular toxicity, which can cause lactic acidosis. These dangerous levels are known to occur in patients with significant renal dysfunction who are inappropriately given metformin. Consequently, metformin is contraindicated for use in patients with significant renal dysfunction. After the adverse events occurred, three clinical trials that were ongoing

at the time were stopped while one Phase 1 clinical trial which did not combine CS-917 with metformin continued and was completed. It was subsequently determined that the two patients who experienced the lactic acidosis had blood levels of metformin that were elevated compared to other patients in the clinical trial who received metformin before administration of CS-917. After CS-917 administration, when the two patients were being administered metformin and CS-917, the metformin blood levels increased significantly into a range that is associated with mitochondrial toxicity and subsequent lactic acidosis. CS-917 blood levels also rose higher than expected.

The reason for the unexpectedly high blood levels of both drugs in these two patients is unknown at this time. In July 2005, after completing a comprehensive review of the program and the events and data surrounding the two serious adverse events, we and Daiichi Sankyo concluded that the lactic acidosis observed in the two patients was likely due to the significantly increased blood levels of metformin described above which in turn likely led to mitochondrial toxicity. Subsequently, Daiichi Sankyo decided that Phase 2b clinical trials of CS-917 could safely resume. In February 2006, after submission of the proposed clinical trial protocol to the FDA and approval by institutional review boards, or IRBs, a Phase 2b clinical trial of CS-917 was initiated. This Phase 2b clinical trial provides for measurement of HbA1c, the endpoint generally required for approval of diabetes product candidates by regulatory agencies. Daiichi Sankyo has conducted and will likely conduct additional studies combining CS-917 with other diabetes drugs to assess both the safety and eventually the potential for enhanced efficacy with the combination. However, further use of CS-917 in combination with metformin will be avoided unless additional data suggests that the elevation of metformin blood levels as seen in the two patients can be avoided through patient exclusion or through the administration of CS-917 at lower doses or through other means. Should CS-917 eventually be approved and the use of CS-917 in combination with metformin remains an issue, the FDA may require additional measures be taken during marketing, such as prominent warning labels known as black-box warnings, physician education programs and/or other steps regarding concomitant use of CS-917 and metformin.

In February 2006, we initiated Phase 1 clinical trials of our second-generation product candidate for diabetes, MB07803, which works by the same mechanism as CS-917.

It is also possible that CS-917 and MB07803 may cause other side effects. In certain preclinical studies, as expected based on the mechanism of these compounds, fasted animals treated with CS-917 showed pronounced hypoglycemia, a condition involving abnormally low blood glucose levels that can lead to coma or death. Hypoglycemia has been observed in one patient participating in a clinical trial that involved multi-day administration of the highest dose of CS-917 tested to date in patients (400 milligrams twice a day). This dose is above what is expected to be used in Phase 3 clinical trials if warranted. However, we cannot yet rule out the possibility that CS-917 may increase a patient s susceptibility to hypoglycemia, including the potential for severe hypoglycemia, by inhibiting gluconeogenesis, especially in elderly patients who are already prone to develop this condition. Some rodent models of diabetes studied in preclinical trials of CS-917 demonstrated, at glucose lowering doses, increased levels of fat molecules known as triglycerides, which are associated with an increased risk of cardiovascular disease. Elevated triglyceride levels have not been observed in human clinical trials to date. Other side effects observed during early clinical trials of CS-917 included nausea and vomiting.

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

MB07811 is a HepDirect prodrug of a potent liver-selective thyroid hormone receptor modulator (a mimetic) discovered by us. Thyroid hormone and thyroid hormone mimetics are known to exhibit a wide array of physiological actions involving a variety of organs that can be assessed in pre-clinical animal studies. Both beneficial and undesirable effects can be inferred from studies of humans with hyperthyroidism (elevated thyroid hormone). The development of liver-selective thyroid receptor modulators for the treatment of hyperlipidemia is a novel approach seeking to exploit the beneficial hepatic effects while avoiding toxicities related

to systemic exposure of thyromimetic agents. Successful development of MB07811 will require finding a dose range in humans that provides adequate benefit and an acceptable safety profile, that is known as an acceptable Therapeutic Index.

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

- we may be unable to obtain additional financing on acceptable terms, if at all,
- our stock price could decline,
- our collaborators may ultimately terminate development of our partnered products, may further decide not to develop backup product candidates and may terminate our agreements,
- if these agreements were terminated we may determine not to further develop the affected product candidates due to resource constraints and may not be able to establish additional collaborations for their further development on acceptable terms, if at all,
- if we were to later continue the clinical trials of these product candidates and receive regulatory approval, earlier findings may significantly limit their marketability and thus significantly lower our potential future revenues from their sale,
- we may be subject to product liability or stockholder litigation, and
- we may be unable to attract and retain key employees.

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

- regulatory authorities may withdraw their approval of the product, or we may decide to cease marketing and sale of the product voluntarily,
- we may be required to change the way the product is administered, conduct additional clinical trials, change the labeling of the product, or change the product s manufacturing facilities, and
- our reputation may suffer.

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

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

We have entered into collaborations with Valeant and Daiichi Sankyo for the development and commercialization of pradefovir and CS-917, respectively. Valeant and Daiichi Sankyo have agreed to finance the clinical trials for pradefovir and CS-917, respectively, and, if they are approved, manufacture and market them. In December 2006, Valeant assigned its rights to pradefovir to Schering Corporation subject to customary closing conditions, including the expiration or early termination of the waiting period under the HSR Act applicable to the transaction. Accordingly, we are currently dependent on Valeant and Daiichi Sankyo to gain FDA and other foreign regulatory agency approval of, and to commercialize, pradefovir and CS-917, and will be similarly dependent on Schering following the completion of the assignment described above. We have also entered into two collaborations with Merck and a collaboration with Idenix. The first collaboration with Merck seeks to develop and commercialize new products for the treatment of hepatitis C infection and the second seeks to develop and commercialize new products to treat

8

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

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

Our agreement with Daiichi Sankyo contains certain rights and restrictions regarding our access to and use of confidential data and information generated by Daiichi Sankyo. We have initiated Phase 1 clinical trials of MB07803, a second-generation gluconeogenesis inhibitor to which Daiichi Sankyo has no rights and that may be a direct competitor to CS-917. Because of this competitive situation and with our consent, the transfer to us of confidential information and data related to CS-917 from Daiichi Sankyo has already been reduced and we expect that further reductions in information flow will occur. This situation may limit our ability to (i) provide information regarding clinical results unless they are publicly released by Daiichi Sankyo, (ii) influence decisions made at Daiichi Sankyo regarding CS-917 and (iii) accurately track Daiichi Sankyo s diligence on the development program.

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

- we do not achieve our objectives under our collaboration agreements,
- we are unable to obtain patent protection for the product candidates or proprietary technologies we discover in our collaborations,
- we are unable to manage multiple simultaneous product discovery and development collaborations,
- our potential collaborators are less willing to expend their resources on our programs due to their focus on other programs or as a result of general market conditions,
- our collaborators become competitors of ours or enter into agreements with our competitors,
- we or our collaborators encounter regulatory hurdles that prevent commercialization of our product candidates,
- we develop products and processes or enter into additional collaborations that conflict with the business objectives of our other collaborators,

- consolidation in our target markets limits the number of potential collaborators, or
- we are unable to negotiate additional collaboration agreements under terms satisfactory to us.

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

The assignment of Valeant s rights to pradefovir to Schering may not occur as currently anticipated.

In December 2006, Valeant assigned its rights to pradefovir to Schering Corporation, subject to customary closing conditions, including the expiration or early termination of the waiting period under the HSR Act applicable to the transaction. We have no control over when, if at all, the closing conditions will be satisfied and the assignment completed. If the assignment is significantly delayed or does not occur as currently anticipated, the future development of pradefovir may be adversely impacted and our business results may be harmed.

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

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

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

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

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

- unwillingness on the part of a collaborator to pay us research funding, milestone payments or royalties we believe are due to us under our collaboration agreement,
- uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations, or disagreements with our collaborators regarding the protection of intellectual property rights,

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

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

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

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

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

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

- delays in obtaining regulatory approval to commence a clinical trial,

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

- delays in manufacturing sufficient quantities of a product candidate or other materials necessary to conduct the clinical trial,

- delays in obtaining institutional review board approval to conduct a clinical trial at a prospective site,

- delays in recruiting and enrolling patients to participate in a clinical trial, and

- the failure of our collaborators to adequately resource our product candidates due to their focus on other programs or as a result of general market conditions.

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

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

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

- unforeseen safety issues, or
- lack of adequate funding to continue the clinical trial.

If we experience significant delays in the commencement or completion of clinical testing, our product development costs may increase, we may lose any competitive advantage associated with early market entry and our ability to generate significant revenues may be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

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

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

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

We used our HepDirect technology to discover pradefovir, MB07133, MB07811 and applied this technology in certain other programs as well. We used our NuMimetic technology to identify CS-917 and MB07803. We intend to use these and future proprietary technologies to expand our product pipeline in the future. We also may leverage our HepDirect and other liver-targeting technology through strategic alliances and collaborations with other companies, such as our hepatitis C collaborations with Merck and Idenix in which we are applying our technology to certain Merck and Idenix compounds. Our proprietary technologies are subject to many of the same risks as our product candidates, including risks related to:

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

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

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

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

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

- a product candidate may not be safe and effective,
- FDA or other foreign regulatory agency officials may not find the data from preclinical testing and clinical trials sufficient,
- the FDA or other foreign regulatory agency may not approve of our third-party manufacturers processes or facilities, or
- the FDA or other foreign regulatory agency may change its approval policies or adopt new regulations.

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

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

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

- issue warning letters or other notices of possible violations,
- impose civil or criminal penalties or seek disgorgement of revenue or profits,
- suspend regulatory approval,
- suspend any ongoing clinical trials,

- refuse to approve pending applications or supplements to approved applications filed by us or our collaborators,
- impose restrictions on operations, including costly new manufacturing requirements, or
- seize or detain products or require a product recall.

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

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

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

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

We are aware of many competitive products currently marketed or under development that are used to treat some of the diseases we have targeted. If CS-917 and/or MB07803 are ultimately determined