METABASIS THERAPEUTICS INC
Form S-3
May 09, 2008

**As filed with the Securities and Exchange Commission on May 9, 2008**

**Registration No. 333-**

# UNITED STATES

# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

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# FORM S-3

**REGISTRATION STATEMENT**

**UNDER**

**THE SECURITIES ACT OF 1933**

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# METABASIS THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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| **Delaware** | **33-0753322** |
| --- | --- |
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification Number) |

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**11119 North Torrey Pines Road**

**La Jolla, CA 92037**

**(858) 587-2770**

(Address, including zip code, and telephone number, including

area code, of registrant s principal executive offices)

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**Paul K. Laikind, Ph.D.**

**President and Chief Executive Officer**

**Metabasis Therapeutics, Inc.**

**11119 North Torrey Pines Road**

**La Jolla, CA 92037**

**(858) 587-2770**

(Name, address, including zip code, and telephone number, including

area code, of agent for service)

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**Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

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 o | Accelerated filer x |
| Non-accelerated filer o<br>(Do not check if a smaller reporting company) | Smaller reporting company o |

**CALCULATION OF REGISTRATION FEE**

| Title of each class of securities to be registered | Amount to be registered (1) | Proposed maximum offering price per share (2) | Proposed maximum aggregate offering price (2) | Amount of registration fee (3) |
|---|---|---|---|---|
| Common Stock, $0.001 par value per share | 4,170,939 shares | $ 2.31 | $ 9,634,869.09 | $ 379 |
| Common Stock, $0.001 par value per share, issuable upon the exercise of warrants | 1,057,196 shares | $ 2.31 | $ 2,442,122.76 | $ 96 |

| | | | | |
|---|---|---|---|---|
| Total | 5,228,135 shares | $ 2.31 | $ 12,076,991.85 | $ 475 |

(1) Based upon the estimated maximum number of shares of common stock that may be sold by the selling stockholders. Pursuant to Rule 416(a) under the Securities Act this registration statement also registers such additional shares of the registrant s common stock as may hereafter be offered or issued to prevent dilution resulting from stock splits, stock dividends, recapitalizations or certain other capital adjustments.

(2) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(c) of the Securities Act. The price per share and aggregate offering price are based upon the average of the high and low sales prices of the Registrant s common stock on May 6, 2008, as reported on the Nasdaq Stock Market.

(3) Calculated by multiplying $39.30 by the proposed maximum aggregate offering price.

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**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

**The information in this prospectus is not complete and may be changed. The selling stockholders may not sell the securities under this prospectus until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the registrant is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.**

**SUBJECT TO COMPLETION, DATED MAY 9, 2008**

**PRELIMINARY PROSPECTUS**

**5,228,135 Shares**

**Common Stock**

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This prospectus relates to the offer and sale, from time to time, of up to 5,228,135 shares of Metabasis Therapeutics, Inc. common stock held by the selling stockholders listed on page 28 of this prospectus, including common stock issuable upon exercise of warrants. The selling stockholders purchased the common stock and warrants to purchase common stock from us in our April 2008 warrant exchange and concurrent private placement. We will not receive any proceeds from the sale of the shares by the selling stockholders.

For a description of the plan of distribution of the shares, see page 32 of this prospectus.

Our common stock is listed on the Nasdaq Stock Market under the symbol MBRX. On May 8, 2008, the last reported sale price for our common stock was $2.09 per share.

**Our business and an investment in our common stock involve significant risks. These risks are described under the caption Risk Factors beginning on page 3 of this prospectus.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2008.

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**You should rely only on the information contained or incorporated by reference in this prospectus and any applicable prospectus supplement. We have not, and the selling stockholders have not, authorized anyone to provide you with additional information or information different from that contained or incorporated by reference in this prospectus and any applicable prospectus supplement. The selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted.**

**The information contained in this prospectus is accurate only as of the date of this prospectus and information appearing in any applicable prospectus supplement is accurate only as of the date of the applicable prospectus supplement. Additionally, information from other documents incorporated by reference in this prospectus or any applicable prospectus supplement is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of the prospectus or prospectus supplement 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 appearing under 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 discovering, developing and commercializing novel drugs by applying our proprietary technologies, scientific expertise and unique capabilities for targeting the liver and liver pathways. We have established a broad pipeline of product candidates and advanced research programs targeting large markets with significant unmet needs. Our product pipeline includes product candidates and advanced research 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 research 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 technologies.

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

Under our strategic plan we will focus our internal resources primarily on our clinical and advanced research core metabolic disease programs. This includes funding the further clinical evaluation of our core assets, MB07803 and MB07811, with a focus on achieving key milestones. Continued development of these core assets thereafter will require significant resources. Therefore, we plan to establish strategic collaborations for these core assets at appropriate times to secure additional resources, accelerate progress and share risk. In addition, we plan to advance additional metabolic disease product candidates discovered by our research group into clinical development either independently, or potentially with current or future strategic collaborators.

In order to reduce future expenses and to minimize the potential dilution associated with financing internal development, we intend to license pradefovir and MB07133 for further development and commercialization.

We currently do not have strategic collaborations in place related to our core assets, MB07803 or MB07811, and we intend to license our non-core assets, pradefovir and MB07133. We retain worldwide commercialization rights to all of the compounds that we have generated from our past and current research programs, with the exception of any potential future product candidates covered by our collaborations with Merck & Co., Inc., or Merck, and Idenix Pharmaceuticals, Inc., or Idenix. 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 exclusive marketing rights to our collaborators in exchange for up-front fees, milestones and royalties on future sales, if any.

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, CA 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. 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.

## RISK FACTORS

*You should consider carefully the following information about the risks described below, together with the other information contained or incorporated by reference in this prospectus and in our other filings with the Securities and Exchange Commission, before you decide to invest in our common stock. We believe the risks described below are the risks that are material to us as of the date of this prospectus. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.*

### Risks Related to our Business

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

We have expended significant time, money and effort in the development of our core metabolic disease assets, MB07803 and MB07811, and our non-core liver disease assets, pradefovir and MB07133. Clinical trials conducted to date have provided initial evidence of safety with all of our product candidates and initial evidence of efficacy in certain 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 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, MB07803 and MB07811, 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 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. 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

- 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 collaborative partner on CS-917, that results from a completed Phase 2b 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 March 2008 the FDA released draft guidance regarding clinical trials for product candidates that treat diabetes, which may result in more stringent requirements for the clinical testing and regulatory approval of such product candidates.

We currently do not have strategic collaborations in place for any of our current product candidates. 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 non-core assets, pradefovir and MB07133, and certain metabolic disease advanced research programs 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 all of the potential product candidates that may be based upon our technologies, including MB07803, MB07811, pradefovir and MB07133, and as a component of our strategic plan, we plan to enter into additional collaborative agreements to assist in the development and commercialization of some or all of these product candidates. However, our discussions with potential collaborators may not lead to the establishment of new collaborations on acceptable terms, if at all, or it may take longer than expected to establish new collaborations, leading to development and commercialization delays, 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 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.

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 and was slightly increased at the intermediate dose levels. The low dose levels were considered no-effect dose levels in both studies. As a result of numerous factors which may include these findings, we entered into an agreement with Schering and Valeant Pharmaceuticals North America, or 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 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 significantly increased blood levels of 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. To date, no incidents of lacticemia, lactic acidosis, hypoglycemia or other significant adverse side effects have been observed in clinical trials of MB07803.

The unique nature of our proprietary technologies including HepDirect and NuMimetic 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.

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,

- 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 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 Idenix 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 Idenix, 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 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 type 2 diabetes and potentially other metabolic diseases. Our collaboration with Idenix seeks to develop and commercialize new products for the treatment of hepatitis C infection. Although our collaborations with Merck and Idenix have not yet yielded any product candidates, should they ultimately be successful, we will be dependent on Merck and/or Idenix, as applicable, for further development and commercialization of any resulting product candidates. In October 2007, the sponsored research term of our collaboration agreement with Idenix was ended upon the first anniversary of the agreement in accordance with its terms. While the sponsored research portion of our collaboration with Idenix ended, certain compounds are under evaluation for further development.

We have limited control over the amount and timing of resources that Merck, Idenix 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 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 these product candidates for further development and commercialization.

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 proprietary technologies we discover in our collaborations,

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

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

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

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

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

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

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

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

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

The objective of our hepatitis C collaboration with Merck has been to discover product candidates for the treatment of this disease by applying our technology to certain compounds provided by Merck.

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

Our agreement with Merck to develop and commercialize new products to treat 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. Similarly, our agreement with Idenix to develop and commercialize new products to treat hepatitis C infection may include the development of compounds owned or controlled by Idenix. In October 2007, the sponsored research term of our collaboration agreement with Idenix ended upon the first anniversary of the agreement in accordance with its terms. While the sponsored research portion of our collaboration with Idenix ended, certain compounds are under evaluation for further development. Idenix may not choose to develop the compounds discovered during the research term, should it do so and then decide to terminate 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 Merck, Idenix or any future collaborators, they may act in their self-interest, which may be adverse to our best interests. Any such disagreement between us and a collaborator could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating sufficient revenues to achieve or maintain profitability:

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

- uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations or independently pursuing the development and/or commercialization of product candidates, or disagreements with our collaborators regarding the protection of intellectual property rights,

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

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

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

We intend to use our proprietary technologies and our knowledge and expertise to develop and commercialize novel drugs to address some of the world s most widespread and costly chronic diseases. Our goal is to expand our core metabolic disease clinical development pipeline by

continuing to develop and move additional new drug compounds into clinical development. However, the process of researching and discovering drug compounds is expensive, time-consuming and unpredictable. Data from our current research programs may not support the clinical development of our lead compounds or other compounds from these programs, and we may not identify any additional drug compounds suitable for recommendation for clinical development. Moreover, any drug compounds we recommend for clinical development may not demonstrate, through preclinical testing, indications of safety and potential efficacy, that such drug compounds warrant advancement into clinical trials. Such findings would potentially impede our ability to maintain or expand our clinical development pipeline. Our ability to identify new drug compounds and advance them into clinical development also depends upon our ability to fund our research and development operations, and we cannot be certain that additional funding will be available on acceptable terms, or at all.

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

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

- obtaining regulatory approval to commence a clinical trial,
- reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites,
- manufacturing sufficient quantities of a product candidate or other materials necessary to conduct the clinical trial,
- obtaining institutional review board approval to conduct a clinical trial at a prospective site,
- recruiting and enrolling patients to participate in a clinical trial, and
- the failure of our collaborators to adequately resource our product candidates due to their focus on other programs or as a result of general market conditions.

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

- failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols,
- inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold,

- unforeseen safety issues, or

- lack of adequate funding to continue the clinical trial.

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

***We rely on third parties 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 MB07803 and 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 pradefovir or MB07133 and intend to license these product candidates for further development and commercialization. We may rely on strategic collaborators for the development of our core metabolic disease assets, MB07803 and MB07811, 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 Idenix have not yet yielded product candidates, should they be successful, we will be dependent on Merck and/or Idenix, as applicable, to conduct the development of any

resulting product candidates. If Merck, Idenix 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.

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

We used our NuMimetic technology to identify MB07803. We used our HepDirect technology to discover pradefovir, MB07811 and MB07133, and have applied it in certain other programs as well. We intend to use these and future proprietary technologies to expand our product pipeline in the future. We may also 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 applied 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 and may be influenced by the results of other similar or competitive products. 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.

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 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:

- metformin, which is a member of the biguanide drug class, related to guanidine and currently is the most widely prescribed first line therapy for type 2 diabetes,

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

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

- PPARs, which improve insulin sensitivity by activating certain genes involved in fat synthesis and carbohydrate metabolism,

- incretin mimetics, which lower glucose levels by increasing the levels of certain naturally occurring hormones from the pancreas, including glucagon-like peptide-1, or GLP-1, a peptide that facilitates the response of the pancreas and liver to fluctuations in glucose levels by its action on pancreatic beta and alpha cells. This drug class includes dipeptidyl peptidase IV, or DPP-IV inhibitors, and BYETTA® (exenatide) injection. DPP-IV is an enzyme in the bloodstream that cleaves and inactivates GLP-1. Inhibition of DPP-IV thus increases the half-life of endogenous GLP-1 by preventing cleavage and inactivation of GLP-1. BYETTA is an injectable medication that exhibits many of the same glucose regulating actions of GLP-1. The overall effect of drugs in this class is to enhance glucose-dependent insulin secretion and suppress inappropriate glucagon secretion,

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

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

- combination therapies, which combine metformin with members of several or one of the above-mentioned classes, particularly sulfonylureas and PPARs.

Metformin is a drug that inhibits liver glucose production like MB07803 but does so through an unknown mechanism. Because it does not cause weight gain, metformin is often prescribed as a first line therapy to obese patients with type 2 diabetes, who are reported to comprise more than 90% of patients newly diagnosed with type 2 diabetes. Generic forms of metformin have recently become available. Accordingly, unless MB07803 demonstrates significant benefits when compared to metformin or demonstrates that it can be used in the patient population who do not tolerate and/or adequately respond to metformin treatment, the price required to effectively compete with the generic form of metformin may be so low that it may limit the market s potential or make it uneconomical to market MB07803. In addition, many companies are developing novel therapies that target diabetes. These companies may develop and introduce products competitive with or superior to MB07803.

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. Lipitor (atorvastatin; a statin marketed by Pfizer) 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 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 HBV, 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 HBV.

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

Nexavar (sorafenib), a chemotherapy approved for treating kidney cancer, received FDA approval in November, 2007 for the treatment of primary liver cancer. This follows the European Medicines Agency s, or EMEA, decision in October of the same year to approve Nexavar in the same indication for Europe. Nexavar is now the only drug approved for primary liver cancer in the United States or Europe.

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.

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

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

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

Our ability to develop and commercialize our products depends in part on our ability to manufacture, or arrange for collaborators or other third parties to manufacture, our products at a competitive cost, in accordance with regulatory requirements and in sufficient quantities for development and eventual commercialization. We have relied on a number of suppliers to manufacture sufficient quantities of MB07803 and 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, 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 MB07803 and MB07811, we will rely on our current suppliers to manufacture these compounds. However, we do not have long-term supply agreements with these third parties, and we may not be able to enter into new supply agreements with them in a timely manner or on acceptable terms, if at all. These third parties may also be subject to capacity constraints that would cause them to limit the amount of these compounds that we can purchase. While we believe alternative sources to manufacture these compounds are readily available, in the event we have to seek such alternative sources we will incur costs associated with identifying and qualifying one or more alternate suppliers. In addition, any resulting interruption or delay we experience in the supply of MB07803 or MB07811 may impede the development of these compounds.

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

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

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

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

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

- our ability to provide acceptable evidence of safety and efficacy,
- relative convenience and ease of administration,
- the prevalence and severity of any adverse side effects,
- restrictions on use in combination with other products,
- availability of alternative treatments,

- pricing and cost effectiveness 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,

- 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 will be managed by private health insurers and other managed care organizations, will result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenues. It is also possible that other similar proposals will be adopted.

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

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

Since we became an independent company in 1999, we have increased the number of our full-time employees from 50 to 124 as of March 31, 2008. We may need to decrease the number of our full-time employees in the future in response to adverse business events. Reducing our workforce may lead to additional unanticipated attrition. If our future staffing is inadequate because of additional unanticipated attrition or because we failed to retain the staffing level required to accomplish our business objectives we may be delayed or unable to continue the development or commercialization of our product candidates, which could impede our ability to generate revenues and achieve or maintain 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 commercialization of our product candidates. We employ these individuals on an at-will basis and their employment can be terminated by us or them at any time, for any reason and with or without notice, subject to the terms of their stock restriction agreements and severance agreements.

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

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

scientific advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

**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 or commercialization efforts and affect our ability to continue as a going concern.***

We intend to use our existing cash reserves, proceeds received in April 2008 from our warrant exchange and concurrent private placement, proceeds received in March 2008 from our venture debt facility, proceeds from our ongoing collaboration with Merck, our Committed Equity Financing Facility, or CEFF, and proceeds from other planned financing and business development activities to execute our strategic plan through 2008. Under our strategic plan we will need to secure additional cash proceeds through future strategic collaborations and the CEFF or other financing sources to fund certain studies on the MB07803 and MB07811 programs in 2008. In the event we are not able to generate sufficient financing through the use of our CEFF or other planned financing and business development activities we have the ability and intent to, and will be required to, delay, scale back or eliminate some or all of our research or development programs and other outlays of cash in order to meet our cash requirements through 2008. 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. Alternatively, we may determine that seeking additional resources through traditional financing transactions may be appropriate to achieve certain key value-driving development milestones. No assurances can be made that additional funding through any resources including, our CEFF, will be available when needed. Failure to obtain adequate financing and to curtail or delay cash expenditures adequately will have a significant negative impact on our future operations. 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,
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights,
- the costs and timing of regulatory approvals,

- the costs of establishing or contracting for sales and marketing capabilities, 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 public or private equity offerings, debt financings, grants or corporate collaboration and licensing arrangements, as well as through interest income earned on cash balances.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research and development programs or our commercialization efforts and we may be unable to continue as a going concern.

***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 March 31, 2008, we had an accumulated deficit of approximately $161.1 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.

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

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

- successful completion of ongoing development activities for our product candidates,
- achievement of regulatory approval for our product candidates,
- successful completion of our current and future strategic collaborations, and
- successful sales, manufacturing, distribution and marketing of our products.

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

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

We may raise additional funds through public or private equity offerings, our CEFF, corporate collaboration and licensing arrangements, debt financings or grants. For example, we have an effective shelf registration statement on file with the Securities and Exchange Commission which allow 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 technologies, or grant licenses on terms that are not favorable to us.

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

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.

***Our quarterly operating results and stock price may fluctuate significantly.***

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

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

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

- changes in the use assumptions or the use of different valuation methods in the application of SFAS No. 123R in future periods.

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

***Our 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 we 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. 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 our Intellectual Property**

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

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

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

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

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

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

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

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

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

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

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

- our issued patents may not be valid or enforceable,

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

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

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

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

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

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

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

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

- substantial damages for infringement, including treble damages and attorneys fees, as well as damages for products developed using allegedly infringing drug discovery tools or methods, which we may have to pay if a court

decides that the product or proprietary technology at issue infringes on or violates the third party s rights,

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

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

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

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

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

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

**Risks Related to Other Legal Matters**

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

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

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials, and will face an even greater risk if we sell our product candidates commercially. An individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates,
- injury to our reputation,
- withdrawal of clinical trial participants,
- costs of related litigation,
- substantial monetary awards to patients or other claimants,
- loss of revenues, and

- the inability to commercialize our product candidates.

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

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

Our research and development and manufacturing activities involve the use of biological and hazardous materials. Although we believe our safety procedures for handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot entirely eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of these materials. If one of our employees was accidentally injured from the use, storage, handling or disposal of these materials, the medical costs related to his or her treatment would be covered by our workers compensation insurance policy. While our property and casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination, we do carry separate pollution legal liability coverage that is intended to cover third party claims for bodily injury, property damage and remediation costs. However, in the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our insurance and/or resources.

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

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

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

- changes in the regulatory status of our product candidates, including the status and results of our development activities,

- establishment of new collaborative arrangements,

- events affecting Merck, Idenix or any future collaborators,

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

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

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

- variations in our quarterly operating results,

- changes in securities analysts estimates of our financial performance,

- changes in accounting principles,

- issuances of new equity securities by us, pursuant to our effective shelf registration 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, and

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

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

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

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

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

Our executive officers, directors and holders of 5% or more of our outstanding common stock, beneficially owned approximately 82% of our common stock as of March 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 advances their best interests and not necessarily those of other stockholders.

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

A large portion of our shares are held by a small number of persons and investment funds. In addition, these persons and funds hold warrants to purchase 2,833,338 shares of common stock that, if exercised, will result in these additional shares becoming available for sale. Moreover, several of our stockholders and warrant holders have rights, subject to some conditions, to require us to file registration statements covering the unregistered shares they currently hold or may acquire upon exercise of warrants, or to include these shares in registration statements that we

may file for ourselves or other stockholders. For example, we are filing a registration statement, of which this prospectus is a part, with the Securities and Exchange Commission covering the resale of the shares of common stock issued, and the shares of common stock issuable upon exercise of the warrants issued, in our April 2008 warrant exchange and concurrent private placement. Under the CEFF, an institutional investor is committed to purchase up to $50 million of our common stock over a 36 month period which commenced in December 2006, subject to certain conditions. 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.

**FORWARD-LOOKING STATEMENTS**

This prospectus and the documents incorporated by reference contain forward-looking statements that are based on our management s beliefs and assumptions and on information currently available to our management. Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities, the effects of future regulation and the effects of competition. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as anticipates, believes, could, estimates, expects, intends, may, plans, pote projects, should, will, would , can, continue, and the negative of these terms or other comparable terminology 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 Risk Factors. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management s beliefs and assumptions only as of the date of this prospectus. You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended, or the Securities Act.

## USE OF PROCEEDS

We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders. The proceeds from the sale of the common stock offered pursuant to this prospectus are solely for the accounts of the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees and fees and expenses of our counsel and our accountants.

A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase our common stock. Upon any exercise for cash of the warrants, the selling stockholders will pay us the exercise price of the warrants. The cash exercise price of the warrants is $2.69 per share of our common stock. The warrants are also exercisable on a cashless basis. We will not receive any cash payment from the selling stockholders upon any exercise of the warrants on a cashless basis.

## SELLING STOCKHOLDERS

We are registering for resale shares of our common stock which have been issued and sold to the selling stockholders identified below or that may be issued upon exercise of the warrants which have been issued to the selling stockholders identified below. In connection with a warrant exchange and concurrent private placement in April 2008 with certain current investors, we entered into a warrant exercise agreement dated April 14, 2008 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 of the warrant exchange and concurrent private placement. As a result of the April 14, 2008 warrant exercise agreement, warrants for the purchase of 127,557 shares of our common stock with a prior exercise price of $8.70 per share and warrants for the purchase of 1,558,279 shares of our common stock with a prior exercise price of $6.74 per share were exercised at $2.34 per share. Additionally, in connection with the warrant exchange and concurrent private placement, we entered into a securities purchase agreement dated April 14, 2008 pursuant to which we issued and sold to the investors 2,485,103 shares of our common stock at a 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, which warrants become exercisable 180 days following the date of issuance and expire five years from the date of issuance. We received aggregate proceeds from the warrant exchange and concurrent private placement of $9.9 million.

The table below presents information regarding the selling stockholders and the shares that they may offer and sell from time to time under this prospectus. The shares of common stock covered, as to their resale, under this prospectus include shares of common stock issued and sold in the warrant exchange and concurrent private placement and issuable upon exercise of warrants.

This table is prepared based in part on information supplied to us by the selling stockholders identified below as of April 16, 2008. The number of shares in the column Number of Shares Being Offered represents all of the shares that a selling stockholder may offer under this prospectus, and assumes the exercise of all the warrants for common stock issued under the April 14, 2008 securities purchase agreement. In addition, the table assumes that the selling stockholders sell all of such shares. However, because the selling stockholders may offer from time to time all or some of their shares under this prospectus, or in another permitted manner, we cannot assure you as to the actual number of shares that will be sold by the selling stockholders or that will be held by the selling stockholders after completion of the sales. Information concerning the selling stockholders may change from time to time and changed information will be presented in a supplement to this prospectus if and when necessary and required.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the Securities and Exchange Commission under the Securities Exchange Act of 1934, as amended, or the Exchange Act, except that it also includes warrants held by the selling stockholders that become exercisable greater than 60 days following April 16, 2008.

| | Shares Beneficially Owned Prior to Offering (1) | | Number of Shares Being | Shares Beneficially Owned After Offering (1) | |
|---|---|---|---|---|---|
| Selling Stockholders | Number | Percent | Offered (2) | Number | Percent |
| DLJ Capital Corporation (3)(4) | 47,364 | * | 4,509 | 42,855 | * |
| Domain Public Equity Partners, L.P. (5) | 859,567 | 2.5% | 462,517 | 397,050 | 1.1% |
| Hale BioPharma Ventures LLC (6) | 212,152 | * | 16,111 | 196,041 | * |
| InterWest Investors VII, L.P. (7)(8) | 192,907 | * | 72,687 | 120,220 | * |
| InterWest Partners VII, L.P. (8)(9) | 4,029,455 | 11.4% | 1,519,002 | 2,510,453 | 7.2% |
| MPM Asset Management Investors 2000 B LLC (10)(11) | 79,097 | * | 6,004 | 73,093 | * |
| MPM BioVentures GmbH & Co. Parallel-Beteiligungs KG (11)(12) | 1,209,445 | 3.5% | 91,787 | 1,117,658 | 3.2% |
| MPM BioVentures II, L.P. (11)(13) | 379,088 | 1.1% | 28,776 | 350,312 | 1.0% |
| MPM BioVentures II-QP, L.P. (11)(14) | 3,435,413 | 9.8% | 260,718 | 3,174,695 | 9.1% |

| | | | | | |
|---|---|---|---|---|---|
| Playback & Co. c/o Federated Kaufmann Fund, A Portfolio of Federated Equity Funds (15) | 5,103,729 | 14.4% | 2,103,729 | 3,000,000 | 8.6% |

| Selling Stockholders | Shares Beneficially Owned Prior to Offering (1) Number | Percent | Number of Shares Being Offered (2) | Shares Beneficially Owned After Offering (1) Number | Percent |
|---|---|---|---|---|---|
| Red Abbey Venture Partners, L.P. (16) | 743,781 | 2.1% | 267,833 | 475,948 | 1.4% |
| Sprout Capital IX, L.P. (4)(17) | 3,937,061 | 11.2% | 375,827 | 3,561,234 | 10.1% |
| Sprout Entrepreneurs Fund, L.P. (4)(18) | 15,512 | * | 1,478 | 14,034 | * |
| Sprout IX Plan Investors, L.P. (4)(19) | 120,560 | * | 17,157 | 103,403 | * |

* Less than 1%

(1) Shares beneficially owned include (a) shares of common stock and (b) shares of common stock issuable upon exercise of warrants. Percentages are based on 34,930,843 shares of our common stock that were outstanding on April 16, 2008. In calculating the percentage for each selling security holder, the shares represented by item (b) above are treated as shares outstanding for that selling security holder but are not treated as outstanding for any other person.

(2) Number of shares beneficially owned include 1,057,196 shares of common stock issuable upon exercise of warrants received pursuant to the April 14, 2008 securities purchase agreement that are not currently exercisable within 60 days of April 16, 2008 but that will become exercisable 180 days after April 14, 2008.

(3) Includes 937 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 2,809 shares of common stock that DLJ Capital Corporation has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(4) DLJ Capital Corporation and Credit Suisse First Boston Private Equity, Inc. are wholly owned subsidiaries of Credit Suisse (USA), Inc. (formerly, Credit Suisse First Boston (USA), Inc.), a subsidiary of Credit Suisse Holdings (USA), Inc., a member of the NASD and have represented to us that the shares and warrants held by them were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by them, they were not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by them or the common stock issuable upon exercise of the warrants held by them. DLJ Capital Corporation is the managing general partner of Sprout Capital IX, L.P., DLJ Associates IX, L.P. is a general partner of Sprout Capital IX, L.P. and Credit Suisse (USA), Inc. is a limited partner of Sprout Capital IX, L.P. DLJ Capital Corporation is the general partner of Sprout Entrepreneurs Fund, L.P. Credit Suisse First Boston Private Equity, Inc. wholly owns DLJ LBO Plans Management Corporation II, the general partner of Sprout IX Plan Investors, L.P. Nicole Arnaboldi, Philippe Chambon, Robert Finzi, Janet Hickey and Kathleen LaPorte are members of the Sprout Investment Committee and share voting and investment control over the shares held by DLJ Capital Corporation, Sprout Capital IX, L.P., Sprout Entrepreneurs Fund, L.P. and Sprout IX Plan Investors, L.P. and disclaim beneficial ownership of such shares except to the extent of their pecuniary interest therein.

(5) Includes 99,870 shares of common stock issuable upon exercise of warrants received in connection with the

April 14, 2008 securities purchase agreement. Nicole Vitullo and Domain Associates, LLC are the managing members of Domain Public Equity Associates, LLC, the sole general partner of Domain Public Equity Partners, L.P. James C. Blair, Brian H. Dovey, Jesse I. Treu, Kathleen K. Schoemaker, Nicole Vitullo and Brian Halak are the managing members of Domain Associates, LLC and share voting and investment control over the shares held by Domain Public Equity Partners, L.P. and disclaim beneficial ownership of such shares except to the extent of their pecuniary interest therein.

(6) Includes 3,000 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement. David F. Hale, a member of our board of directors, is the chairman and chief executive officer of Hale BioPharma Ventures LLC. Also includes 47,226 shares held by the Hale Family Trust dated February 10, 1986, of which Mr. Hale and Linda C. Hale are trustees, and 148,815 shares that Mr. Hale has the right to acquire from us within 60 days of April 16, 2008 pursuant to

the exercise of stock options. Mr. Hale disclaims beneficial ownership of the shares owned by Hale BioPharma Ventures LLC except to the extent of his pecuniary interest therein.

(7) Includes 14,937 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement.

(8) Arnold L. Oronsky, a member of our board of directors, is a managing director of InterWest Management Partners VII, LLC, the general partner of Inter West Investors VII, L.P. and InterWest Partners VII, L.P. and, together with the other managing directors and venture members of InterWest Management Partners VII, LLC, has shared voting and investment control over the shares owned by InterWest Investors VII, L.P. and InterWest Partners VII, L.P. Dr. Oronsky and the other managing directors and venture members disclaim beneficial ownership of the shares owned by InterWest Investors VII, L.P. and InterWest Partners VII, L.P. except to the extent of their pecuniary interest therein.

(9) Includes 312,173 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement.

(10) Includes 1,094 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 3,375 shares of common stock that MPM Asset Management Investors 2000 B LLC has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(11) MPM Capital, L.P. is a direct or indirect parent and/or control person of MPM Asset Management II LLC, funds managed or advised by it (including MPM BioVentures II, L.P., MPM BioVentures II-QP, L.P., MPM BioVentures GmbH & Co. Parallel Beteiligungs KG, and MPM Asset Management Investors 2000 B LLC) and the general partners of such funds, and may be deemed to beneficially hold the shares owned by such entities. Luke B. Evnin, a member of our board of directors, may be deemed to be a control person of MPM Capital, L.P. as a result of his interest in Medical Portfolio Management LLC, the general partner of MPM Capital, L.P. Dr. Evnin disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein.

(12) Includes 16,718 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 51,614 shares of common stock that MPM BioVentures GmbH & Co. Parallel Beteiligungs KG has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(13) Includes 5,241 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 16,181 shares of common stock that MPM BioVentures II, L.P. has

the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(14) Includes 47,485 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 146,610 shares of common stock that MPM BioVentures II-QP, L.P. has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(15) Includes 416,580 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement. Federated Kaufmann Fund, or FKF, is a portfolio of Federated Equity Funds, a registered investment company. The parent holding company of FKF s advisors is Federated Investors Inc., or FII. FKF s advisor is Federated Equity Management Company of Pennsylvania, or FEMCPA, which has delegated daily management of the fund s assets to Federated Global Investment Management Corp., or FGIMC, as subadvisor. While the officers and directors of FEMCPA have dispositive power over FKF s portfolio securities, they customarily delegate this dispositive power, and therefore the day to day dispositive decisions are made by the portfolio managers of FKF, currently, Lawrence Auriana and Hans P. Utsch. Messrs. Auriana and Utsch disclaim any beneficial ownership of the shares. With respect to voting power, FKF has delegated the authority to vote proxies to FEMCPA. FEMCPA has established a Proxy Voting Committee to cast proxy votes on behalf of FKF in accordance

with proxy voting policies and procedures approved by FKF. FII is a member of the NASD. FKF has represented to us that the shares and warrants held by it were purchased in the ordinary course of business and that at the time of purchase of the shares and warrants held by it, it was not aware of any agreements or understandings, directly or indirectly, with any person to distribute the shares held by it or the common stock issuable upon exercise of the warrants held by it.

(16) Includes 57,214 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement, 128,072 shares of common stock held by Red Abbey Venture Partners (QP), L.P. and 6,945 shares of common stock held by Red Abbey CEO s Fund, L.P. Matt Zuga is the managing member of Red Abbey Venture Partners, LLC, the general partner of Red Abbey Venture Partners, L.P., Red Abbey Venture Partners (QP), L.P. and Red Abbey CEO s Fund, L.P., and disclaims any beneficial ownership of the shares except to the extent of his pecuniary interest therein.

(17) Includes 78,074 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 231,789 shares of common stock that Sprout Capital IX, L.P. has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(18) Includes 308 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 913 shares of common stock that Sprout Entrepreneurs Fund, L.P. has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

(19) Includes 3,565 shares of common stock issuable upon exercise of warrants received in connection with the April 14, 2008 securities purchase agreement and 13,380 shares of common stock that Sprout IX Plan Investors, L.P. has the right to acquire within 60 days of April 16, 2008 pursuant to the exercise of warrants.

## PLAN OF DISTRIBUTION

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, automated interdealer quotation system, market or trading facility on which the shares are traded, in the over-the-counter market, or in private transactions. These dispositions may be at fixed prices that may be changed, at market prices prevailing at the time of sale, at prices related to prevailing market prices, at varying prices determined at the time of sale or at prices otherwise negotiated. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. The selling stockholders may sell the securities using one or more, or a combination of the following methods:

- on the Nasdaq Stock Market (or any other exchange or automated quotation system on which the shares may be listed),
- on the over-the-counter market,
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers,
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction,
- purchases by a broker-dealer as principal and resale by the broker or dealer for its account,
- an exchange distribution in accordance with the rules of the applicable exchange,
- privately negotiated transactions,
- short sales,
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise,

- through the distribution of the common stock by any selling stockholders to its partners, members or stockholders,

- through one or more underwritten offerings on a firm commitment or best efforts basis,

- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share,

- a combination of any such methods of sale, and

- any other method permitted pursuant to applicable law.

In addition, any shares that qualify for sale pursuant to Rule 144 promulgated under the Securities Act may be sold under Rule 144 rather than pursuant to this prospectus.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under a supplement to this prospectus under Rule 424(b) or under any applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors-in-interest as selling

stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus. To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution.

In connection with distributions of the shares of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which institutions may, in turn, engage in short sales of shares of our common stock in the course of hedging the positions they assume with the selling stockholders. The selling stockholders may also sell the shares of our common stock short and redeliver these shares to close out the selling stockholders short positions, or loan or pledge shares of our common stock to broker-dealers that may in turn sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares of our common stock offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the shares of common stock offered by them will be the purchase price of the shares less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering. Upon any exercise of the warrants by payment of cash, however, we will receive the exercise price of the warrants.

The selling stockholders may engage brokers and dealers, and any brokers or dealers may arrange for other brokers or dealers to participate in effecting sales of the securities. These brokers, dealers or underwriters may act as principals, or as an agent of a selling securityholder. Broker-dealers may agree with a selling stockholder to sell a specified number of the securities at a stipulated price per security. If the broker-dealer is unable to sell securities acting as agent for a selling stockholder, it may purchase as principal any unsold securities at the stipulated price. Broker-dealers who acquire securities as principals may thereafter resell the securities from time to time in transactions in any stock exchange or automated interdealer quotation system on which the securities are then listed, at prices and on terms then prevailing at the time of sale, at prices related to the then-current market price or in negotiated transactions. Broker-dealers may use block transactions and sales to and through broker-dealers, including transactions of the nature described above.

To the extent required under the Securities Act, the aggregate amount of selling stockholders securities being offered and the terms of the offering, the names of any agents, brokers, dealers or underwriters and any applicable commission with respect to a particular offer will be set forth in an accompanying prospectus supplement. Any underwriters, dealers, brokers or agents participating in the distribution of the securities may receive compensation in the form of underwriting discounts, concessions, commissions or fees from a selling stockholder and/or purchasers of selling stockholders securities of securities, for whom they may act (which compensation as to a particular broker-dealer might be in excess of customary commissions).

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the shares of common stock or interests therein may be underwriters within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are underwriters within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We will bear substantially all of the costs, expenses and fees in connection with the registration of the shares of common stock, other than any commissions, discounts or other fees payable to broker-dealers in connection with any sale of shares, which will be borne by the selling

stockholder selling such shares of common stock. We have agreed to indemnify the selling stockholders against certain liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

In order to comply with the securities laws of some states, if applicable, the shares of common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the shares may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares of our common stock in the market and to the activities of the selling stockholders. These rules may limit the timing of purchases and sales of the shares by such selling stockholders.

We will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act.

We have agreed with each selling stockholder to keep the registration statement of which this prospectus constitutes a part effective with respect to its shares of our common stock until the earlier of (1) April 14, 2010, (2) the date on which all shares purchased from us, or issuable upon exercise of warrants purchased from us, by such selling stockholders in the private placement may be resold pursuant to Rule 144 of the Securities Act, or (3) the date on which all shares purchased from us, or acquirable upon exercise of warrants purchased from us, by such selling stockholders have been resold.

## LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley Godward Kronish LLP, San Diego, California. As of the date of this prospectus, investment funds affiliated with Cooley Godward Kronish LLP owned 8,230 shares of common stock and warrants to purchase 3,111 shares of common stock having an exercise price of $8.70 per share.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2007 and the effectiveness of our internal control over financial reporting as of December 31, 2007, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act and in accordance therewith, file reports, proxy statements and other information with the Securities and Exchange Commission. Such reports, proxy statements and other information filed by us may be inspected and copied at the Security and Exchange Commission s Public Reference Section located at 100 F Street, N.E., Washington, D.C. 20549. Copies of such material also can be obtained from the Public Reference Section of the Commission at 100 F Street, N.E., Washington, D.C. 20549, at

prescribed rates. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for more information about the operation of the public reference rooms. The Securities and Exchange Commission also makes electronic filings publicly available on the Internet. The Securities and Exchange Commission s Internet address is http://www.sec.gov. The Securities and Exchange Commission s website also contains reports, proxy and information statements and other information regarding us that has been filed with the Securities and Exchange Commission. Our common stock is listed on the Nasdaq Stock Market. Reports, proxy statements and other information concerning us may be inspected at the National Association of Securities Dealers, Inc. at 1735 K Street, N.W., Washington, D.C. 20006.

This prospectus constitutes a part of a registration statement on Form S-3 filed by us with the Securities and Exchange Commission under the Securities Act, including amendments thereto relating to the common stock offered hereby. This prospectus does not contain all of the information set forth in the registration statement.

The Securities and Exchange Commission allows us to incorporate by reference information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the Securities and Exchange Commission will automatically update and supersede this information. Further, all filings we make under the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the Securities and Exchange Commission under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act:

(i) Our Annual Report on Form 10-K for the year ended December 31, 2007, including all material incorporated by reference therein,

(ii) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2008, including all material incorporated by reference therein,

(iii) Our Current Reports on Form 8-K filed on February 1, 2008, February 15, 2008, April 22, 2008, April 25, 2008 and May 1, 2008 (excluding the information furnished pursuant to Item 2.02 thereto), and

(iv) The description of our common stock contained in our Registration Statement on Form 8-A filed on May 28, 2004.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request of such person, a copy of any and all of the documents that have been incorporated by reference in this prospectus (not including exhibits to such documents, unless such exhibits are specifically incorporated by reference in this prospectus or into such documents). Such request may be directed to Metabasis Therapeutics, Inc., 11119 North Torrey Pines Road, La Jolla, CA 92037, (858) 587-2770.

**PART II**

**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. Other Expenses of Issuance and Distribution.**

The following table sets forth all costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the sale of the common stock being registered. All amounts shown are estimates except for the Securities Exchange Commission registration fee.

| | | |
|---|---|---|
| Securities Exchange Commission registration fee | $ | 475 |
| Legal fees and expenses | | 100,000 |
| Accounting fees and expenses | | 20,000 |
| Miscellaneous | | 9,525 |
| Total | $ | 130,000 |

**Item 15. Indemnification of Directors and Officers.**

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law provides that a Delaware corporation may indemnify any persons who are, or are threatened to be made, parties to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person was an officer, director, employee or agent of such corporation, or is or was serving at the request of such person as an officer, director, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation s best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was illegal. A Delaware corporation may indemnify any persons who are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit provided such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation s best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses which such officer or director has actually and reasonably incurred. Our amended and restated certificate of incorporation and amended and restated bylaws, each of which will become effective upon the completion of this offering, provide for the indemnification of our directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability:

- for any transaction from which the director derives an improper personal benefit,

- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law,

- for improper payment of dividends or redemptions of shares, or

- for any breach of a director s duty of loyalty to the corporation or its stockholders.

Our amended and restated certificate of incorporation and amended and restated bylaws include such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director, who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption, may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, we have entered into indemnity agreements with each of our directors and executive officers, that require us to indemnify such persons against any and all expenses (including attorneys fees), witness fees, damages, judgments, fines, settlements and other amounts incurred (including expenses of a derivative action) in connection with any action, suit or proceeding, whether actual or threatened, to which any such person may be made a party by reason of the fact that such person is or was a director, an officer or an employee of Metabasis or any of its affiliated enterprises, provided that such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to our best interests and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification thereunder.

At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

We have an insurance policy covering our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, or otherwise.

**Item 16. Exhibits.**

| 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(2) | | Amended and Restated Bylaws of the Company. |
| 4.1(1) | | Form of Common Stock Certificate. |
| 4.2(1) | | Form of Stock Purchase Warrant issued to participants in the Company s Series D Preferred Stock financing dated October 18, 2001. |
| 4.3(1) | | Form of letter agreement entered into between the Company and its warrantholders. |
| 4.4(1) | | Letter agreement dated October 18, 2001 entered into between the Company and Sprout Capital IX, L.P. and its affiliates. |
| 4.5(1) | | Amended and Restated Investors Rights Agreement dated October 28, 2003, as amended, between the Company and certain of its stockholders. |
| 4.6(3) | | Securities Purchase Agreement dated September 30, 2005, by and among Metabasis Therapeutics, Inc. and the individuals and entities identified on Exhibit A thereto (the ***2005 Securities Purchase Agreement*** ). |
| 4.7(3) | | Form of Warrant issued pursuant to the 2005 Securities Purchase Agreement. |
| 4.8(4) | | Common Stock Purchase Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited. |
| 4.9(5) | | Amendment to Common Stock Purchase Agreement dated February 15, 2008, by and between the Company and Kingsbridge Capital Limited. |
| 4.10(4) | | Registration Rights Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited. |
| 4.11(5) | | Amended and Restated Warrant dated February 15, 2008 issued by the Company to Kingsbridge Capital Limited. |
| 4.12(6) | | Warrant to Purchase Shares of Common Stock dated March 14, 2008 issued by the Company to Oxford Finance Corporation. |
| 4.13(7) | | Form of Warrant Exercise Agreement dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto. |
| 4.14(7) | | Securities Purchase Agreement dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto (the ***2008 Securities Purchase Agreement*** ). |
| 4.15(7) | | Registration Rights Agreement, dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto. |
| 4.16(7) | | Form of Warrant issued pursuant to the 2008 Securities Purchase Agreement. |

| | | |
|---|---|---|
| 5.1 | | Opinion of Cooley Godward Kronish LLP. |
| 23.1 | | Consent of Ernst & Young LLP, independent registered public accounting firm. |
| 23.2 | | Consent of Cooley Godward Kronish LLP. Reference is made to Exhibit 5.1. |
| 24.1 | | Power of Attorney. Reference is made to the signature page hereto. |

(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 Company s Current Report on Form 8-K filed on October 2, 2007.

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

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

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

(6) Incorporated by reference to the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2007 filed on March 17, 2008.

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

**Item 17. Undertakings**

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933,

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement, and

(iii) To include any material information with respect to the distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

Provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the registration statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for purposes of determining any liability under the Securities Act of 1933:

(i) If the registrant is relying on Rule 430B:

(a) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(b) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of 314 securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant s annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on May 9, 2008.

**METABASIS THERAPEUTICS, INC.**

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

**KNOW ALL PERSONS BY THESE PRESENTS,** that each person whose signature appears below hereby constitutes and appoints jointly and severally, Paul K. Laikind, Ph.D. and John W. Beck, C.P.A., and each or any one of them, his or her true and lawful attorney-in-fact and agent, each with the full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any way and all capacities, to sign any and all amendments (including post-effective amendments and registration statements filed pursuant to Rule 462) to this registration statement and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that each said attorney-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed below by the following persons in the capacities and on the dates indicated.

| NAME | | TITLE | | DATE |
|---|---|---|---|---|
| | | | | |
| /s/ Paul K. Laikind | | Director, President, | | May 9, 2008 |
| Paul K. Laikind, Ph.D. | | Chief Executive Officer and Secretary | | |
| | | (Principal Executive Officer) | | |
| | | | | |
| /s/ John W. Beck | | Senior Vice President of Finance, | | May 9, 2008 |
| John W. Beck, C.P.A. | | Chief Financial Officer and | | |
| | | Treasurer (Principal Financial and | | |
| | | Accounting Officer) | | |
| | | | | |
| /s/ David F. Hale | | Chairman of the Board | | May 9, 2008 |
| David F. Hale | | | | |
| | | | | |
| /s/ Daniel D. Burgess | | Director | | May 9, 2008 |
| Daniel D. Burgess, M.B.A. | | | | |
| | | | | |
| /s/ Mark D. Erion | | Executive Vice President of | | May 9, 2008 |
| Mark D. Erion, Ph.D. | | Research and Development, Chief | | |
| | | Scientific Officer and Director | | |

| | | | | |
|---|---|---|---|---|
| | | | | |
| /s/ Luke B. Evnin | | Director | | May 9, 2008 |
| Luke B. Evnin, Ph.D. | | | | |
| | | | | |
| /s/ Arnold L. Oronsky | | Director | | May 9, 2008 |
| Arnold L. Oronsky, Ph.D. | | | | |
| | | | | |
| /s/ William R. Rohn | | Director | | May 9, 2008 |
| William R. Rohn | | | | |
| | | | | |
| /s/ George Schreiner | | Director | | May 9, 2008 |
| George Schreiner, M.D., Ph.D. | | | | |
| | | | | |
| /s/ Elizabeth Stoner | | Director | | May 9, 2008 |
| Elizabeth Stoner, M.D. | | | | |

**EXHIBIT INDEX**

| 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(2) | Amended and Restated Bylaws of the Company. |
| 4.1(1) | Form of Common Stock Certificate. |
| 4.2(1) | Form of Stock Purchase Warrant issued to participants in the Company s Series D Preferred Stock financing dated October 18, 2001. |
| 4.3(1) | Form of letter agreement entered into between the Company and its warrantholders. |
| 4.4(1) | Letter agreement dated October 18, 2001 entered into between the Company and Sprout Capital IX, L.P. and its affiliates. |
| 4.5(1) | Amended and Restated Investors Rights Agreement dated October 28, 2003, as amended, between the Company and certain of its stockholders. |
| 4.6(3) | Securities Purchase Agreement dated September 30, 2005, by and among Metabasis Therapeutics, Inc. and the individuals and entities identified on Exhibit A thereto (the ***2005 Securities Purchase Agreement*** ). |
| 4.7(3) | Form of Warrant issued pursuant to the 2005 Securities Purchase Agreement. |
| 4.8(4) | Common Stock Purchase Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited. |
| 4.9(5) | Amendment to Common Stock Purchase Agreement dated February 15, 2008, by and between the Company and Kingsbridge Capital Limited. |
| 4.10(4) | Registration Rights Agreement dated November 2, 2006 between the Company and Kingsbridge Capital Limited. |
| 4.11(5) | Amended and Restated Warrant dated February 15, 2008 issued by the Company to Kingsbridge Capital Limited. |
| 4.12(6) | Warrant to Purchase Shares of Common Stock dated March 14, 2008 issued by the Company to Oxford Finance Corporation. |
| 4.13(7) | Form of Warrant Exercise Agreement dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto. |
| 4.14(7) | Securities Purchase Agreement dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto (the ***2008 Securities Purchase Agreement*** ). |
| 4.15(7) | Registration Rights Agreement, dated April 14, 2008, by and among the Company and the individuals and entities identified on the signature pages thereto. |
| 4.16(7) | Form of Warrant issued pursuant to the 2008 Securities Purchase Agreement. |
| 5.1 | Opinion of Cooley Godward Kronish LLP. |
| 23.1 | Consent of Ernst & Young LLP, independent registered public accounting firm. |
| 23.2 | Consent of Cooley Godward Kronish LLP. Reference is made to Exhibit 5.1. |

24.1 Power of Attorney. Reference is made to the signature page hereto.

(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 Company s Current Report on Form 8-K filed on October 2, 2007.

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

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

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

(6) Incorporated by reference to the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2007 filed on March 17, 2008.

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