

METABASIS THERAPEUTICS INC
Form 424B2
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Registration No. 333-141977

PROSPECTUS

\$75,000,000

Common Stock Warrants

From time to time, we may sell any of the securities listed above in one or more offerings in amounts, at prices and on the terms that we will determine at the time of the offering, with an aggregate initial offering price of up to \$75,000,000.

We will provide the specific terms of these securities in one or more supplements to this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus and any prospectus supplement carefully before you invest.

Our common stock is traded on the Nasdaq Stock Market under the symbol MBRX. On May 2, 2007, the last reported sales price for our common stock was \$7.98 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Stock Market or any securities market or exchange of the securities covered by the prospectus supplement.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE RISK FACTORS BEGINNING ON PAGE 3.

THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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 May 3, 2007

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

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, we may sell common stock and warrants in one or more offerings up to a total dollar amount of \$75,000,000, of which \$40,000,003.20 is being registered under this registration statement and \$34,999,996.80 was previously registered under our registration statement filed on February 3, 2006. This prospectus provides you with a general description of the securities we may offer. Each time we sell any securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of those securities. We may also add, update or change in a prospectus supplement any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to this offering. You should carefully read both this prospectus and the applicable prospectus supplement together with the additional information described under Where You Can Find More Information before buying securities in this offering.

SUMMARY

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

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

Metabasis Therapeutics, Inc.

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

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

| Product Candidate | Disease Indication |
|----------------------------------|----------------------|
| <i>Metabolic Diseases</i> | |
| CS-917 | type 2 diabetes |
| MB07803 | type 2 diabetes |
| MB07811 | hyperlipidemia |
| <i>Liver Diseases</i> | |
| pradefovir | hepatitis B |
| MB07133 | primary liver cancer |

Our agreements with collaborators may include joint marketing or promotion arrangements of our products. For example, we have retained co-promotion rights for CS-917 in North America with Daiichi Sankyo, Co. Ltd. Alternatively, we may grant exclusive marketing rights to our collaborators in exchange for up-front fees, milestones and royalties on future sales, if any. We have licensed worldwide commercialization rights for pradefovir to Schering Corporation, a subsidiary of Schering-Plough Corporation. We do not have collaborative partnerships for MB07803, MB07133 or MB07811 and are currently independently developing these product candidates. We retain worldwide commercialization rights to all of the compounds generated from our current research programs, with the exception of product candidates covered by our collaborations with Merck & Co., Inc. and Idenix Pharmaceuticals, Inc. We intend to eventually market one or more of the product candidates for which we retain commercialization rights through our own sales force or with a co-promotion partner in the U.S. and through strategic collaborations abroad.

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

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

The Securities We May Offer

We may offer shares of our common stock and warrants to purchase shares of our common stock with a total offering price of up to \$75,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type of security, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the offering: The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

We may sell the securities directly or through underwriters, dealers or agents. We, and our underwriters, dealers or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval. Subject to any preferential rights of any then outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any then outstanding preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

Warrants. We may issue warrants for the purchase of common stock from time to time. We may issue warrants independently or together with common stock, and the warrants may be attached to or separate from the common stock.

The warrants will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplements related to the warrants being offered, as well as the complete forms of warrant agreement and warrant certificate that contain the terms of the warrants. Forms of the warrant agreements and warrant certificate relating to warrants for the purchase of common stock have been filed as exhibits to the registration statement of which this prospectus is a part, and complete forms of the warrant agreement and warrant certificate containing the terms of the warrants being offered will be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

RISK FACTORS

Investing in our securities involves risks. Before deciding whether to invest in our securities, you should consider carefully the risk factors discussed in the section entitled "Risk Factors" contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2006, as filed with the SEC on March 13, 2007, which is incorporated herein by reference in its entirety, as well as any amendment or update thereto reflected in subsequent filings with the SEC. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment.

FORWARD-LOOKING INFORMATION

This prospectus and the documents incorporated herein by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, regarding, among other things, our business, our financial position and the research and development of biopharmaceutical products. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would" or similar expressions. These statements are based largely upon our expectations and projections about future events, and so are subject to certain risks and uncertainties, particularly those inherent in the process of developing and commercializing biopharmaceutical products, that could cause actual results to differ materially from those expressed in or implied by the forward-looking statements. Among the factors that could cause actual results to differ materially from those expressed in or implied by the forward-looking statements are risks and uncertainties incorporated by reference under "Risk Factors" in this prospectus and described in our filings with the SEC.

Although our forward-looking statements reflect good faith beliefs of our management, these statements are based only on facts and circumstances currently known to us. As a result, we cannot guarantee future results, events, levels of activity, performance or achievement as expressed in or implied by our forward-looking statements. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

USE OF PROCEEDS

Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of securities under this prospectus for general corporate purposes, including clinical trial expenses, research and development expenses, general and administrative expenses, manufacturing expenses, and potential acquisitions of companies and technologies that complement our business, although we are not currently a party to any binding agreements or commitments with respect to the acquisition of any companies or technologies. Pending these uses, we expect to invest the net proceeds in investment-grade, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 105,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of March 31, 2007, approximately 30,515,974 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary describes the material terms of our capital stock. The description of capital stock is qualified by reference to our amended and restated certificate of incorporation, as amended, and

our bylaws, as amended, which are incorporated by reference as exhibits into the registration statement of which this prospectus is a part.

Common Stock

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on May 28, 2004 is incorporated herein by reference in its entirety, as well as any amendment or update thereto reflected in subsequent filings with the SEC. See [Where You Can Find More Information](#).

Delaware Anti-Takeover Law and Provisions of our Amended and Restated Certificate of Incorporation and Bylaws

Delaware Anti-Takeover Law. We are subject to Section 203 of the Delaware General Corporation Law. Section 203 generally prohibits a public Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 $\frac{2}{3}$ % of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Amended and Restated Certificate of Incorporation and Bylaws. Provisions of our amended and restated certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise

deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our amended and restated certificate of incorporation and bylaws:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose); and
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

The amendment of any of these provisions generally would require approval by the holders of at least 66 $\frac{2}{3}$ % of our then outstanding common stock.

Nasdaq Stock Market Listing

Our common stock is listed on the Nasdaq Stock Market under the symbol MBRX.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company. The transfer agent and registrar's address is 59 Maiden Lane, New York, New York 10038.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants to purchase common stock that we may offer under this prospectus. Warrants may be offered independently or together with common stock offered by any prospectus supplement, and may be attached to or separate from the common stock. While the terms we have summarized below will generally apply to any future warrants we may offer under this prospectus, we will describe the particular terms of any warrants that we may offer in more detail in the applicable prospectus supplement. The terms of any warrants we offer under a prospectus supplement may differ from the terms we describe below.

We will issue the warrants under a warrant agreement which we will enter into with a warrant agent to be selected by us. We have filed forms of the warrant agreement and the related warrant certificate for the warrants we may offer under this prospectus as exhibits to the registration statement of which this prospectus is a part. The warrant agent will act solely as an agent of ours in connection with the warrants and will not act as an agent for the holders or beneficial owners of the warrants.

The following summaries of material provisions of the warrants and the warrant agreement are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement. We urge you to read the applicable prospectus supplements related to the warrants that we sell under this prospectus, as well as the complete warrant agreement that contains the terms of the warrants.

General

We will describe in the applicable prospectus supplement the following terms relating to the warrants, to the extent applicable:

- the offering price and the aggregate number of warrants offered;
- the total number of shares that can be purchased if a holder of the warrants exercises them;
- the number of warrants being offered with each share of common stock;
- the number of shares of common stock that can be purchased if a holder exercises the warrant and the price at which such common stock may be purchased upon exercise, including, if applicable, any provisions for changes to or adjustments in the exercise price and in the securities or other property receivable upon exercise;
- the terms of any rights to redeem or call, or accelerate the expiration of, the warrants;
- the date on which the right to exercise the warrants begins and the date on which that right expires;
- the federal income tax consequences of holding or exercising the warrants; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the warrants.

Warrants for the purchase of common stock will be in registered form only.

If the warrants are attached to common stock, the prospectus supplement will also describe the date on and after which the holder of the warrants can transfer them separately from the related common stock.

A holder of warrant certificates may exchange them for new certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase common stock are exercised, holders of the warrants will not have any rights of holders of the underlying common stock, including any rights to receive dividends or to exercise any voting rights, except to the extent set forth under **Warrant Adjustments** below.

Exercise of Warrants

Each holder of a warrant is entitled to purchase the number of shares of common stock at the exercise price described in the applicable prospectus supplement. After the close of business on the day when the right to exercise terminates (or a later date if we extend the time for exercise), unexercised warrants will become void.

A holder of warrants may exercise them by following the general procedure outlined below:

- delivering to the warrant agent the consideration required by the applicable prospectus supplement to purchase the underlying common stock;
- properly completing and signing the reverse side of the warrant certificate representing the warrants; and
- delivering the warrant certificate representing the warrants to the warrant agent within five business days of the warrant agent receiving payment of the exercise price.

If you comply with the procedures described above, your warrants will be considered to have been exercised when the warrant agent receives payment of the exercise price, subject to the transfer books for the securities issuable upon exercise of the warrant not being closed on such date. After you have completed those procedures and subject to the foregoing, we will, as soon as practicable, issue and deliver to you the common stock that you purchased upon exercise. If you exercise fewer than all of the warrants represented by a warrant certificate, a new warrant certificate will be issued to you for the unexercised amount of warrants. Holders of warrants will be required to pay any tax or governmental charge that may be imposed in connection with transferring the underlying common stock in connection with the exercise of the warrants.

Amendments and Supplements to the Warrant Agreements

We may amend or supplement a warrant agreement without the consent of the holders of the applicable warrants to cure ambiguities in the warrant agreement, to cure or correct a defective provision in the warrant agreement, or to provide for other matters under the warrant agreement that we and the warrant agent deem necessary or desirable, so long as, in each case, such amendments or supplements do not materially adversely affect the interests of the holders of the warrants.

Warrant Adjustments

Unless the applicable prospectus supplement states otherwise, the exercise price of, and the number of securities covered by a warrant will be adjusted proportionately if we subdivide or combine our common stock. In addition, unless the prospectus supplement states otherwise, if we, without payment for:

- issue capital stock or other securities convertible into or exchangeable for common stock, or any rights to subscribe for, purchase or otherwise acquire any of the foregoing, as a dividend or distribution to holders of our common stock;
- pay any cash to holders of our common stock other than a cash dividend paid out of our current or retained earnings;

- issue any evidence of our indebtedness or rights to subscribe for or purchase our indebtedness to holders of our common stock; or
- issue common stock or preferred stock or additional stock or other securities or property to holders of our common stock by way of spinoff, split-up, reclassification, combination of shares or similar corporate rearrangement,

then the holders of warrants will be entitled to receive upon exercise of the warrants, in addition to the common stock otherwise receivable upon exercise of the warrants and without paying any additional consideration, the amount of stock and other securities and property such holders would have been entitled to receive had they held the common stock issuable under the warrants on the dates on which holders of the common stock received or became entitled to receive such additional stock and other securities and property.

Except as stated above, the exercise price and number of securities covered by a warrant, and the amounts of other securities or property to be received, if any, upon exercise of those warrants, will not be adjusted or provided for if we issue those securities or any securities convertible into or exchangeable for those securities, or securities carrying the right to purchase those securities or securities convertible into or exchangeable for those securities.

Holders of warrants may have additional rights under the following circumstances:

- certain reclassifications, capital reorganizations or changes of the common stock;
- certain share exchanges, mergers, or similar transactions involving us and which result in changes of the common stock; or
- certain sales or dispositions to another entity of all or substantially all of our property and assets.

If one of the above transactions occurs and holders of our common stock are entitled to receive stock, securities or other property with respect to or in exchange for their common stock, the holders of the warrants then outstanding will be entitled to receive upon exercise of their warrants the kind and amount of shares of stock and other securities or property that they would have received upon the applicable transaction if they had exercised their warrants immediately before the transaction.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus in any of three ways (or in any combination):

- to or through underwriters or dealers;
- directly to a limited number of purchasers or to a single purchaser; or
- through agents.

Each time we offer and sell securities, we will provide a prospectus supplement that will set forth the terms of the offering of the securities covered by this prospectus, including:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any underwriting discounts or commissions or agency fees and other items constituting underwriters or agents compensation;
- the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers; and

- any securities exchanges or markets on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Underwriters or dealers may offer and sell the offered securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. If underwriters or dealers are used in the sale of any securities, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters or dealers. Generally, the underwriters or dealers' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters or dealers will be obligated to purchase all of the securities if they purchase any of the securities, unless otherwise specified in the prospectus supplement. We may use underwriters with whom we have a material relationship. We will describe the nature of any such relationship in the prospectus supplement, naming the underwriter.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, dealers and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents, dealers and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

All warrants we offer will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying securities so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq Stock Market may engage in passive market making transactions on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the applicable securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security. If all independent

bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon 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 5,940 shares of common stock having a weighted average exercise price of \$7.44 per share.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2006, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's web site at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's public reference room at 100 F Street, NE., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the SEC's public reference room in Washington, D.C. by calling the SEC at 1-800-SEC-0330.

The SEC allows us to incorporate by reference into this prospectus the information in documents we file with it, which means that we can disclose important information to you by referring you to those documents. Any statement contained in any document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus, to the extent that a statement contained in or omitted from this prospectus, or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering is completed:

- Our Annual Report on Form 10-K for the year ended December 31, 2006 which was filed on March 13, 2007, including all material incorporated by reference therein;
- Our Current Report on Form 8-K which was filed on April 27, 2007; and
- 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, California 92037, (858) 587-2770.

All documents that we file with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination of the offering of the securities offered in this prospectus shall be deemed incorporated by reference into this prospectus and to be a part of this prospectus from the respective date of filing such documents.

We have filed with the SEC a registration statement on Form S-3 under the Securities Act covering the securities described in this prospectus. This prospectus does not contain or incorporate by reference all of the information included in the registration statement, some of which is contained in exhibits included with or incorporated by reference into the registration statement. The registration statement, including the exhibits contained or incorporated by reference therein, can be read at the SEC web site or at the SEC office referred to above. Any statement made or incorporated by reference in this prospectus concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified in its entirety by reference to the actual document.