

HOLLIS EDEN PHARMACEUTICALS INC /DE/
 Form 424B5
 November 08, 2006
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Filed pursuant to Rule 424(b)(5)
 Registration No. 333-135095

PROSPECTUS SUPPLEMENT NO. 1

(TO PROSPECTUS DATED JUNE 16, 2006)

4,800,000 Shares

HOLLIS-EDEN PHARMACEUTICALS, INC.

Common Stock

Warrants to Purchase Common Stock

We are offering up to 4,000,000 shares of our common stock at a price per share of \$6.50 and warrants to purchase up to an additional 800,000 shares of our common stock at a price per share of \$8.75.

Our common stock is listed on The Nasdaq Global Market under the symbol `HEPH`. On November 7, 2006, the last reported sale price of our common stock on The Nasdaq Global Market was \$7.34 per share.

Our business and an investment in our common stock involve significant risks. These risks are described under the headings Risk Factors on page S-1 of this prospectus supplement and beginning on page 2 of the accompanying prospectus.

Rodman & Renshaw, LLC and Canaccord Adams, Inc. (collectively, the Placement Agents) have been retained to act as agents for us in connection with the arrangement of this transaction. We have agreed to pay the Placement Agents the aggregate placement agent fees set forth in the table below. The Placement Agents are not required to sell any specific number or dollar amount of these shares but will use commercially reasonable efforts to arrange for the sale of all of the shares offered hereby. See Plan of Distribution in this prospectus supplement.

| | Per Share (1) | Maximum Offering (1) |
|----------------------------------|---------------|----------------------|
| Price to the public | \$ 6.50 | \$ 26,000,000 |
| Placement agent fees | \$ 0.39 | \$ 1,560,000 |
| Proceeds, before expenses, to us | \$ 6.11 | \$ 24,440,000 |

(1) This table does not reflect any proceeds to us from the warrants we are offering, and we will not receive any proceeds with respect to such warrants unless and until such warrants are exercised. If the warrants were fully exercised, we would receive additional proceeds of \$7,000,000 (assuming that the warrants are exercised for cash, and not using the cashless exercise feature described on page S-13). We will not pay the Placement Agents any fee with respect to shares of our common stock issued upon exercise of the warrants. We estimate that the total expenses of this offering, excluding placement agent fees, will be approximately \$85,000. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agent fees and proceeds to us, if any, are not presently determinable and may be substantially less than the maximum amounts set forth above.

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

Rodman & Renshaw, LLC

Canaccord Adams, Inc.

As Placement Agents

The date of this prospectus supplement is November 7, 2006

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This prospectus supplement is a supplement to the accompanying prospectus that is also part of this document. This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may sell shares of our stock up to an aggregate amount of \$75,000,000 in one or more offerings. In this prospectus supplement, we provide you with specific information about the terms of this offering and certain other information. You should read this prospectus supplement, along with the accompanying prospectus, carefully before you invest. Both documents contain important information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus. You should read both this prospectus supplement and the accompanying prospectus together with additional information described under the heading, **Where You Can Find More Information**.

You should rely only on the information we have provided or incorporated by reference in this prospectus supplement or in the accompanying prospectus. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus. This prospectus supplement is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information contained in this prospectus supplement and in the accompanying prospectus is accurate only as of their respective dates and that any information we have incorporated by reference is accurate only as of the date of the document

incorporated by reference, regardless of the time of delivery of this prospectus supplement or the accompanying prospectus or any sale of shares of our common stock.

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ABOUT THIS PROSPECTUS SUPPLEMENT

We provide information to you about this offering of shares of our common stock in two separate documents:

the accompanying prospectus, which provides general information, some of which may not apply to this offering; and

this prospectus supplement, which provides specific information regarding the terms of this offering.

Generally, when we refer to this prospectus, we are referring to both documents combined. Additional information is incorporated by reference in this prospectus. See *Where You Can Find More Information*. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement.

RISK FACTORS

Any investment in shares of our common stock involves significant risks. You should consider carefully the following information about these risks, together with the other information contained in this prospectus supplement, the accompanying prospectus and the additional information in our reports and other documents on file with the SEC that are incorporated by reference, before you decide to buy any shares of our common stock. The following risk factors relate to this offering and are in addition to the risk factors appearing in the accompanying prospectus.

If we do not obtain government regulatory approval for our products, we cannot sell our products and we will not generate revenues.

Our principal development efforts are currently centered around a proprietary class of small compounds which we believe shows promise for the treatment of diseases and disorders in which the body is unable to mount an appropriate immune response. However, all drug candidates require approval by the FDA before they can be commercialized in the U.S. as well as approval by various foreign government agencies before they can be commercialized in other countries. These regulations change from time to time and new regulations may be adopted. None of our drug candidates have been approved for commercial sale. We may incur significant additional operating losses for the foreseeable future as we fund development, preclinical and clinical testing and other expenses in support of regulatory approval of our drug candidates. While limited clinical trials of our drug candidates have been conducted to date, significant additional trials are required, and we may not be able to demonstrate that these drug candidates are safe or effective. If we are unable to demonstrate the safety and effectiveness of a particular drug candidate to the satisfaction of regulatory authorities, the drug candidate will not obtain required government approval. If we do not receive FDA or foreign approvals for our drug candidates, we will not be able to sell products and will not generate revenues. If we receive regulatory approval of one of our drug candidates, such approval may impose limitations on the indicated uses for which we may market the resulting product, which may limit our ability to generate significant revenues. Further, U.S. or foreign regulatory agencies could change existing, or promulgate new, regulations at any time which may affect our ability to obtain approval of our drug candidates or require significant additional costs to obtain such approvals. In addition, if regulatory authorities determine that we or a partner conducting research and development activities on our behalf have not complied with regulations in the research and development of one of our drug candidates, then they may not approve the drug candidate and we will not be able to market and sell it. If we were unable to market and sell our drug candidates, our business and results of operations would be materially and adversely affected.

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If we do not successfully commercialize our products, we may never achieve profitability.

We have experienced significant operating losses to date because of the substantial expenses we have incurred to acquire and fund development of our drug candidates. We have never had operating revenues and have never commercially introduced a product. Our accumulated deficit was approximately \$183.6 million as of September 30, 2006. Our net losses for fiscal years 2005, 2004 and 2003 were approximately \$29.4 million, \$24.8 million and \$25.7 million, respectively. Many of our research and development programs are at an early stage. Potential drug candidates are subject to inherent risks of failure. These risks include the possibilities that no drug candidate will be found safe or effective, meet applicable regulatory standards or receive the necessary regulatory clearances. Even safe and effective drug candidates may never be developed into commercially successful drugs. If we are unable to develop safe, commercially viable drugs, we may never achieve profitability. If we become profitable, we may not remain profitable.

The market for treating Acute Radiation Syndrome is uncertain.

We do not believe any drug has ever been approved and commercialized for the treatment of acute radiation syndrome. In addition, the incidence of large-scale exposure to nuclear or radiological events has been low. Accordingly, even if NEUMUNE[®], our lead drug candidate to treat ARS, is approved by the FDA, we cannot predict with any certainty the size of this market. The initial potential market for NEUMUNE is largely dependent on the size of stockpiling orders, if any, procured by government agencies. While a number of governments have historically stockpiled drugs to treat indications such as smallpox, anthrax exposure, plague, tularemia and certain long-term effects of radiation exposure, we are unaware of any significant stockpiling orders for drugs to treat ARS. On December 9, 2005, the U.S. Department of Health and Human Services (DHHS) issued a Request for Proposal (RFP) which specified an initial potential stockpiling order of up to 100,000 treatment regimens, which is substantially lower than we had anticipated. While we have responded to the RFP, we cannot guarantee that we will be able to meet the requirements set forth in the RFP or that we will receive any resulting stockpiling orders. A decision by any department of the U.S. Government to enter into a commitment to purchase NEUMUNE, whether before or after FDA approval, is largely out of our control. Our development plans and timelines may vary substantially depending on whether we receive such a commitment and the size of such commitment, if any. In addition, even if NEUMUNE is approved by regulatory authorities, we cannot guarantee that we will receive any stockpiling orders for NEUMUNE, that any such order would be profitable to us or that NEUMUNE will achieve market acceptance by the general public.

As a result of our intensely competitive industry, we may not gain enough market share to be profitable.

The biotechnology and pharmaceutical industries are intensely competitive. We have numerous competitors in the U.S. and elsewhere. Because we are pursuing potentially large markets, our competitors include major multinational pharmaceutical companies, specialized biotechnology firms and universities and other research institutions. Several of these entities have already successfully marketed and commercialized products that will compete with our products, assuming that our products gain regulatory approval. Companies such as Amgen Inc. have developed or are developing products to boost neutrophils or platelets after chemotherapy. A large number of companies, including Merck & Company, Inc., Pfizer Inc., Johnson & Johnson Inc. and Amgen Inc. are also developing and marketing new drugs for the treatment of chronic inflammatory conditions. Companies such as GlaxoSmithKline, Merck & Company, Inc., Roche Pharmaceuticals, Pfizer Inc. and Abbott Laboratories have significant market share for the treatment of a number of infectious diseases such as HIV. In addition, biotechnology companies such as Gilead Sciences Inc., Chiron Corporation and Vertex Pharmaceuticals Inc., as well as many others, have marketed products or research and development programs in these fields.

Many of these competitors have greater financial and other resources, larger research and development staffs and more effective marketing and manufacturing organizations than we do. In addition, academic and government institutions have become increasingly aware of the commercial value of their research findings. These institutions are now more likely to enter into exclusive licensing agreements with commercial enterprises, including our competitors, to develop and market commercial products.

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Our competitors may succeed in developing or licensing technologies and drugs that are more effective or less costly than any we are developing. Our competitors may succeed in obtaining FDA or other regulatory approvals for drug candidates before we do. If competing drug candidates prove to be more effective or less costly than our drug candidates, our drug candidates, even if approved for sale, may not be able to compete successfully with our competitors' existing products or new products under development. If we are unable to compete successfully, we may never be able to sell enough products at a price sufficient to permit us to generate profits.

We may need to raise additional money before we achieve profitability; if we fail to raise additional money, it could be difficult or impossible to continue our business.

As of September 30, 2006, our cash and cash equivalents totaled approximately \$47.4 million. In February 2006, we completed an offering of common stock and warrants to purchase common stock, pursuant to which we received net proceeds of approximately \$24.4 million. Based on our current plans, we believe these financial resources, and interest earned thereon, will be sufficient to meet our operating expenses and capital requirements for at least the next 12 months. However, changes in our research and development plans or other events affecting our operating expenses may result in the expenditure of such cash before that time. We may require substantial additional funds in order to finance our drug discovery and development programs, fund operating expenses, pursue regulatory clearances, develop manufacturing, marketing and sales capabilities, and prosecute and defend our intellectual property rights. We may seek additional funding through public or private financing or through collaborative arrangements with strategic partners.

You should be aware that in the future:

we may not obtain additional financial resources when necessary or on terms favorable to us, if at all; and

any available additional financing may not be adequate.

If we cannot raise additional funds when needed, or on acceptable terms, we will not be able to continue to develop our drug candidates.

Failure to protect our proprietary technology could impair our competitive position.

We own or have obtained a license to numerous U.S. and foreign patents and foreign patent applications. Our success depends in part on our ability to obtain and defend patent rights and other intellectual property rights that are important to our ability to commercialize our drug candidates, if approved and our ability to operate our business without infringing the proprietary rights of third parties. We place considerable importance on obtaining patent protection for significant new technologies, products and processes. Legal standards relating to the validity of patents covering pharmaceutical and biotechnology inventions and the scope of claims made under such patents are still developing. In some of the countries in which we intend to market our drug candidates, if approved, pharmaceuticals are either not patentable or have only recently become patentable. Past enforcement of intellectual property rights in many of these countries has been limited or non-existent. Future enforcement of patents and proprietary rights in many other countries may be problematic or unpredictable. Moreover, the issuance of a patent in one country does not assure the issuance of a similar patent in another country. Claim interpretation and infringement laws vary by nation, so the extent of any patent protection is uncertain and may vary in different jurisdictions. Our domestic patent position is also highly uncertain and involves complex legal and factual questions. The applicant or inventors of subject matter covered by patent applications or patents owned by or licensed to us may not have been the first to invent or the first to file patent applications for such inventions. Due to uncertainties regarding patent law and the circumstances surrounding our patent applications, the pending or future patent applications we own or have licensed may not result in the issuance of any patents. Existing or future patents owned by or licensed to us may be challenged, infringed upon, invalidated, found to be unenforceable or circumvented by others. Further, any rights we may have under any issued patents may not

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provide us with sufficient protection against similar competitive products or technologies that do not infringe on patents or otherwise cover commercially valuable products or processes.

Litigation or other disputes regarding patents and other proprietary rights may be expensive, cause delays in bringing products to market and harm our ability to operate.

The manufacture, use or sale of our drug candidates may infringe on the patent rights of others. If we are unable to avoid infringement of the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming and can preclude, delay or suspend commercialization of products. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, or fail to successfully defend an infringement action or have the patents we are alleged to infringe declared invalid, we may

incur substantial money damages;

encounter significant delays in bringing our drug candidates to market;

be precluded from participating in the manufacture, use or sale of our drug candidates or methods of treatment without first obtaining licenses to do so; and/or

not be able to obtain any required license on favorable terms, if at all.

In addition, if another party claims the same subject matter or subject matter overlapping with the subject matter that we have claimed in a U.S. patent application or patent, we may decide or be required to participate in interference proceedings in the U.S. Patent and Trademark Office in order to determine the priority of invention. Loss of such an interference proceeding would deprive us of patent protection sought or previously obtained and could prevent us from commercializing our products. Participation in such proceedings could result in substantial costs, whether or not the eventual outcome is favorable. These additional costs could adversely affect our financial results.

Litigation may be expensive and time consuming and may adversely affect our operations.

From time to time, we may be involved in litigation relating to claims arising out of our operations in the normal course of business. Participation in such proceedings is time consuming and could result in substantial costs, whether or not the eventual outcome is favorable. These additional costs could adversely affect our financial results.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we also rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Existing pricing regulations and reimbursement limitations may reduce our potential profits from the sale of our products.

The requirements governing product licensing, pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries,

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the pricing review period begins after product-licensing approval is granted. As a result, we may obtain regulatory approval for a drug candidate in a particular country, but then be subject to price regulations that reduce our profits from the sale of the product. In some foreign markets pricing of prescription pharmaceuticals is subject to continuing government control even after initial marketing approval. In addition, certain governments may grant third parties a license to manufacture our product without our permission. Such compulsory licenses may be on terms that are less favorable to us and would likely have the effect of reducing our revenues.

Varying price regulation between countries can lead to inconsistent prices and some re-selling by third parties of products from markets where products are sold at lower prices to markets where those products are sold at higher prices. Any practice of exploiting price differences between countries could undermine our sales in markets with higher prices and reduce the sales of our future products, if any.

While we do not have any applications for regulatory approval of our drug candidates currently pending, any decline in the size of the markets in which we may in the future sell commercial products, assuming our receipt of the requisite regulatory approvals, could cause the perceived market value of our business and the price of our common stock to decline.

Our ability to commercialize our drug candidates successfully also will depend in part on the extent to which reimbursement for the cost of our drug candidates and related treatments will be available from government health administration authorities, private health insurers and other organizations. Third-party payers are increasingly challenging the prices charged for medical products and services. If we succeed in bringing any of our drug candidates to the market, such drug candidates may not be considered cost effective and reimbursement may not be available or sufficient to allow us to sell such drug candidates on a profitable or competitive basis.

Delays in the conduct or completion of our preclinical or clinical studies or the analysis of the data from our preclinical or clinical studies may result in delays in our planned filings for regulatory approvals, or adversely affect our ability to enter into collaborative arrangements.

The current status of our drug candidates is set forth below. We have either completed or are in the midst of:

animal efficacy studies with NEUMUNE for the treatment of radiation exposure;

Phase I clinical trials with NEUMUNE in the United States and the Netherlands;

Phase II clinical trials with IMMUNITIN in South Africa and Phase I/II clinical trials with IMMUNITIN in the United States for the treatment of HIV/AIDS; and

Phase II clinical trials with IMMUNITIN in Thailand for the treatment of malaria.

We may encounter problems with some or all of our completed or ongoing studies that may cause us or regulatory authorities to delay or suspend our ongoing studies or delay the analysis of data from our completed or ongoing studies. We rely, in part, on third parties to assist us in managing and monitoring our preclinical and clinical studies. We generally do not have control over the amount and timing of resources that our business partners devote to our drug candidates. Our reliance on these third parties may result in delays in completing or failure to complete studies if third parties fail to perform their obligations to us. If the results of our ongoing and planned studies for our drug candidates are not available when we expect or if we encounter any delay in the analysis of the results of our studies for our drug candidates:

we may not have the financial resources to continue research and development of any of our drug candidates; and

we may not be able to enter into collaborative arrangements relating to any drug candidate subject to delay in regulatory filing.

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Any of the following reasons, among others, could delay or suspend the completion of our ongoing and future studies:

delays in enrolling volunteers;

interruptions in the manufacturing of our drug candidates or other delays in the delivery of materials required for the conduct of our studies;

lower than anticipated retention rate of volunteers in a trial;

unfavorable efficacy results;

serious side effects experienced by study participants relating to the drug candidate;

new communications from regulatory agencies about how to conduct these studies; or

failure to raise additional funds.

If the manufacturers of our drug candidates do not comply with current Good Manufacturing Practices regulations, or cannot produce sufficient quantities of our drug candidates to enable us to continue our development, we will fall behind on our business objectives.

Manufacturers producing our drug candidates must follow current Good Manufacturing Practices regulations enforced by the FDA and foreign equivalents. If a manufacturer of our drug candidates does not conform to current Good Manufacturing Practices regulations and cannot be brought up to such a standard, we will be required to find alternative manufacturers that do conform. This may be a long and difficult process, and may delay our ability to receive FDA or foreign regulatory approval of our drug candidates.

We also rely on our manufacturers to supply us with a sufficient quantity of our drug candidates to conduct clinical trials. If we have difficulty in the future obtaining our required quantity and quality of supply, we could experience significant delays in our development programs and regulatory process.

Our ability to achieve any significant revenue may depend on our ability to establish effective sales and marketing capabilities.

Our efforts to date have focused on the development and evaluation of our drug candidates. As we continue preclinical and clinical studies and seek to commercialize our drug candidates, we may need to build a sales and marketing infrastructure. As a company, we have no experience in the sales and marketing of pharmaceutical products. If we fail to establish a sufficient marketing and sales force or to make alternative arrangements to have our drug candidates marketed and sold by others on attractive terms, it will impair our ability to commercialize our drug candidates and to enter new or existing markets. Our inability to effectively enter these markets would materially and adversely affect our ability to generate significant revenues.

If we were to lose the services of Richard B. Hollis, or fail to attract or retain qualified personnel in the future, our business objectives would be more difficult to implement, adversely affecting our operations.

Our ability to successfully implement our business strategy depends highly upon our Chief Executive Officer, Richard B. Hollis. The loss of Mr. Hollis' services could impede the achievement of our objectives. We also highly depend on our ability to hire and retain qualified scientific and technical personnel. The competition for these employees is intense. Thus, we may not be able to continue to hire and retain the qualified personnel needed for our business. Loss of the services of or the failure to recruit key scientific and technical personnel could adversely affect our business, operating results and financial condition.

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We may face product liability claims related to the use or misuse of our drug candidates, which may cause us to incur significant losses.

We are currently exposed to the risk of product liability claims due to administration of our drug candidates in clinical trials, since the use or misuse of our drug candidates during a clinical trial could potentially result in injury or death. If we are able to commercialize our products, we will also be subject to the risk of losses in the future due to product liability claims in the event that the use or misuse of our commercial products results in injury or death. We currently maintain liability insurance on a claims-made basis. Because we cannot predict the magnitude or the number of claims that may be brought against us in the future, we do not know whether the insurance policies' coverage limits are adequate. The insurance is expensive, difficult to obtain and may not be available in the future on acceptable terms, or at all. Any claims against us, regardless of their merit, could substantially increase our costs and cause us to incur significant losses.

Our securities could be subject to extreme price fluctuations that could adversely affect your investment.

The market prices for securities of life sciences companies, particularly those that are not profitable, are highly volatile. Publicized events and announcements may have a significant impact on the market price of our common stock. For example:

biological or medical discoveries by competitors;

public concern about the safety of our drug candidates;

delays in the conduct or analysis of our preclinical or clinical studies;

unfavorable results from preclinical or clinical studies;

delays in obtaining or failure to obtain purchase orders of our drug candidates;

announcements in the scientific and research community;

changes in the potential commercial markets for our drug candidates;

unfavorable developments concerning patents or other proprietary rights;

unfavorable domestic or foreign regulatory or governmental developments or actions; or

broader economic, industry and market trends unrelated to our performance.

may have the effect of temporarily or permanently driving down the price of our common stock. In addition, the stock market from time to time experiences extreme price and volume fluctuations which particularly affect the market prices for emerging and life sciences companies, such as ours, and which are often unrelated to the operating performance of the affected companies. For example, our stock price has ranged from \$4.09 to \$16.50 between January 1, 2004 and November 1, 2006.

These broad market fluctuations may adversely affect the ability of a stockholder to dispose of his shares at a price equal to or above the price at which the shares were purchased. In addition, in the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Any litigation against our company, including this type of litigation, could

result in substantial costs and a diversion of management's attention and resources, which could materially adversely affect our business, financial condition and results of operations.

We may be delisted from The Nasdaq Global Market, which could materially limit the trading market for our common stock.

Our common stock is quoted on The Nasdaq Global Market. In order to continue to be included in The Nasdaq Global Market, a company must meet Nasdaq's maintenance criteria. We may not be able to continue to meet these listing criteria. Failure to meet Nasdaq's maintenance criteria may result in the delisting of our

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common stock from The Nasdaq Global Market. If our common stock is delisted, in order to have our common stock relisted on The Nasdaq Global Market we would be required to meet the criteria for initial listing, which are more stringent than the maintenance criteria. Accordingly, if we were delisted we may not be able to have our common stock relisted on The Nasdaq Global Market. If our common stock is removed from listing on The Nasdaq Global Market, it may become more difficult for us to raise funds.

Because stock ownership is concentrated, you and other investors will have minimal influence on stockholders' decisions.

Assuming that outstanding warrants and options have not been exercised, Richard B. Hollis, our Chief Executive Officer, owns approximately 9% of our outstanding common stock as of September 30, 2006. Assuming that Mr. Hollis exercises all of his outstanding warrants and options that vest within 60 days of September 30, 2006, Mr. Hollis would beneficially own approximately 14% of our outstanding common stock. As a result, Mr. Hollis may be able to significantly influence our management and all matters requiring stockholder approval, including the election of directors. Such concentration of ownership may also have the effect of delaying or preventing a change in control of our company.

Substantial sales of our stock may impact the market price of our common stock.

Future sales of substantial amounts of our common stock, including shares that we may issue upon exercise of options and warrants, could adversely affect the market price of our common stock. Further, if we raise additional funds through the issuance of common stock or securities convertible into or exercisable for common stock, the percentage ownership of our stockholders will be reduced and the price of our common stock may fall.

Issuing preferred stock with rights senior to those of our common stock could adversely affect holders of common stock.

Our charter documents give our board of directors the authority to issue shares of preferred stock without a vote or action by our stockholders. The board also has the authority to determine the terms of preferred stock, including price, preferences and voting rights. The rights granted to holders of preferred stock may adversely affect the rights of holders of our common stock. For example, a series of preferred stock may be granted the right to receive a liquidation preference—a pre-set distribution in the event of a liquidation—that would reduce the amount available for distribution to holders of common stock. In addition, the issuance of preferred stock could make it more difficult for a third party to acquire a majority of our outstanding voting stock. As a result, common stockholders could be prevented from participating in transactions that would offer an optimal price for their shares.

We have broad discretion over the use of the net proceeds from this offering.

We have broad discretion to allocate the net proceeds of this offering. We expect a major use of these proceeds will be research and development. The timing and amount of our actual expenditures, however, are subject to change and will be based on many factors, including:

progress with our preclinical and clinical trials;

the time and costs involved in obtaining regulatory approvals for the marketing of any of our drug candidates;

the costs of manufacturing any of our drug candidates; and

the costs involved in preparing, filing, prosecuting, maintaining and enforcing patents or defending ourselves against competing technological and market developments.

Our management will determine, in its sole discretion, how to allocate these proceeds. If we do not wisely allocate the proceeds, our ability to carry out our business plan may be harmed.

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FORWARD-LOOKING INFORMATION

This prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference contain some forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as anticipate, estimate, plans, projects, continuing, ongoing, expects, management believes, we believe, we intend, or may. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference.

You should be aware that our actual results could differ materially from those contained in the forward-looking statements due to a number of factors, including:

failure to achieve positive results in clinical trials involving our drug candidates;

failure to obtain government regulatory approvals for our drug candidates;

our ability to obtain stockpiling orders for our drug candidates from U.S. and foreign governments;

competitive factors;

our ability to raise additional capital;

uncertainty regarding our patents and patent rights;

relationships with our consultants, academic collaborators and other third-party service providers; and

our ability to enter into future collaborative agreements.

Because the risk factors referred to above, as well as the risk factors on page S-1 of this prospectus supplement and beginning on page 2 of the accompanying prospectus, could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by us or on our behalf, you should not place undue reliance on any forward-looking statements. Further, any forward-looking statement speaks only as of the date on which it is made. Moreover, new factors that may impact those forward-looking statements may emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of any single factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock we are offering will be approximately \$24.4 million, assuming we sell the maximum number of shares offered hereby. Net proceeds is what we expect to receive after paying the placement agent fees and other expenses of the offering. Because there is no minimum offering amount required as a condition to closing this offering, the actual public offering amount, placement fees and proceeds to us, if any, are not presently determinable and may be substantially less than the maximum amount set forth above. We will not receive any proceeds from the warrants we are offering unless and until such warrants are exercised. If the warrants were fully exercised, we would receive additional proceeds of \$7.0 million. We will not pay the placement agents any fee with respect to shares of our common stock issued upon exercise of the warrants.

We currently intend to use the net proceeds from this offering for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we are not currently planning or negotiating any such transactions. Pending these uses, the net proceeds will be deposited primarily in a money market mutual fund with a large financial institution.

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Our net tangible book value on September 30, 2006 was approximately \$44.8 million, or \$1.79 per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares outstanding.

Assuming we sell all of the 4,000,000 shares of common stock offered by us by this prospectus supplement, at the offering price of \$6.50 per share and after deducting the placement agent fees and estimated offering expenses, our pro forma net tangible book value on September 30, 2006 would have been \$69.1 million, or \$2.38 per share. The adjustments made to determine pro forma net tangible book value per share are the following:

An increase in total assets to reflect the net proceeds of the offering assuming we sell the maximum number of shares offered hereby as described under Use of Proceeds.

The addition of the number of shares offered by this prospectus supplement to the number of shares outstanding, assuming we sell the maximum number of shares offered hereby.

Our pro forma net tangible book value per share calculation assumes no exercise of the warrants offered hereby.

The following table illustrates the pro forma increase in net tangible book value of \$0.59 per share and the dilution (the difference between the offering price per share and net tangible book value per share) to new investors:

| | |
|---|-------------|
| Offering price per share | \$ 6.50 |
| Net tangible book value per share as of September 30, 2006 | \$ 1.79 |
| Increase in net tangible book value per share attributable to the offering | 0.59 |
| Pro forma net tangible book value per share as of September 30, 2006, after giving effect to the offering | 2.38 |
| Dilution per share to new investors in the offering | \$ 4.12 |

The following table shows the difference between existing stockholders and new investors with respect to the number of shares purchased from us, the total consideration paid and the average price paid per share. The table assumes that we have sold all of the 4,000,000 shares of common stock offered by us by this prospectus supplement at the offering price of \$6.50 per share. This table also assumes no exercise of the warrants offered hereby.

| | Shares Purchased | | Total Consideration | | Average Price |
|-----------------------|-------------------|-------------|-----------------------|-------------|----------------|
| | Number | Percent | Amount | Percent | Per Share |
| Existing stockholders | 24,969,711 | 86.2% | \$ 228,800,000 | 89.8% | \$ 9.16 |
| New investors | 4,000,000 | 13.8 | 26,000,000 | 10.2 | 6.50 |
| Total | 28,969,711 | 100% | \$ 254,800,000 | 100% | \$ 8.80 |

The number of shares of our common stock to be outstanding after the offering is based on 24,969,711 shares outstanding as of September 30, 2006 and excludes:

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6,787,387 shares of common stock issuable upon the exercise of outstanding stock options with a weighted average exercise price of \$8.89 per share;

1,761,924 shares of common stock available for future issuance upon exercise of outstanding warrants at a weighted average exercise price of \$9.27 per share;

1,033,126 shares of common stock available for future grant under our stock option plans; and

97,900 shares of common stock available for matching contributions under our 401(k) plan.

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Table of Contents**PLAN OF DISTRIBUTION**

We are offering the shares of common stock and warrants to purchase shares of common stock through placement agents. Subject to the terms and conditions contained in the placement agency agreement, dated November 7, 2006, Rodman & Renshaw, LLC and Canaccord Adams, Inc. have agreed to act as placement agents for the sale of up to 4,000,000 shares of our common stock and warrants to purchase up to an additional 800,000 shares of our common stock. The placement agents are not purchasing or selling any shares by this prospectus supplement and the accompanying prospectus, nor is it required to arrange the purchase or sale of sell any specific number or dollar amount of the shares, but has agreed to use reasonable efforts to arrange for the sale of all of the shares and warrants offered hereby.

The placement agents propose to arrange for the sale to one or more purchasers of the shares of common stock and the warrants to purchase shares of our common stock offered pursuant to this prospectus supplement and the accompanying prospectus through direct purchase agreements between the purchasers and us. We will pay the placement agents a total commission equal to 6.0% of the gross proceeds of the sales of shares of common stock. The placement agents will not receive any commission with respect to the warrants offered hereby or the shares of our common stock issuable upon exercise of the warrants.

The following table shows the per share and total commissions we will pay to the placement agents in connection with the sale of the shares offered pursuant to this prospectus supplement and the accompanying prospectus, assuming the purchase of all of the shares offered hereby.

| | |
|------------------------|--------------|
| Per share | \$ 0.39 |
| Maximum offering total | \$ 1,560,000 |

Because there is no minimum offering amount required as a condition to closing in this offering, the actual total offering commissions, if any, are not presently determinable and may be substantially less than the maximum amount set forth above.

Our obligation to issue and sell shares to the purchasers is subject to the conditions set forth in the purchase agreements, which may be waived by us in our discretion. A purchaser's obligation to purchase shares is subject to conditions set forth in the purchase agreement as well, which also may be waived.

We currently anticipate that the sale of up to 4,000,000 shares will be completed on November 13, 2006. We estimate the total expenses of this offering which will be payable by us, excluding the commissions, will be approximately \$85,000.

We have agreed to indemnify the placement agents and purchasers against liabilities under the Securities Act of 1933, as amended.

The placement agency agreement with Rodman & Renshaw, LLC and Canaccord Adams, Inc. is included as an exhibit to our Current Report on Form 8-K that will be filed with the Securities and Exchange Commission in connection with the consummation of this offering.

In order to facilitate the offering of the common stock, the placement agents may engage in transactions that stabilize, maintain or otherwise affect the market price of our common stock. Any of these activities may maintain the market price of our common stock at a level above that which might otherwise prevail in the open market. The placement agents are not required to engage in these activities and if commenced, may end any of these activities at any time. Neither we nor the placement agents make any representation or prediction as to the effect that these transactions may have on the market price of our common stock. These transactions may occur on The Nasdaq Global Market or otherwise.

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DESCRIPTION OF WARRANTS

We are offering warrants to purchase up to 800,000 shares of common stock at an exercise price of \$8.75 per share, exercisable at any time after the date that is six months following issuance and before the fourth anniversary of issuance.

If at any time after one year from the date of issuance of the warrants there is no effective registration statement registering, or no current prospectus available for, the resale of the warrant shares, then the warrants may also be exercised at such time by means of a cashless exercise, in which event the holder would receive upon exercise the number of shares determined by dividing:

the difference between the volume-weighted average price of a share of our common stock on the trading day preceding exercise and the exercise price of the warrant, multiplied by the number of warrant shares issuable under the warrant pursuant to an exercise of the warrant for cash; by

the volume-weighted average price of a share of our common stock on the trading day preceding exercise.

The number of shares deliverable and/or the exercise price of the warrants are subject to adjustment to reflect stock splits and dividends, distributions on our common stock, and similar corporate actions. The holders of the warrants are entitled to 20 days notice before the record date for certain distributions to holders of our common stock. If certain fundamental transactions, such as a merger, consolidation sale of substantially all of our assets, tender offer or exchange offer with respect to our common stock or reclassification of our common stock, the holders of the warrants will be entitled to receive thereafter in lieu of our common stock, the consideration (if different from common stock), that the holders of our common stock received due to such fundamental transaction. In addition, in the event of certain kinds of fundamental transaction, the holders of the warrants will have the option, exercisable within 30 days after the consummation of the fundamental transaction, to receive an amount of cash equal to the value of the warrants as determined in accordance with a formula specified in the warrants.

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LEGAL MATTERS

The validity of the issuance of the shares of common stock being offered hereby will be passed upon for us by Cooley Godward Kronish LLP, San Diego, California.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended. Therefore, we file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of common stock we are offering under this prospectus supplement and accompanying prospectus. This prospectus supplement and accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement and accompanying prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information at the SEC's public reference rooms in Washington, D.C., New York, NY and Chicago, IL. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC's website at <http://www.sec.gov>. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, N.W., Washington, D.C. 20006.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information that we file with it, 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 supplement and accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with the statements made in the accompanying prospectus or the information incorporated by reference, the statements made in the accompanying prospectus are deemed modified or superseded by the statements made in this prospectus supplement, while information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference into this prospectus supplement the documents listed below and any future filings we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement but prior to the termination of the offering of the shares covered by this prospectus supplement and accompanying prospectus.

We incorporate by reference the documents listed below, except as modified by this prospectus supplement and the accompanying prospectus, and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering (other than information furnished under Item 2.02, Item 7.01 or Item 8.01 of Form 8-K).

Our Annual Report on Form 10-K for the year ended December 31, 2005;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2006, June 30, 2006 and September 30, 2006;

Our Current Reports on Form 8-K which were filed on June 26, 2006, September 27, 2006 and November 3, 2006; and

The description of our common stock included in our registration statement on Form S-4, No. 333-18725, as amended.

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You may request a copy of these filings at no cost, by writing or telephoning us at the following address or telephone number:

Hollis-Eden Pharmaceuticals, Inc.

4435 Eastgate Mall, Suite 400

San Diego, CA 92121

Attn: Chief Accounting Officer

(858) 587-9333

Information contained on our website is not part of this prospectus supplement. You should rely only on the information we have provided or incorporated by reference in this prospectus supplement or in the accompanying prospectus.

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

Subject to completion, dated June 16, 2006

\$75,000,000

HOLLIS-EDEN PHARMACEUTICALS, INC.

Common Stock

Warrants to Purchase Common Stock

From time to time, we may sell common stock and/or warrants to purchase common stock.

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

Our common stock is currently traded on The Nasdaq National Market under the trading symbol HEPH. The applicable prospectus supplement will contain information, where applicable, as to any other listing (if any) on The Nasdaq Stock Market's National Market or any securities exchange of the securities covered by the prospectus supplement.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. SEE RISK FACTORS BEGINNING ON PAGE 2.

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

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. 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 those underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement or, if the offering will be an "at the market" offering, in a post-effective amendment. The net proceeds we expect to receive from any sale of our securities under this prospectus 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.

Prospectus dated

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may sell shares of our common stock and warrants in one or more offerings up to a total aggregate dollar amount of \$75,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell common stock and/or warrants to purchase common stock, we will provide a prospectus supplement that will contain more specific information, as set forth below under The Securities We May Offer. We may also add, update or change in a prospectus supplement or post-effective amendment any of the information contained in this prospectus. Please carefully read both this prospectus and any prospectus supplement together with the additional information described below under Where You Can Find More Information.

The SEC 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 that we incorporate by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

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PROSPECTUS SUMMARY

This summary highlights some information from this prospectus, and it may not contain all of the information that is important to you. You should read the following summary together with the more detailed information regarding our company, our securities and our financial statements and notes to those statements appearing elsewhere in this prospectus or incorporated here by reference. Together, these documents describe the specific terms of the securities we are offering.

Overview

Hollis-Eden Pharmaceuticals, Inc. is a development-stage pharmaceutical company engaged in the discovery, development and commercialization of a proprietary new class of small molecule compounds that act as cellular signalers that drive biological function. These compounds, which are derived from our Hormonal Signaling Technology Platform, are metabolites or synthetic analogs of adrenal steroid hormones. We are developing these compounds with the goal of restoring the biological activity of cellular signaling pathways disrupted by disease and aging. In investigational studies, these compounds have been demonstrated in humans to possess several properties with potential therapeutic benefit they regulate innate and adaptive immunity, reduce nonproductive inflammation, and stimulate cell proliferation.

Our lead product candidate, NEUMUNE (HE2100), is entering late-stage development for the treatment of Acute Radiation Syndrome, or ARS, a life-threatening condition resulting from exposure to high levels of radiation following a nuclear or radiological incident. In addition, we have filed an Investigational New Drug application with the U.S. Food and Drug Administration, or FDA, to begin clinical trials with NEUMUNE in patients at high risk of developing healthcare-acquired infections.

We are also profiling optimized second-generation compounds for potential clinical development in a broad spectrum of therapeutic categories including hematology, metabolic disorders, autoimmune disorders, pulmonary diseases, oncology and infectious diseases.

Hollis-Eden Pharmaceuticals, HE2000, HE2100, HE2200, HE2300, HE2400, IMMUNITIN, NEUMUNE, PHOSPHONOL, REVERSIONEX and the Hollis-Eden Pharmaceuticals stylized logo are trademarks of Hollis-Eden Pharmaceuticals, Inc. This prospectus also includes trademarks owned by other parties. All other trademarks mentioned are the property of their respective owners.

Our principal executive offices are located at 4435 Eastgate Mall, Suite 400, San Diego, CA 92121, and our telephone number is (858) 587-9333. We are incorporated in Delaware.

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RISK FACTORS

An investment in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the risks described in the section entitled "Risk Factors" in our most recent annual report on Form 10-K, which has been filed with the SEC and is incorporated herein by reference along with any amendments or updates thereto reflected in subsequent filings with the SEC. You should also read carefully all of the other information contained in this prospectus, any applicable prospectus supplement, or incorporated by reference in this prospectus. The risks and uncertainties described in our filings with the SEC or in the applicable prospectus supplement and are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of the risks or uncertainties described in our filings with the SEC or in the applicable prospectus supplement or any such additional risks and uncertainties actually occur, our business, results of operations and financial condition could be materially and adversely affected. In that case, the trading price of our securities could decline, and you might lose all or part of your investment.

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FORWARD-LOOKING INFORMATION

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as anticipate, estimate, plans, projects, continuing, ongoing, expect, management believes, we believe, we intend and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus.

You should be aware that our actual results could differ materially from those contained in the forward-looking statements due to a number of factors, including:

failure to achieve positive results in clinical trials involving our drug candidates;

failure to obtain government regulatory approvals for our drug candidates;

competitive factors;

our ability to raise additional capital;

uncertainty regarding our patents and patent rights;

relationships with our consultants, academic collaborators and other third-party service providers; and

our ability to enter into future collaborative agreements.

Because the risk factors referred to above, as well as the risk factors beginning on page 2 of this prospectus, could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by us or on our behalf, you should not place undue reliance on any forward-looking statements. Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to publicly release any revision to the forward-looking statements or reflect events or circumstances after the date of this prospectus. Moreover, new factors that may impact those forward-looking statements may emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of any single factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

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USE OF PROCEEDS

Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of the securities offered hereby for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we currently are not planning or negotiating any such transactions. Pending these uses, the net proceeds will be deposited primarily in a money market mutual fund with a large financial institution.

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THE SECURITIES WE MAY OFFER

We may offer shares of our common stock and warrants to purchase shares of our common stock in one or more offerings from time to time under this prospectus up to a total aggregate dollar amount of \$75,000,000 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 securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

aggregate principal amount or aggregate offering price;

voting or other rights, if any;

exercise prices, if any; and

important federal income tax considerations.

A prospectus supplement or post-effective amendment also may add, update or change information contained in this prospectus or in documents we have incorporated by reference.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

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

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. You should read the description of our common stock included under DESCRIPTION OF CAPITAL STOCK.

Warrants. We may issue warrants to purchase shares of our common stock from time to time. Our board of directors shall determine the terms of the warrants, including exercise prices, exercise periods, redemption or call rights, and the effect on the warrants of a merger, consolidation, sale for other disposition of our business.

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DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 50 million shares of common stock, \$0.01 par value, and 10 million shares of preferred stock, \$0.01 par value.

Common Stock

As of June 12, 2006, there were 24,886,916 shares of our common stock outstanding. The holders of our common stock are entitled to one vote per share on all matters submitted to a vote of our stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of our common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive ratably any dividends out of assets legally available therefor as our board of directors may from time to time determine. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding shares of preferred stock. Holders of our common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of our common stock are fully paid and nonassessable.

Preferred Stock

Our certificate of incorporation authorizes 10,000,000 shares of preferred stock; 4,000 shares have been designated 5% series A convertible preferred stock and 300,000 shares as series B junior participating preferred stock. There are currently no shares of preferred stock outstanding. Under our certificate, our board has the authority, without further action by stockholders, to issue up to 9,696,000 additional shares of preferred stock in one or more series and to fix or alter the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon any wholly unissued series of preferred stock, and to establish from time to time the number of shares constituting any such series or any of them; and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of such series then outstanding. The issuance of preferred stock could adversely affect the voting power of holders of our common stock and reduce the likelihood that such holders will receive dividend payments and payment upon liquidation. Such issuance could have the effect of decreasing the market price of our common stock. The issuance of preferred stock could also have the effect of delaying, deterring or preventing a change in control. We have no present plans to issue any shares of preferred stock.

Warrants

As of June 12, 2006, there were outstanding warrants to purchase an aggregate of 1,783,738 shares of our common stock at a weighted average exercise price of \$9.26 per share.

Anti-Takeover Provisions

Delaware Law. We are governed by the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 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 the business combination is approved in a prescribed manner. A business combination includes a merger, asset sale or other transactions resulting in a financial benefit to the stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years, did own, 15% or more of the corporation's voting stock. The statute could have the effect of delaying, deferring or preventing a change in our control.

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Certificate of Incorporation and Bylaw Provisions. Our certificate of incorporation and bylaws provide that the board of directors will be divided into three classes of directors, with each class serving a staggered three-year term. The classification system of electing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us and may maintain the composition of the board of directors, as the classification of the board of directors generally increases the difficulty of replacing a majority of directors. Our certificate provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by any consent in writing. In addition, our bylaws provide that special meetings of our stockholders may be called only by the Chairman of the board of directors, 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. Our certificate also specifies that the authorized number of directors may be changed only by resolution of the board of directors and does not include a provision for cumulative voting for directors. Under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares may be able to ensure the election of one or more directors. These and other provisions contained in our amended certificate and bylaws could delay or discourage certain types of transactions involving an actual or potential change in control of us or our management, including transactions in which stockholders might otherwise receive a premium for their shares over then current prices. Such provisions could also limit the ability of stockholders to remove current management or approve transactions that stockholders may deem to be in their best interests and could adversely affect the price of our common stock.

Stockholders Rights Plan. We have 300,000 shares of series B junior participating preferred stock authorized and reserved for issuance in connection with our stockholder rights plan set forth in our Rights Agreement dated November 15, 1999 with American Stock Transfer and Trust Company, as rights agent. Each outstanding share of common stock has one preferred stock purchase right. The rights expire on November 14, 2009 unless exchanged or redeemed prior to that date. Our board may extend the expiration date.

If any person or group, except Richard Hollis, acquires 15% or more of our common stock, the rights holders will be entitled to receive upon exercise, the number of shares of common stock that, at that time, have a market value equal to twice the purchase price of the right. The shares of preferred stock acquired upon exercise of a purchase right are not redeemable and are entitled to preferential quarterly dividends. They are also entitled to preferential rights in the event of liquidation. Finally, if any business combination occurs in which our common shares are exchanged for shares of another company, each preferred share will be entitled to receive 100 times the amount received per common share of our company.

If we are acquired in a business combination, the purchase rights holders will be entitled to acquire, for the purchase price, the number of shares of common stock of the acquiring corporation that, at the time, have a market value equal to twice the purchase price of the right. Our board has the right to redeem the purchase rights in certain circumstances for \$.01 per share, subject to adjustment.

The rights plan is designed to protect our stockholders in the event of unsolicited offers to acquire us and other coercive takeover tactics, which, in the board's opinion, would impair its ability to represent our stockholders' interests. The rights plan may make an unsolicited takeover more difficult or less likely to occur or may prevent a takeover, even though the takeover may offer our stockholders the opportunity to sell their stock at a price above the prevailing market rate and may be favored by a majority of our stockholders.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer and Trust. Its address is 59 Maiden Lane, Plaza Level, New York, New York 10038, and its telephone number is (718) 921-8124.

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DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement or post-effective amendment, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement which includes this prospectus or as an exhibit to a current report on Form 8-K.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

the aggregate number of warrants offered;

the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreement and warrants may be modified;

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.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of our common stock, including the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the number of shares of common stock that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5:00 P.M. Pacific time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

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PLAN OF DISTRIBUTION

We may sell the securities being offered hereby through underwriters or dealers, through agents, or directly to one or more purchasers from time to time. The prospectus supplement will describe the terms of the offering of the securities, including:

the name or names of any underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

any initial public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

In addition, if we engage in an at the market offering, we will file a post-effective amendment to the registration statement of which this prospectus is a part, naming the underwriter or underwriters. Only underwriters named in a prospectus supplement or post-effective amendment are underwriters of the securities offered thereby.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell them from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the securities of the series offered by a prospectus supplement or post-effective amendment. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in a prospectus supplement or post-effective amendment, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in a prospectus supplement or post-effective amendment.

Unless a prospectus supplement or post-effective amendment states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in a prospectus supplement or post-effective amendment pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in a prospectus supplement or post-effective amendment.

We may provide agents and underwriters with indemnification against certain civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to such liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

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The warrants to purchase common stock that we may 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 overallocation, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Overallocation involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security 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 National Market may engage in passive market making transactions in the securities on The Nasdaq National 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 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.

In compliance with guidelines of the National Association of Securities Dealers, or NASD, the maximum consideration or discount to be received by any NASD member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Cooley Godward LLP, San Diego, California.

EXPERTS

The financial statements and management's report on the effectiveness of internal control over financial reporting incorporated by reference in this prospectus have been audited by BDO Seidman, LLP, an independent registered public accounting firm, to the extent and for the periods set forth in their reports incorporated herein by reference, and are incorporated herein in reliance upon such reports given upon the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of common stock and warrants to purchase common stock we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy this registration statement, as well as our reports, proxy statements and other information at the SEC's public reference rooms in Washington, D.C., New York, NY and Chicago, IL. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC's Web site at <http://www.sec.gov>. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, N.W., Washington, D.C. 20006.

INCORPORATION BY REFERENCE

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended (the Exchange Act), and file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any reports, proxy statements and other information we file at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. You may also access filed documents at the SEC's web site at www.sec.gov.

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.

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We are incorporating by reference some information about us that we file with the SEC. We are disclosing important information to you by referencing those filed documents. Any information that we reference this way is considered part of this prospectus. The information in this prospectus supersedes information incorporated by reference that we have filed with the SEC prior to the date of this prospectus, while information that we file with the SEC after the date of this prospectus that is incorporated by reference will automatically update and supersede the information in this prospectus.

We incorporate by reference the documents listed below, except as modified by this registration statement, and any future documents we file with the SEC under Section 13 (a), 13(c), 14 or 15 (d) of the Exchange Act, after the date of this prospectus and before the termination of this offering:

Annual Report on Form 10-K for the year ended December 31, 2005;

Quarterly Report on Form 10-Q for the quarter ended March 31, 2006;

Notice of Annual Meeting and Proxy Statement for the 2006 Annual Meeting of Stockholders to be held on June 9, 2006; and

Current Reports on Form 8-K filed January 31, 2006, February 1, 2006 and February 2, 2006.

You may request a copy of these filings at no cost, by writing or telephoning us at the following address or telephone number:

Hollis-Eden Pharmaceuticals, Inc.

4435 Eastgate Mall, Suite 400

San Diego, CA 92121

Attn: Chief Accounting Officer

(858) 587-9333

Information contained on our website is not part of this prospectus. You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement or post-effective amendment. We have not authorized anyone to provide you with information different from that contained in this prospectus or any prospectus supplement or post-effective amendment. The information contained in this prospectus and any prospectus supplement or post-effective amendment is accurate only as of the date of this prospectus and any prospectus supplement or post-effective amendment and, with respect to material incorporated by reference herein or in any prospectus supplement or post-effective amendment, the dates of such referenced material.