

ARENA PHARMACEUTICALS INC
Form 424B5
November 29, 2006

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The information contained in this preliminary prospectus supplement is not complete and may be changed. The registration statement filed with the Securities and Exchange Commission relating to these securities has been declared effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**This filing is made pursuant to Rule 424(b)(5)
under the Securities Act of 1933 in connection
with Registration No. 333-137030**

Subject to Completion, Dated November 29, 2006

8,000,000 Shares

\$ per share

Common Stock

We are offering 8,000,000 shares of our common stock.

Our common stock is listed on the Nasdaq Global Market under the symbol "ARNA." On November 27, 2006, the last reported sale price of our common stock was \$14.13 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement.

| | <u>Per Share</u> | <u>Total</u> |
|-------------------------------------|------------------|--------------|
| Public offering price | \$ | \$ |
| Underwriting discount | \$ | \$ |
| Proceeds, before expenses, to Arena | \$ | \$ |

The underwriters may also purchase up to an additional 1,200,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover over-allotments.

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

The underwriters expect to deliver the shares against payment in New York, New York on _____, 2006.

CIBC World Markets

Sole Book-Running Manager

Cowen and Company

Piper Jaffray

Co-Lead Managers

Needham & Company, LLC

Leerink Swann & Company

Fortis Securities

Morgan Joseph

Oppenheimer & Co.

The date of this prospectus supplement (to the prospectus dated September 12, 2006) is

, 2006

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We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement.

You should rely only on information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

Arena Pharmaceuticals®, Arena® and our corporate logo are registered service marks of Arena. CART is an unregistered service mark of Arena. All other brand names or trademarks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective holders.

Prospectus Supplement Summary

This summary highlights selected information contained in other parts of this prospectus supplement and the accompanying prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our shares. You should read the entire prospectus supplement and accompanying prospectus and the documents incorporated by reference herein and therein carefully.

Arena Pharmaceuticals, Inc.

We are a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing oral drugs in four major therapeutic areas: cardiovascular, central nervous system, inflammatory and metabolic diseases. Our most advanced product candidate, lorcaserin hydrochloride, or lorcaserin, is being investigated in a Phase 3 clinical trial program for the treatment of obesity. Our broad pipeline of novel compounds targeting known and orphan G protein-coupled receptors, an important class of validated drug targets, includes compounds being evaluated independently and with our partners, Ortho-McNeil Pharmaceutical, Inc. and Merck & Co., Inc.

Lorcaserin is a selective 5-HT_{2C} serotonin receptor agonist under investigation for the treatment of obesity. We recently initiated the first of three planned Phase 3 pivotal trials evaluating the efficacy and safety of lorcaserin. This first trial, known as BLOOM (Behavioral modification and Lorcaserin for Overweight and Obesity Management), is a double-blinded, randomized and placebo-controlled trial that is expected to include approximately 100 centers in the United States and to enroll approximately 3,000 overweight and obese patients. A Phase 2b clinical trial demonstrated that treatment with lorcaserin produced a highly statistically significant, progressive and dose-dependent weight loss over a 12-week period. An assessment of echocardiograms for patients in this trial indicated that lorcaserin had no apparent effect on heart valves or pulmonary artery pressure.

We are developing APD125, a selective 5-HT_{2A} serotonin receptor inverse agonist for the treatment of insomnia. We have completed a Phase 1 clinical program of APD125 and expect to initiate a Phase 2 clinical trial of this drug candidate in the first half of 2007. We also expect to initiate a clinical trial for APD791, our drug candidate intended for the treatment and the prevention of arterial thromboembolic diseases such as acute coronary syndrome, in the first half of 2007.

In addition to our internal programs, we have active partnerships with two major pharmaceutical companies: Ortho-McNeil and Merck. Our Ortho-McNeil partnership is focused on diabetes, and our most advanced drug candidate in this partnership is APD668, an Arena-discovered, orally administered drug candidate that is in a Phase 1 clinical trial for the treatment of type 2 diabetes. Our Merck partnership is focused on niacin receptor agonists as treatments for atherosclerosis and other disorders, and several orally administered drug candidates are under evaluation.

Our goal is to discover, develop and commercialize novel, orally administered drugs that address major unmet medical needs by targeting GPCRs. GPCRs are a class of receptors that mediate the majority of cell-to-cell communication in humans. A high percentage of today's prescription drugs target one or more GPCRs, and we believe that approved GPCR-based drugs target about 60, or 30%, of the approximately 190 known non-sensory GPCRs. We believe our GPCR-focused technologies and integrated discovery and development capabilities will allow us to continue to build our pipeline of unique and selective drug candidates.

We intend to commercialize our drug candidates independently and with partners. We have not received regulatory approval for, or generated commercial revenues from, marketing or selling drugs.

Our Research & Development Programs

We have built a broad drug candidate pipeline that targets large and attractive market opportunities in several therapeutic areas. The following table summarizes our current independent and partnered development programs and selected research programs:

| Program (Indication) | Development Status | Next Potential Milestone | Commercial Rights |
|---|--------------------|----------------------------|-------------------|
| Lorcaserin (obesity) | Phase 3 | First DSMB review | Arena |
| APD125 (insomnia) | Phase 1 complete | Initiate Phase 2 | Arena |
| APD791 (arterial thrombosis) | Preclinical | Initiate Phase 1 | Arena |
| APD668 (diabetes) | Phase 1 | Initiate Phase 2 | Ortho-McNeil |
| MK-0354 (undisclosed)(1) | Preclinical | Reinitiate clinical trials | Merck |
| Niacin receptor agonist (atherosclerosis; raise HDL)(1) | Preclinical | Initiate Phase 1 | Merck |
| Type 2 diabetes & obesity | Research | | Arena |
| Wakefulness promoter | Research | | Arena |
| Cardioprotection | Research | | Arena |
| Cytokine & immune cell modulators | Research | | Arena |

Note: The table above does not list all of our research programs.

- (1) Merck discontinued development of MK-0354 for the treatment of atherosclerosis after a Phase 2 clinical trial completed in 2006, but is evaluating MK-0354 for continued development for an undisclosed indication under our partnership. Merck is also continuing to evaluate other niacin receptor agonists for the treatment of atherosclerosis and other disorders under our partnership.

Corporate Information

We were incorporated in Delaware in April 1997, and our principal executive offices are located at 6166 Nancy Ridge Drive, San Diego, California 92121. Our telephone number is (858) 453-7200 and website address is <http://www.arenapharm.com>. Information contained in, or accessible through, our website does not constitute a part of this prospectus supplement or the accompanying prospectus.

The Offering

| | |
|--|---|
| Common stock to be offered | 8,000,000 shares |
| Common stock to be outstanding after this offering | 55,449,825 shares |
| Use of proceeds | We intend to use the net proceeds from this offering for the clinical and preclinical development of our drug candidates, for discovery research for new drug candidates and for general corporate purposes, including working capital. |

Nasdaq Global Market symbol ARNA

The number of shares of common stock to be outstanding after this offering as reflected in the table above is based on the actual number of shares outstanding as of September 30, 2006, which was 47,449,825, and does not include, as of that date:

5,213,978 shares of common stock issuable upon conversion of our Series B-1 Preferred at a conversion price of \$7.50 per share;

1,740,525 shares of common stock issuable upon conversion of our Series B-2 Preferred at a conversion price of \$7.00 per share;

1,106,344 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$10.00 per share;

829,856 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$15.49 per share;

4,541,207 shares of common stock issuable upon the exercise of outstanding options at a weighted average exercise price of \$9.40 per share;

5,470,925 shares of common stock available for future issuance under our 2006 Long-Term Incentive Plan;

736,795 shares of common stock available for future issuance under our 2001 Employee Stock Purchase Plan, as amended; and

114,169 shares of common stock available for future issuance under our Deferred Compensation Plan.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their over-allotment option.

Summary Consolidated Financial Data

The following table sets forth our summary consolidated financial data. This data has been derived from our audited consolidated financial statements for the years ended December 31, 2003, 2004 and 2005, and our unaudited consolidated financial statements for the nine-month periods ended September 30, 2005 and 2006, and as of September 30, 2006, all of which are incorporated by reference into this prospectus supplement. You should read this information in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes, which are incorporated by reference into this prospectus supplement. Certain prior period amounts have been reclassified to conform to current period presentations. The results of operations for interim periods are not necessarily indicative of operating results for the full year.

| | Years Ended December 31, | | | Nine Months Ended September 30, | |
|---|--|-------------|-------------|------------------------------------|-------------|
| | 2003 | 2004 | 2005 | 2005 | 2006 |
| | (Unaudited) | | | | |
| | (In thousands, except for per share amounts) | | | | |
| Consolidated Statements of Operations Data: | | | | | |
| Revenues: | | | | | |
| Total revenues | \$ 12,834 | \$ 13,686 | \$ 23,233 | \$ 17,357 | \$ 25,870 |
| Operating Expenses: | | | | | |
| Research and development | 52,867 | 58,579 | 79,710 | 58,923 | 65,293 |
| General and administrative | 9,808 | 11,066 | 13,122 | 8,399 | 13,238 |
| Amortization of acquired technology | 1,621 | 1,825 | 1,537 | 1,153 | 1,153 |
| Total operating expenses | 64,296 | 71,470 | 94,369 | 68,475 | 79,684 |
| Interest income (expense) and other, net | 4,403 | (208) | 3,235 | 2,287 | 3,455 |
| Net loss | (47,059) | (57,992) | (67,901) | (48,831) | (50,359) |
| Dividends on redeemable convertible preferred stock | (27) | (1,437) | (1,813) | (1,313) | (1,511) |
| Accretion of discount related to redeemable convertible preferred stock | (36) | (1,852) | (7,372) | (7,372) | |
| Net loss allocable to common stockholders | \$ (47,122) | \$ (61,281) | \$ (77,086) | \$ (57,516) | \$ (51,870) |
| Net loss per share allocable to common stockholders, basic and diluted | \$ (1.74) | \$ (2.40) | \$ (2.24) | \$ (1.69) | \$ (1.14) |
| Shares used in calculating net loss per share allocable to common stockholders, basic and diluted | 27,159 | 25,528 | 34,378 | 34,065 | 45,620 |

September 30, 2006

| | Actual | As Adjusted |
|--|------------|----------------|
| (In thousands) | | |
| Consolidated Balance Sheet Data (unaudited): | | |
| Cash, cash equivalents and short-term investments available for sale | \$ 250,812 | \$ 357,482 |
| Working capital | 233,769 | 340,439 |
| Total assets | 331,230 | 437,901 |
| Financing obligation, including deferred interest | 13,630 | 13,630 |
| Accumulated deficit | (297,762) | (297,762) |
| Stockholders' equity | 235,285 | 341,956 |

(1)

A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) the amounts representing cash, cash equivalents and short-term investments available for sale, total assets and stockholders' equity by \$7.6 million.

The as adjusted consolidated balance sheet data gives effect to the sale of 8,000,000 shares of common stock offered by us in this offering at an assumed public offering price of \$14.13 per share (the closing price of our common stock on November 27, 2006) after deducting the underwriting discount and our estimated offering expenses.

The actual and as adjusted consolidated balance sheet data does not give effect to any redemption of our outstanding Series B-1 Preferred. The holders of our Series B-1 Preferred can require us at any time to redeem all or some of their outstanding shares of Series B-1 Preferred. The aggregate redemption price at September 30, 2006 was approximately \$39.1 million, and accrues interest at 4.0% annually. We may be able to satisfy a portion of this amount with shares of our common stock if certain criteria are met.

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Risk Factors

You should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, before you make a decision to invest in our common stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to Our Business

We will need additional funds to conduct our planned research and development efforts, and we may not be able to obtain such funds.

We had losses of \$51.9 million for the nine months ended September 30, 2006 and we had an accumulated deficit of \$297.8 million from our inception in April 1997 through September 30, 2006. Our losses have resulted in large part from the significant research and development expenditures we have made in seeking to identify and validate new drug targets and develop compounds that could become marketed drugs.

We expect that our operating expenses over the next several years will be significant and that we will continue to have significant operating losses in the near term, even if we or our collaborators are successful in advancing our compounds or partnered compounds.

We do not have any commercially available drugs. It takes many years and potentially hundreds of millions of dollars to successfully develop a preclinical or early clinical compound into a marketed drug. We have substantially less money than we need to successfully develop a compound into a marketed drug. Additional funding may not be available to us or may not be available on terms that you or we believe are favorable. If additional funding is not available, we may have to delay, reduce the scope of or eliminate one or more of our research or development programs.

Our stock price could decline significantly based on the results and timing of clinical trials and nonclinical studies of, and decisions affecting, our lead drug candidates.

Results of clinical trials and nonclinical studies of our lead drug candidates may not be viewed favorably by us or third parties, including investors, analysts and potential collaborators. The same may be true of how we design the clinical trials of our lead drug candidates and regulatory decisions affecting those clinical trials. Biotechnology company stock prices have declined significantly when such results and decisions were unfavorable or perceived negatively or when a drug candidate did not otherwise meet expectations.

We have commenced a Phase 3 clinical trial program for our obesity drug candidate, lorcaserin. Results from this program may be negative, may not meet expectations or may be perceived negatively. The design of these clinical trials (which may change significantly and be more expensive than currently anticipated depending on our clinical results and regulatory decisions) may also be viewed negatively by third parties. We may not be successful in completing these clinical trials on our projected timetable, if at all.

We will need to conduct additional preclinical studies to address manufacturing and formulation issues before the Food and Drug Administration, or FDA, will allow us to initiate our planned Phase 2

clinical trial for APD125. Assuming the data generated in the additional preclinical studies are favorable, we expect to be able to start the Phase 2 trial in the first half of 2007, but we cannot be sure when, if ever, the trial will proceed.

Failure to initiate or delays in our clinical trials of lorcaserin, APD125, APD668, APD791 or any of our other drug candidates, or unfavorable results or decisions or negative perceptions regarding any of such trials, could cause our stock price to decline significantly.

Clinical trials for our drug candidates are expensive, time consuming, uncertain and susceptible to change, interruption, delay or termination.

Clinical trials are very expensive, time consuming and difficult to design and implement. Even if the results of our clinical trials are favorable, we estimate that the clinical trials of our most advanced drug candidates, including those being developed by our collaborators, will continue for several years and may take significantly longer than expected to complete. In addition, the FDA, other regulatory authorities, our collaborators, or we may suspend, delay or terminate our clinical trials at any time for various reasons, including:

lack of effectiveness of any drug candidate during clinical trials;

side effects experienced by study participants or other safety issues;

slower than expected rates of patient recruitment and enrollment or lower than expected patient retention rates;

delays or inability to manufacture or obtain sufficient quantities of materials for use in clinical trials;

inadequacy of or changes in our manufacturing process or compound formulation;

delays in obtaining regulatory approvals to commence a study, or "clinical holds" or delays requiring suspension or termination of a study by a regulatory agency, such as the FDA, after a study is commenced;

changes in applicable regulatory policies and regulations;

delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;

uncertainty regarding proper dosing;

unfavorable results from on-going clinical trials and preclinical studies;

failure of our clinical research organizations to comply with all regulatory and contractual requirements or otherwise fail to perform their services in a timely or acceptable manner;

scheduling conflicts with participating clinicians and clinical institutions;

failure to construct appropriate clinical trial protocols;

insufficient data to support regulatory approval;

inability or unwillingness of medical investigators to follow our clinical protocols; or

difficulty in maintaining contact with subjects during or after treatment, which may result in incomplete data.

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There is typically a high rate of attrition from the failure of drug candidates proceeding through clinical trials. We may suffer significant setbacks in our advanced clinical trials similar to a number of other companies in the pharmaceutical and biotechnology industries that have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If we or our collaborators abandon or are delayed in our development efforts related to lorcaserin, APD125, APD668, APD791 or any other drug candidate, we may not be able to generate sufficient revenues to continue our operations at the current level or become profitable, our reputation in the industry and in the investment community would likely be significantly damaged, it may not be possible to complete financings, and our stock price would likely decrease significantly.

Our drug candidates are subject to extensive regulation, and we may not receive required regulatory approvals for our drug candidates.

The clinical development, manufacturing, labeling, packaging, storage, record-keeping, advertising, promotion, export, marketing and distribution of our drug candidates are, and any resulting drugs will be, subject to extensive regulation by the FDA and other regulatory agencies in the United States. Neither our collaborators nor we are permitted to market our drug candidates in the United States until we receive regulatory approval from the FDA. Neither our collaborators nor we have received marketing approval for any of our drug candidates. Specific preclinical data, chemical data, a proposed clinical study protocol and other information must be submitted to the FDA as part of an investigational new drug, or IND, application, and clinical trials may commence only after the IND application becomes effective. To market a new drug in the United States, we must submit to the FDA and obtain FDA approval of a New Drug Application, or NDA. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding manufacturing, process and controls to demonstrate the safety and effectiveness of the drug candidate.

We do not expect any drugs resulting from our research and development efforts to be commercially available for many years, if ever. Our most advanced drug candidates, including lorcaserin and APD125, have not completed the large, pivotal Phase 3 clinical trials for efficacy and safety that are required for FDA approval. Also, we have not previously filed NDAs with the FDA, nor have we previously conducted large scale Phase 3 clinical trials, which are significantly larger and more complex than earlier stage trials. This lack of experience may impede our ability to successfully complete these trials and obtain FDA approval in a timely manner, if at all, for our drug candidates for which development and commercialization is our responsibility. Even if we believe the data collected from clinical trials of our drug candidates are promising, such data may not be sufficient to support approval by the FDA or any other U.S. or foreign regulatory authority. As a result, we cannot predict when or whether regulatory approval will be obtained for any drug we develop. Our business and reputation may be harmed by any failure or significant delay in receiving regulatory approval for the sale of any drugs resulting from our drug candidates.

In order to market any drugs outside of the United States, we and our collaborators must comply with numerous and varying regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with FDA approval as well as additional presently unanticipated risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects associated with regulatory approval in the United States, including the risk

that our drug candidates may not be approved for all indications requested and that such approval may be subject to limitations on the indicated uses for which the drug may be marketed.

The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and our current drug candidates may not have favorable results in later studies or trials.

Preclinical studies and Phase 1 and Phase 2 clinical trials are not primarily designed to test the efficacy of a drug candidate, but rather to test safety, to study pharmacokinetics and pharmacodynamics, and to understand the drug candidate's side effects at various doses and schedules. To date, long-term safety and efficacy have not yet been demonstrated in clinical trials for any of our drug candidates. Favorable results in our early studies or trials may not be repeated in later studies or trials, including continuing preclinical studies and large-scale clinical trials, and our drug candidates in later-stage trials may fail to show desired safety and efficacy despite having progressed through earlier-stage trials. In particular, preclinical data and the limited clinical results that we have obtained for lorcaserin and APD125 may not predict results from studies in larger numbers of subjects drawn from more diverse populations treated for longer periods of time. They also may not predict the ability of lorcaserin or APD125 to achieve or sustain the desired effects in the intended population or to do so safely. Unfavorable results from ongoing preclinical studies or clinical trials could result in delays, modifications or abandonment of ongoing or future clinical trials. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Negative or inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be delayed, repeated or terminated. In addition, we may report top-line data from time to time, which is based on a preliminary analysis of key efficacy and safety data, and is subject to change following a more comprehensive review of the data related to the applicable clinical trial.

Our development of lorcaserin may be adversely impacted by cardiovascular side effects previously associated with fenfluramine and dexfenfluramine.

We have developed lorcaserin to more selectively stimulate the 5-HT_{2C} serotonin receptor because we believe this may avoid the cardiovascular side effects associated with fenfluramine and dexfenfluramine, two serotonin-releasing agents and non-selective serotonin receptor agonists, both of which were withdrawn from the market in 1997 after reported incidences of heart valve disease and pulmonary hypertension associated with their usage. We may not be correct in this belief, however, and lorcaserin's selectivity profile may not avoid the undesired side effects. Moreover, the potential relationship between the activity of lorcaserin and the activity of fenfluramine and dexfenfluramine may result in increased FDA regulatory scrutiny of the safety of lorcaserin and may raise potential adverse publicity in the marketplace, which could affect clinical enrollment or ultimately sales if lorcaserin is approved for sale.

Many of our research and development programs are in early stages of development, and may not result in the commencement of clinical trials.

Many of our research and development programs are in the discovery or preclinical stage of development. The process of discovering compounds with therapeutic potential is expensive, time consuming and unpredictable. Similarly, the process of conducting preclinical studies of compounds that we discover requires the commitment of a substantial amount of our technical and financial resources and personnel. We may not discover additional compounds with therapeutic potential, and any of the compounds for which we are conducting preclinical studies may not result in the

commencement of clinical trials. For example, in December 2005 we announced the commencement of preclinical studies with our anti-platelet compound, APD791, under investigation for the treatment and the prevention of arterial thromboembolic diseases such as acute coronary syndrome. We cannot be certain that results sufficiently favorable to justify commencement of Phase 1 studies will be obtained in these preclinical investigations. If we are unable to identify and develop new drug candidates, we may not be able to maintain a clinical development pipeline or generate revenues.

The technologies on which we rely may not result in the discovery or development of commercially viable drugs.

Our GPCR technologies include technologies that allow us to discover drug-like compounds that act on receptor subtypes of known GPCRs and novel GPCRs where the native ligands have not been identified. These methods of identifying, prioritizing and screening molecular targets are unproven, and may not result in the regulatory approval and commercialization of any therapeutic products. We do not believe that there are any drugs on the market that have been discovered or developed using our proprietary technologies. If we are unable to identify additional drug candidates using our proprietary drug discovery technologies, we may not be able to maintain a clinical development pipeline or generate revenues.

Another company, organization or individual could have, or could develop, a technology targeting GPCRs to discover and develop compounds into drugs more effectively or efficiently than our screening and other technologies. Such a technology could render our technologies, in particular our constitutively activated receptor technology, or CART, and Melanophore technology, obsolete or noncompetitive.

If we are not successful in achieving milestones under our collaborations or in advancing our lead programs, we may have to curtail some of our activities.

If we are not successful in achieving additional milestones under our collaboration with Merck or our diabetes collaboration with Ortho-McNeil or developing or partnering lorcasein or APD125 or any of our other lead programs, we may not be able to raise additional capital or generate significant partnering revenues in the short term. If we do not receive additional capital or partnering revenues, we may need to license some or all of our programs on financial terms that are unfavorable to us. Also, without additional capital or partnering revenues, we would need to re-evaluate our strategy of moving multiple drug discovery and development programs forward while at the same time maintaining our research and discovery capabilities. Based on such evaluation, we may need to significantly curtail some of our current and planned programs and expenditures. We do not know what programs, if any, we would need to curtail, but we believe narrowing our pipeline would reduce our opportunities for success.

Our revenues depend upon the actions of our existing and potential collaborators.

Our revenues were \$23.2 million for the year ended December 31, 2005, and were \$25.9 million for the nine months ended September 30, 2006. Our revenues depend upon the success of our existing collaborations and on our ability to enter into new collaborations. We will receive little additional revenues from our existing collaborators if our own or our collaborators' research, development or, ultimately, marketing efforts are unsuccessful, or if our agreements are terminated early. Typically, our collaborators (and not us) control the development of compounds into drugs after we have met early preclinical scientific milestones. In addition, we may not have complete access to information about the results and status of our collaborators' clinical trials and regulatory programs and strategies. We

are not entitled to the more significant milestone payments under our agreements until our collaborators have advanced compounds in clinical testing. Our partners may not devote adequate resources to the development of our compounds and may not develop or implement a successful clinical or regulatory strategy. Only two of our partners, Merck and Ortho-McNeil, have advanced our drug candidates into clinical testing and paid us the applicable milestone payments. We cannot guarantee that any of the other development, approval or sales milestones in our existing or future collaborations will be achieved, or that we will receive any payments for the achievement of those other milestones.

For the year ended December 31, 2005, and for the nine months ended September 30, 2006, 100% of our revenues were from our collaborations with Merck and Ortho-McNeil. Absent any new collaborators, we expect all of our revenues for 2006 to be derived from our collaborations with Merck and Ortho-McNeil. Our revenues will be materially impacted if:

our agreement with either Merck or Ortho-McNeil is terminated;

our collaborators do not devote their time and financial resources to develop compounds under our collaborations;

our collaborators dispute whether we have achieved a milestone, rights to a particular receptor or compound, or other terms of our agreements;

our collaborators use alternative technologies to our technologies and compete with us in developing drugs; or

our collaborators experience failures in the discovery or development of compounds identified with our technologies or in the clinic or marketplace with other products that cause them to discontinue or slow down our collaboration.

Our ability to enter into new collaborations depends on the outcomes of our preclinical and clinical testing. We do not control these outcomes. In addition, even if our testing is successful, pharmaceutical companies may not partner with us on terms that we believe are acceptable until we have advanced our drug candidates into the clinic and, possibly, through later-stage clinical trials, if at all.

Our collaboration agreements with Merck and Ortho-McNeil may be terminated in certain circumstances.

The term of our amended collaborative research program with Merck is until October 21, 2007. Merck can terminate this program: (i) for "Technical Grounds", by giving 30 days prior notice, if both Merck and we agree that Technical Grounds have occurred; or (ii) in the event of our change in control (as defined in the agreement), by giving 30 days prior notice. Technical Grounds include circumstances where: (1) our joint research committee (a committee comprised of an equal number of Merck and our representatives) concludes that (a) a significant adverse event affecting all the targets, all program compounds and all active compounds under the program has arisen during the conduct of the program, or (b) continuation of the program is no longer scientifically promising because the role of all the targets proves incorrect, or none of the targets are valid as a suitable target for development of a pharmaceutical product; or (2) Merck's patent department, upon consultation with our patent attorneys, makes a reasonable determination that valid third-party patent rights block the achievement of significant program goals.

In addition, either party can terminate the agreement if the other party breaches its material obligations under the agreement by causes and reasons within its control, has not cured such breach

within 90 days of receiving a letter requesting such cure, and there is no dispute as to whether such breach has occurred. In lieu of terminating the agreement, however, Merck can terminate the research program and certain other aspects of the agreement after giving 90 days prior notice if we materially breach our obligations during the course of the program and fail to cure such breach, if such default cannot be cured within such 90-day period, or if we do not commence and diligently continue good faith efforts to cure such default during such period.

The term of the research program under our agreement with Ortho-McNeil is until December 20, 2007. We and Ortho-McNeil each have the right to terminate the agreement early if the other party commits an uncured material breach of its obligations. Further, Ortho-McNeil may terminate the agreement without cause during the term of the research program, provided that in such event it pays us the balance of its research funding obligation for the initial term of the research program in a lump sum, unless the termination is due to a change of control of Arena (as defined in the agreement), in which case Ortho-McNeil may terminate either the agreement or the research program under the agreement without the payment of additional research funding to us. At any time after the end of the research program, Ortho-McNeil may terminate the agreement by providing us at least 60 days prior written notice. Upon termination of the agreement, all rights to the compounds developed under the collaboration will revert to us.

We may have conflicts with our prospective, current or past collaborators that could delay or prevent the development or commercialization of our drug candidates.

We may have conflicts with our prospective, current or past collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, or the ownership of intellectual property. If any conflicts arise with Ortho-McNeil, Merck or any other prospective, current or past collaborator, such collaborator may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our drug candidates, and in turn prevent us from generating revenues:

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

uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations;

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

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

Drug discovery and development is intensely competitive in the therapeutic areas on which we focus. If our competitors develop treatments that are approved faster, marketed better or demonstrated to be more effective or safer than our drug candidates, our commercial opportunities will be reduced or eliminated.

We focus our efforts on GPCRs. Because GPCRs are an important target class for drug discovery efforts, we believe that many pharmaceutical and biotechnology companies and other organizations have internal drug discovery programs focused on GPCRs. Many of the drugs that our collaborators or we are attempting to discover and develop would compete with existing therapies. In addition,

many companies are pursuing the development of new drugs that target the same diseases and conditions that we target. Many of our competitors, particularly large pharmaceutical companies, have substantially greater research and development capabilities and greater financial, scientific and human resources than we do. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before we do for the same indication may achieve a significant competitive advantage, including certain patent and FDA marketing exclusivity rights. In addition, our competitors may develop drugs with fewer side effects, more desirable characteristics (such as route of administration or frequency of dosing) or greater efficacy than our drug candidates or drugs, if any, for the same indication. Any results from our research and development efforts, or from our joint efforts with our existing or any future collaborators, may not compete successfully with existing or newly discovered products or therapies.

Setbacks and consolidation in the pharmaceutical and biotechnology industries, and our or our collaborators' inability to obtain third-party coverage and adequate reimbursement, could make partnering more difficult and diminish our revenues.

Setbacks in the pharmaceutical and biotechnology industries, such as those caused by safety concerns relating to high-profile drugs like Vioxx and Celebrex, competition from generic drugs, litigation, and industry consolidation may have an adverse effect on us. For example, pharmaceutical companies may be less willing to enter into new collaborations or continue existing collaborations if they are integrating a new operation as a result of a merger or acquisition or if their therapeutic areas of focus change following a merger. Moreover, our and our collaborators' ability to commercialize future drugs will depend in part on government regulation and the availability of coverage and adequate reimbursement from third-party payers, including government payers, such as the Medicaid and Medicare programs. Government and third-party payers are increasingly attempting to contain healthcare costs by limiting coverage and reimbursement levels for new drugs. These efforts may limit our commercial opportunities by reducing the amount a potential collaborator is willing to pay to license our programs or drug candidates in the future due to a reduction in the potential revenues from drug sales.

We rely on third parties to conduct our clinical trials. If those parties do not successfully carry out their contractual duties or meet expected deadlines, our drug candidates may not advance in a timely manner or at all.

In the course of our discovery, preclinical testing and clinical trials, we have relied and continue to rely on third parties, including laboratories, investigators, clinical research organizations and manufacturers to perform critical services for us. For example, we have relied, and expect to continue to rely, on contract clinical sites to conduct our clinical trials for lorcaserin and APD125. Clinical research organizations have been, and we expect will continue to be, responsible for many aspects of the trials, including finding and enrolling subjects for testing and administering the trials. These third parties may not be available when we need them or, if they are available, may not comply with all regulatory and contractual requirements or may not otherwise perform their services in a timely or acceptable manner. These independent third parties may also have relationships with other commercial entities, some of which may compete with us. As a result of our dependence on third parties, we may face delays or failures outside of our direct control. These risks also apply to the development activities of our collaborators, and we do not control our collaborators' research and development, clinical trials or regulatory activities. We do not expect any drugs resulting from our collaborators' research and development efforts to be commercially available for many years, if ever.

We or a third-party manufacturer may encounter failures or difficulties that could delay the clinical development or regulatory approval of our drug candidates, or their ultimate commercial production if approved.

We and third parties manufacture our drug candidates. Should we obtain FDA approval for any of our drug candidates, we expect to rely on third-party manufacturers for commercial production. Any performance failure on the part of us or a third-party manufacturer could delay clinical development or regulatory approval of our drug candidates. We or third-party manufacturers may encounter difficulties involving production yields, regulatory compliance, quality control and quality assurance, as well as shortages of qualified personnel. Approval of our drug candidates could be delayed, limited or denied if the FDA does not approve our or a third-party manufacturer's processes or facilities. Manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration of the U.S. Department of Justice, or DEA, and corresponding state and foreign authorities to ensure strict compliance with current good manufacturing practices and other applicable government regulations and corresponding foreign standards. We do not have control over a third-party manufacturer's compliance with these regulations and standards. If one of our manufacturers fails to maintain compliance, the production of our drug candidates could be interrupted or suspended, or our product could be recalled or withdrawn, resulting in delays, additional costs and potentially lost revenues.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time we consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of compounds or technologies. Additional potential transactions we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could harm our operations and financial results.

Our efforts will be seriously jeopardized if we are unable to retain and attract key employees.

Our success depends on the continued contributions of our principal management, development and scientific personnel, and the ability to hire and retain key personnel, particularly in the clinical development area as we transition more of our programs from research into drug development. We face intense competition for such personnel. The loss of services of any principal member of our management or scientific staff, particularly Jack Lief, our President and Chief Executive Officer, and Dominic P. Behan, Ph.D., our Senior Vice President and Chief Scientific Officer, could adversely impact our operations and ability to raise additional capital. To our knowledge, neither Mr. Lief nor Dr. Behan plans to leave, retire or otherwise disassociate with us in the near future.

We may encounter significant delays or problems with our chemical development facility.

We have a chemical development facility for process research, scale-up and production of intermediates and other compounds for research and development purposes, and production of active pharmaceutical ingredients for use in clinical trials. We may encounter delays and problems in operating our chemical development facility due to:

governmental approvals, permits and regulation of the facility;

accidents during operation of the facility;

failure of equipment for the facility;

delays in receiving raw materials from suppliers;

natural or other disasters; or

other factors inherent in operating a complex manufacturing facility.

We may not be able to operate our chemical development facility in a cost-effective manner or in a time frame that is consistent with our expected future manufacturing needs. If this were the case, we would need to seek alternative means to fulfill our manufacturing needs, which could delay progress on our programs.

We use biological materials, hazardous materials, chemicals and radioactive compounds.

Our research and development activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. These materials and various wastes resulting from their use are stored at our facility pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause:

interruption of our research and development efforts;

injury to our employees and others;

environmental damage resulting in costly clean up; and

liabilities under federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products.

In such an event, we may be held liable for any resulting damages, and any such liability could exceed our resources. Although we carry insurance in amounts and type that we consider commercially reasonable, we do not have insurance coverage for losses relating to an interruption of our research and development efforts caused by contamination, and we cannot be certain that the coverage or coverage limits of our insurance policies will be adequate.

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

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

decreased demand for our drug;

injury to our reputation;

withdrawal of clinical trial subjects;

costs of related litigation;

substantial monetary awards to subjects or other claimants;

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loss of revenues; and

the inability to commercialize our drug candidates.

We have limited product liability insurance that covers our clinical trials. We intend to expand our insurance coverage to include the sale of drugs if marketing approval is obtained for any of our drug candidates. However, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost, and we may not have insurance coverage that will be adequate to satisfy any liability that may arise.

Laws and regulations relating to public companies may be costly and impact our ability to attract and retain directors and executive officers.

Laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002 and rules adopted by the Securities and Exchange Commission, or SEC, and by the Nasdaq Global Market, may result in increased costs to us. These laws, rules and regulations could make it more difficult or costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to their requirements.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

Our laboratories, offices and chemical development facility are located in the same business park in San Diego. We depend on our facilities and on our collaborators, contractors and vendors for the continued operation of our business. Natural disasters or other catastrophic events, including terrorist attacks, power interruptions, wildfires and other fires, actions of animal rights activists, earthquakes and wars could disrupt our operations or those of our collaborators, contractors and vendors. Even though we believe we carry commercially reasonable business interruption and liability insurance, and our contractors may carry liability insurance, that protect us in certain events, we might suffer losses as a result of business interruptions that exceed the coverage available under our and our contractors' insurance policies or for which we or our contractors do not have coverage. For example, we are not insured against a terrorist attack. Any natural disaster or catastrophic event could have a significant negative impact on our operations and financial results. Moreover, any such event could delay our research and development programs.

Even if any of our drug candidates receives regulatory approval, our drug candidates will still be subject to extensive post-market regulation.

If we or our collaborators receive regulatory approval for our drug candidates, we will also be subject to ongoing FDA obligations and continued regulatory review, such as continued adverse event reporting requirements. We may also be subject to additional FDA post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize such drugs.

If any of our drug candidates receive United States regulatory approval, the FDA may still impose significant restrictions on the indicated uses for which such drugs may be marketed or impose ongoing requirements for potentially costly post-approval studies. In addition, regulatory agencies subject a drug, its manufacturer and the manufacturer's facilities to continual review and inspections. The

subsequent discovery of previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured, may result in restrictions on the marketing of that drug, including withdrawal of the drug from the market. Failure to comply with applicable regulatory requirements may result in:

issuance of warning letters by the FDA;

imposition of fines and other civil penalties;

criminal prosecutions;

injunctions, suspensions or revocations of marketing licenses;

suspension of any ongoing clinical trials;

suspension of manufacturing;

delays in commercialization;

refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our collaborators;

refusals to permit drugs to be imported or exported to or from the United States;

restrictions on operations, including costly new manufacturing requirements; and

product recalls or seizures.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

New accounting pronouncements may impact our future results of operations.

In December 2004, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards, or SFAS No. 123R, "Share-Based Payment." This statement, which became effective for us on January 1, 2006, changed how we account for share-based compensation, will negatively impact our results of operations and may negatively impact our stock price.

Through December 31, 2005, we accounted for share-based payments to employees and directors using the intrinsic value method. Under this method, we generally did not recognize any compensation related to stock option grants we issued under our equity compensation plans or the discounts we provided under our employee stock purchase plan.

On January 1, 2006, we adopted SFAS No. 123R using the modified-prospective transition method. Under this method, prior period results are not restated. Compensation cost recognized subsequent to adoption includes: (i) compensation cost for all share-based payments granted prior to, but unvested as of, January 1, 2006, based on the grant-date fair value, estimated in accordance with the original provisions of SFAS No. 123, and (ii) compensation cost for all share-based payments granted subsequent to January 1, 2006, based on the grant-date fair value, estimated in accordance with the provisions of SFAS No. 123R. SFAS No. 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow. SFAS No. 123R may also delay when we may

become profitable.

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Future changes in GAAP, including pronouncements relating to revenue recognition, might have a significant effect on our reported results, including reporting of transactions completed before the effective date of such pronouncements.

Risks Relating to Our Intellectual Property

Our success is dependent on intellectual property rights held by us and third parties and our interest in these rights is complex and uncertain.

Our success will depend on our own and on our collaborators' abilities to obtain, secure and defend patents. In particular, the patents directed to our most advanced drug candidates and other compounds discovered using our technologies or that are otherwise part of our collaborations are important to commercializing drugs. We have numerous U.S. and foreign patent applications pending for our technologies, including patent applications on drug lead discovery techniques using CART, genetically altered GPCRs, GPCRs that we have discovered, new uses for previously discovered GPCRs, and compounds discovered using CART and Melanophore and other technologies. The procedures for obtaining a patent in the United States and in most foreign countries are complex. These procedures require an analysis of the scientific technology related to the invention and many sophisticated legal issues. Obtaining patent rights outside the United States often requires the translation of highly technical documents and an improper translation may lead to the loss of, or otherwise jeopardize, the patent protection of our inventions. Ensuring adequate quality of translators and foreign patent attorneys is often very challenging. Consequently, the process for having our patents issue will be difficult, complex and time consuming. Our patent position is very uncertain and we do not know when, or if, we will obtain additional patents for our technologies, or if the scope of the patents obtained will be sufficient to protect our drugs.

In addition, other entities may challenge the validity or enforceability of our patents and patent applications in litigation or administrative proceedings. Even the issuance of a patent is not conclusive as to its validity or enforceability. We cannot make assurances as to how much protection, if any, will be given to our patents if we attempt to enforce them or they are challenged. It is possible that a competitor or a generic pharmaceutical provider may successfully challenge our patents and those challenges may result in reduction or elimination of our patents' coverage.

There is no assurance that any of our patent applications will issue, or that any of the patents will be enforceable or will cover a drug or other commercially significant technology or method, or that the patents will be held to be valid for their expected terms.

In 2000, the United States Patent and Trademark Office began issuing broad patent claims that could allow patent holders to control the use of all drugs that modulate a particular drug target or GPCR, regardless of whether the infringing drug bears any structural resemblance to a chemical compound known to the patent holder at the time of patent filing. We believe that the question of whether these new patent claims are valid is controversial and the subject of litigation. Whether we or our competitors are able to obtain and enforce such patent claims, particularly as they apply to the GPCRs that are the subject of our drug development activities, may have a significant impact on our potential revenues from any drugs that we are able to develop.

We also rely on confidentiality agreements and trade secrets to protect our technologies. However, such information is difficult to protect. We require our employees to contractually agree not to improperly use our confidential information or disclose it to others, but we may be unable to determine if our employees have conformed or will conform to their legal obligations under these agreements. We also enter into confidentiality agreements with prospective collaborators,

collaborators, service providers and consultants, but we may not be able to adequately protect our trade secrets or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of this information. Many of our employees and consultants were, and many of them may currently be, parties to confidentiality agreements with other pharmaceutical and biotechnology companies, and the use of our technologies could violate these agreements. In addition, third parties may independently discover our trade secrets or proprietary information.

Some of our academic institution licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. We generally seek to prevent our partners from disclosing scientific discoveries before we have the opportunity to file patent applications on such discoveries. In some of our collaborations we do not have control over our partners' ability to disclose their own discoveries under the collaboration and in some of our academic collaborations we are limited to relatively short periods to review a proposed publication and file a patent application. If we cannot maintain the confidentiality of our technologies and other confidential information in connection with our collaborations, our ability to receive patent protection or protect our proprietary information will be impaired.

A dispute regarding the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be costly and result in delays in our research and development activities.

Our commercial success also depends upon our ability to develop and manufacture our drug candidates and market and sell drugs, if any, and conduct our research and development activities without infringing or misappropriating the proprietary rights of others. There are many patents and patent applications filed, and that may be filed, by others relating to drug discovery and development programs that could be determined to be similar, identical or superior to ours or our licensors or collaborators. We may be exposed to future litigation by others based on claims that our drug candidates, technologies or activities infringe the intellectual property rights of others. Numerous United States and foreign issued patents and pending patent applications owned by others exist in the area of GPCRs, including some which purport to allow the patent holder to control the use of all drugs that modulate a particular drug target or GPCR, regardless of whether the infringing drug bears any structural resemblance to a chemical compound known to the patent holder at the time of patent filing. Numerous United States and foreign issued patents and pending patent applications owned by others also exist in the therapeutic areas in, and for the therapeutic targets for, which we are developing drugs. These could materially affect our ability to develop our drug candidates or sell drugs, and our activities, or those of our licensors or collaborators, could be determined to infringe these patents. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our drug candidates or technologies may infringe. There also may be existing patents, of which we are not aware, that our drug candidates or technologies may infringe. Further, there may be issued patents and pending patent applications in fields relevant to our business, of which we are or may become aware, that we believe we do not infringe or that we believe are invalid or relate to immaterial portions of our overall drug discovery and development efforts. We cannot assure you that others holding any of these patents or patent applications will not assert infringement claims against us for damages or seeking to enjoin our activities. We also cannot assure you that, in the event of litigation, we will be able to successfully assert any belief we may have as to non-infringement, invalidity or immateriality, or that any infringement claims will be resolved in our favor.

In addition, others may infringe or misappropriate our proprietary rights, and we may have to institute costly legal action to protect our intellectual property rights. We may not be able to afford the costs of enforcing or defending our intellectual property rights against others.

Other organizations, companies and individuals are seeking proprietary positions on genomics information that overlap with the government-sponsored project to sequence the human genome. Our activities, or those of our licensors or collaborators, could be affected by conflicting positions that may exist between any overlapping genomics information made available publicly as a result of the government-sponsored project and genomics information that other organizations, companies or individuals consider to be proprietary.

There could also be significant litigation and other administrative proceedings in our industry that affect us regarding patent and other intellectual property rights. Any legal action or administrative action against us, or our collaborators, claiming damages or seeking to enjoin commercial activities relating to our drug discovery and development programs could:

require us, or our collaborators, to obtain a license to continue to use, manufacture or market the affected drugs, methods or processes, which may not be available on commercially reasonable terms, if at all;

prevent us from importing, making, using, selling or offering to sell the subject matter claimed in patents held by others and subject us to potential liability for damages;

consume a substantial portion of our managerial, scientific and financial resources; or

be costly, regardless of the outcome.

Furthermore, because of the substantial amount of pre-trial document and witness discovery required in connection with intellectual property litigation, there is risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

We have been contacted from time to time by third parties regarding their intellectual property rights, sometimes asserting that we may need a license to use their technologies. If we fail to obtain any required licenses or make any necessary changes to our technologies, we may be unable to develop or commercialize some or all of our drug candidates.

We cannot protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on all of our drug discovery technologies and all of our potential drug candidates throughout the world would be prohibitively expensive. Competitors may use our technologies to develop their own drugs in jurisdictions where we have not obtained patent protection. These drugs may compete with our drugs, if any, and may not be covered by any of our patent claims or other intellectual property rights. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to "work" the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or

government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our drug candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patents and other intellectual property protection, particularly those relating to biotechnology and/or pharmaceuticals, which makes it difficult for us to stop the infringement of our patents. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Risks Relating to Our Securities

Our stock price will likely be volatile, and your investment in our stock could decline in value.

Our stock price has fluctuated historically. From January 1, 2004 to November 27, 2006, the market price of our stock was as low as \$3.48 per share and as high as \$20.68 per share.

Very few biotechnology drug candidates being tested will ultimately receive FDA approval, and a biotechnology company may experience a significant drop in its stock price based on a clinical trial result or regulatory action. Our stock price may fluctuate significantly, depending on a variety of factors, including:

the success or failure of, or other results or decisions affecting, our clinical trials;

the timing of the discovery of drug leads and the development of our drug candidates;

the entrance into a new collaboration or the modification or termination of an existing collaboration;

the timing and receipt by us of milestone and royalty payments or failing to achieve and receive the same;

changes in our research and development budget or the research and development budgets of our existing or potential collaborators;

the introduction of new drug discovery techniques or the introduction or withdrawal of drugs by others that target the same diseases and conditions that we or our collaborators target;

regulatory actions;

expenses related to, and the results of, litigation and other proceedings relating to intellectual property rights or other matters; and

accounting changes, including the expense impact of SFAS No. 123R.

We are not able to control all of these factors. Period-to-period comparisons of our financial results are not necessarily indicative of our future performance. In addition, if our revenues or results of operations in a particular period do not meet stockholders' or analysts' expectations, our stock price may decline and such decline could be significant.

Holders of our Series B Preferred can require us to redeem their Series B Preferred.

On December 24, 2003, we completed a private placement of (i) 3,500 shares of our Series B-1 Preferred, (ii) seven-year warrants to purchase 1,486,200 shares of our common stock at an exercise price of \$10.00 per share (subject to weighted-average adjustment in certain circumstances) and (iii) unit warrants to purchase \$11.5 million of our Series B-2 Preferred and additional seven-year warrants to purchase 450,000 shares of our common stock at an exercise price of \$10.00 per share (subject to weighted-average adjustment in certain circumstances). On April 22, 2005, the investors exercised their unit warrants in full.

The holders of our Series B-1 Preferred can require us at any time to redeem all or some of their shares of Series B-1 Preferred at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties. The stated value is the original holder's investment plus any dividends settled by increasing the stated value at the time the dividend is payable. The aggregate redemption price of our Series B-1 Preferred at September 30, 2006 was approximately \$39.1 million, and accrues interest at 4.0% annually.

The holders of our Series B-2 Preferred will be entitled to require us to redeem their shares of Series B-2 Preferred at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties if, following the 21st month anniversary of the original issue date of the Series B-2 Preferred, the average of the closing prices of our common stock for any 30 consecutive trading days is below \$7.00 per share, which is the conversion price for the Series B-2 Preferred. The aggregate redemption price of our Series B-2 Preferred at September 30, 2006 was approximately \$12.2 million, and accrues interest at 4.0% annually.

Also, the holders of the Series B-2 Preferred may require us to redeem their shares if we issue common stock or common stock equivalents for an effective net price to us per share less than approximately \$5.33 (excluding, among other things, certain common stock and common stock equivalents issued or issuable (i) to our officers, directors, employees or consultants, (ii) in connection with certain strategic partnerships or joint ventures, and (iii) in connection with certain mergers and acquisitions). "Effective net price" is not defined in the Certificate of Designations governing our Series B-2 Preferred. The holders of our Series B-2 Preferred may assert that effective net price should be calculated as the amount we receive after paying any discounts and other expenses related to any such issuance.

At the option of any holder of any Series B Preferred, any Series B Preferred held by such holder may be converted into common stock based on the applicable conversion price then in effect for such shares of Series B Preferred.

In addition to the foregoing redemption rights, at any time following the occurrence of a "Triggering Event", a holder of the Series B Preferred may require us to repurchase all or any portion of the Series B Preferred then held by such holder at a price per share equal to the greater of 115.0% of the stated value or the market value (as calculated under the Certificate of Designations for the Series B-1 Preferred and the Series B-2 Preferred) of such shares of Series B Preferred plus all accrued but unpaid dividends thereon to the date of payment. "Triggering Event" is specifically defined in the Certificate of Designations for the Series B-1 Preferred and the Series B-2 Preferred, and includes any of the following events: (i) immediately prior to a bankruptcy event; (ii) we fail for any reason to timely deliver a certificate evidencing any securities to a purchaser or the exercise or conversion rights of the holders are otherwise suspended for other than a permissible reason; (iii) any of certain events of default (as set forth in the Registration Rights Agreement with the Series B Preferred holders) occur and remain uncured for 60 days; (iv) we fail to make any cash payment required under the Series B Preferred transaction documents and such failure is not timely cured;

(v) the issuance of a going concern opinion by our independent registered public accounting firm that is not timely cured; (vi) we breach a section of the Series B Preferred purchase agreement relating to indebtedness and subordination; or (vii) we default in the timely performance of any other obligation under the Series B Preferred transaction documents and such default is not timely cured.

We will also be required to redeem any shares of the Series B Preferred that remain outstanding on the fifth anniversary of their issuance at a price equal to the amount of the original holder's original investment, plus all accrued but unpaid dividends thereon to the date of such payment.

If we are required to redeem all or some of the currently outstanding shares of our Series B Preferred, we may be able to pay a portion of the redemption price using shares of our common stock if certain enumerated conditions are satisfied, including:

we have sufficient number of shares of common stock available for issuance;

the shares of common stock to be issued are registered under an effective registration statement or are otherwise available for sale under Rule 144(k) under the Securities Act of 1933, as amended, or Securities Act;

our common stock is listed on the Nasdaq Global Market or other eligible market;

the shares to be issued can be issued without violating the rules of the Nasdaq Global Market or any applicable trading market or a provision of our Certificate of Designations for the Series B Preferred; and

no bankruptcy event has occurred.

If we are permitted to satisfy a portion of a redemption by using shares of our common stock, and if we elect to do so, the number of shares to be issued to holders of Series B Preferred will be determined by dividing their cash redemption price by the lesser of the conversion price or 95.0% of the average of the volume weighted average price of our common stock for either 10 or 15 trading days.

There can be no assurance that if we have to redeem our Series B Preferred, that we will be able to pay a portion of the redemption price using shares of our common stock. If we use common stock to redeem a portion of the Series B Preferred, your ownership interest may be significantly diluted. If we are required or elect to redeem shares of the Series B Preferred using cash, we may not have sufficient cash to redeem these shares or to continue our planned research and discovery activities. In such event we may try to raise additional capital by issuing new stock, but there can be no assurance that capital will be available on acceptable terms or at all.

There are a substantial number of shares of our common stock eligible for future sale in the public market, and the sale of these shares could cause the market price of our common stock to fall.

There were 47,449,825 shares of our common stock outstanding as of September 30, 2006. The outstanding shares of our Series B-1 Preferred are convertible into up to 5,213,978 shares of common stock at \$7.50 per share of common stock. The outstanding shares of our Series B-2 Preferred are convertible into up to 1,740,525 shares of common stock at \$7.00 per share of common stock. Holders of Series B Preferred are entitled to receive a 4.0% annual dividend that is payable by issuing common stock or by increasing the amount of common stock that is issuable upon conversion of the Series B Preferred. In connection with the Series B Preferred financing, we issued warrants to acquire 1,936,200 shares of common stock at an exercise price of \$10.00 per share to the two purchasers in our Series B Preferred financing. As of September 30, 2006, 1,106,344 of such warrants are outstanding. Such warrants provide that if the closing price of our common stock is equal to or above

\$14.00 per share for 30 consecutive trading days, upon 10 trading days' prior written notice, we will have the right to, and the warrant holders will have the right to require us to, call and cancel any unexercised portion of the warrants (subject to certain conditions). Following such a call notice, we would be obligated to issue to the warrant holder an exchange warrant entitling the holder to purchase shares of our common stock equal to the "Call Amount" (as such term is defined in the warrants). This exchange warrant would contain the same terms and conditions as the original warrant, except that the maturity date would be seven years from the date of issuance of such exchange warrant and the exercise price would be equal to 130% of the average of the volume weighted average prices of our common stock for the five trading days preceding the original warrant cancellation date.

On March 31, 2006, following our call notice to one of our two warrant holders, Smithfield Fiduciary LLC, such holder exercised its warrants to purchase 829,856 shares of our common stock. In connection with this exercise in full of its warrants, Smithfield claimed that it was entitled to receive exchange warrants that would include a provision that could require us to issue additional exchange warrants in the future. We disagreed with this interpretation and, on June 30, 2006, we entered into a Settlement Agreement and Release with Smithfield. As part of the Settlement Agreement and Release, (a) Smithfield and we provided each other with a release of any claims relating to (i) Smithfield's demand for, and our non-issuance of, exchange warrants, and (ii) any breach or default under certain of our agreements on account of the foregoing, (b) we issued Smithfield a seven-year warrant to purchase 829,856 shares of our common stock at an initial exercise price of \$15.49 per share, and (c) we filed a registration statement covering the sale of the shares of common stock issuable under the new warrant. The new warrant does not contain any right for us, or for the holder to require us, to call the warrant, nor does it provide the holder the right to receive any exchange warrants in the future.

In addition, as of September 30, 2006, there were 4,541,207 options to purchase shares of our common stock issued and outstanding under our Equity Compensation Plans at a weighted average exercise price of \$9.40, 5,470,925 additional shares of common stock issuable under our 2006 Long-Term Incentive Plan, 736,795 shares of common stock reserved for issuance under our 2001 Employee Stock Purchase Plan and 114,169 shares issuable under our Deferred Compensation Plan. A substantial number of the shares described above, when issued upon exercise, will be available for immediate resale in the public market. The market price of our common stock could decline as a result of such resales due to the increased number of shares available for sale in the market.

Any future equity or debt issuances by us may have dilutive or adverse effects on our existing stockholders.

We have financed our operations, and we expect to continue to finance our operations, primarily by issuing and selling our common stock or securities convertible into or exercisable for shares of our common stock. In light of our need for additional financing, we may issue additional shares of common stock or additional convertible securities that could dilute your ownership in our company and may include terms that give new investors rights that are superior to yours. Moreover, any issuances by us of equity securities may be at or below the prevailing market price of our common stock and in any event may have a dilutive impact on your ownership interest, which could cause the market price of our common stock to decline. The terms of our Series B Preferred limit our ability to engage in certain equity issuances.

We may also raise additional funds through the incurrence of debt, and the holders of any debt we may issue would have rights superior to your rights in the event we are not successful and are forced

to seek the protection of bankruptcy laws. The terms of our Series B Preferred limits our ability to incur debt.

Our largest stockholders may take actions that are contrary to your interests, including selling their stock.

A small number of our stockholders hold a significant amount of our outstanding stock. These stockholders may support competing transactions and have interests that are different from yours. Sales of a large number of shares of our stock by these large stockholders or other stockholders within a short period of time could adversely affect our stock price.

We may have disagreements with our warrant holders.

We previously had a disagreement with one of our two warrant holders regarding whether such holder was entitled to receive exchange warrants following the exercise of its warrants in full. Although we entered into a Settlement Agreement and Release with this holder, we may have a similar dispute with the other warrant holder. Moreover, we may be involved with other disagreements with our warrant holders in the future. Such disagreements may lead to litigation which may be expensive and consume management's time, or involve settlements, the terms of which may not be favorable to us.

Provisions of our Series B Preferred may prevent or make it more difficult for us to raise funds or take certain other actions.

Provisions of our Series B Preferred require us to obtain approval of the preferred stockholders, or otherwise trigger rights of first refusal or payment provisions, to (i) offer or sell new securities, other than in specified underwritten offerings or strategic partnerships or joint venture and certain other exceptions, (ii) sell or issue common stock or securities issuable into common stock below certain prices, (iii) incur debt or allow liens on our property, other than certain permitted debt and liens, (iv) amend our certificate of incorporation so as to affect adversely any rights of the preferred stockholders, (v) authorize or create a new class of stock that will be senior or equal to the Series B Preferred in terms of dividends, redemption or distribution of assets, (vi) use more than \$25.0 million in cash for acquisitions, or (vii) take certain other actions. These provisions may make it more difficult for us to take certain corporate actions and could delay, discourage or prevent future financings.

Our rights agreement and certain provisions in our charter documents and Delaware law could delay or prevent a change in management or a takeover attempt that you may consider to be in your best interest.

We have adopted certain anti-takeover provisions, including a stockholders' rights agreement, dated as of October 30, 2002, between us and Computershare Trust Company, Inc., as Rights Agent, as amended. The rights agreement will cause substantial dilution to any person who attempts to acquire us in a manner or on terms not approved by our board of directors.

The rights agreement and Certificate of Designations for the Series B Preferred, as well as other provisions in our certificate of incorporation and bylaws and under Delaware law, could delay or prevent the removal of directors and other management and could make more difficult a merger,

tender offer or proxy contest involving us that you may consider to be in your best interest. For example, these provisions:

allow our board of directors to issue preferred stock without stockholder approval;

limit who can call a special meeting of stockholders;

eliminate stockholder action by written consent; and

establish advance notice requirements for nomination for election to the board of directors or for proposing matters to be acted upon at stockholders meetings.

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

We intend to use the net proceeds from this offering:

for the clinical and preclinical development of our product candidates;

for discovery research for new product candidates; and

for general corporate purposes, including working capital.

Our management will, however, have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock. The proceeds may be used to pay the redemption price for some or all of the outstanding Series B-1 Preferred, if the holders elect to have their preferred stock redeemed.

Forward-Looking Statements

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain "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, or the Exchange Act. These forward-looking statements can generally be identified as such because the context of the statement will include words such as "may," "will," "intends," "plans," "believes," "anticipates," "expects," "estimates," "predicts," "potential," "continue," "likely," "unlikely" or "opportunity," the negative of these words or words of similar import. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in the "Business" section of this prospectus supplement and the "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for the quarters ended subsequent to our filing of such Annual Report on Form 10-K with the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those noted in "Risk Factors" above.

In addition, past financial or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this prospectus supplement or the filing of the accompanying prospectus or documents incorporated by reference herein and therein that include 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 \$106.7 million. If the underwriters exercise the over-allotment option in full, the net proceeds of the shares we sell will be approximately \$122.7 million. "Net proceeds" is what we expect to receive after paying the underwriting discount and other expenses of this offering. For the purpose of estimating net proceeds, we are assuming that the public offering price will be \$14.13 per share (the closing price of our common stock on November 27, 2006). A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) the net proceeds to us from this offering by \$7.6 million.

We intend to use the net proceeds from this offering for the clinical and preclinical development of our product candidates, for discovery research for new product candidates, and for general corporate purposes, including working capital.

The timing and amount of our actual expenditures will be based on many factors, including the timing and success of our clinical trials, whether we partner any of our internal programs and whether we choose to curtail some of our research activities. As a result, we will retain broad discretion in determining how we will allocate the net proceeds from this offering.

Until we use the net proceeds of this offering, we intend to invest the funds in short-term, investment grade, interest-bearing securities.

Dividend Policy

We have never paid any cash dividends on our capital stock. We anticipate that we will retain earnings, if any, to support operations and to finance the growth and development of our business. Therefore, we do not expect to pay cash dividends in the foreseeable future. In addition, we are prohibited from paying cash dividends on any of our capital stock other than our Series B Preferred, which accrues interest at 4.0% annually, without the approval of the holders of the Series B Preferred.

Capitalization

The following table shows:

our capitalization on September 30, 2006; and

our capitalization on September 30, 2006, assuming the completion of this offering at an assumed public offering price of \$14.13 per share (the closing price of our common stock on November 27, 2006), less the underwriting discount and estimated offering expenses payable by us.

| | September 30, 2006 | |
|---|----------------------------|-------------------|
| | Actual | As Adjusted(1) |
| | (In thousands) (Unaudited) | |
| Financing obligation, including deferred interest | \$ 13,630 | \$ 13,630 |
| Redeemable convertible preferred stock | 51,288 | 51,288 |
| Common stock, \$.0001 par value; 142,500,000 shares authorized, 47,449,825 issued and outstanding, actual; 142,500,000 shares authorized, 55,449,825 shares issued and outstanding, as adjusted | 5 | 6 |
| Additional paid-in capital | 556,172 | 662,842 |
| Treasury stock | (23,070) | (23,070) |
| Accumulated other comprehensive loss | (60) | (60) |
| Accumulated deficit | (297,762) | (297,762) |
| | 235,285 | 341,956 |
| Total capitalization | \$ 300,203 | \$ 406,874 |

(1) A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) each of additional paid-in capital, stockholders' equity and total capitalization by \$7.6 million.

The number of shares of common stock as reflected in the actual and as adjusted columns above is based on the actual number of shares outstanding as of September 30, 2006, and does not include, as of that date:

5,213,978 shares of common stock issuable upon conversion of our Series B-1 Preferred at a conversion price of \$7.50 per share;

1,740,525 shares of common stock issuable upon conversion of our Series B-2 Preferred at a conversion price of \$7.00 per share;

1,106,344 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$10.00 per share;

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829,856 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$15.49 per share;

4,541,207 shares of common stock issuable upon the exercise of outstanding options at a weighted average exercise price of \$9.40 per share;

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5,470,925 shares of common stock available for future issuance under our 2006 Long-Term Incentive Plan;

736,795 shares of common stock available for future issuance under our 2001 Employee Stock Purchase Plan, as amended;
and

114,169 shares of common stock available for future issuance under our Deferred Compensation Plan.

The actual and as adjusted column data does not give effect to any redemption of our outstanding Series B-1 Preferred. The holders of our Series B-1 Preferred can require us at any time to redeem all or some of their outstanding shares of Series B-1 Preferred. The aggregate redemption price at September 30, 2006, was approximately \$39.1 million, and accrues interest at 4.0% annually. We may be able to satisfy a portion of this amount with shares of our common stock if certain criteria are met.

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Dilution

Our unaudited net tangible book value on September 30, 2006 was approximately \$228.5 million, or \$4.82 per share of common stock. "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 common stock shares outstanding.

After giving effect to the sale of 8,000,000 shares of common stock offered by us in this offering (at an assumed public offering price of \$14.13 per share, the closing price of our common stock on November 27, 2006), our pro forma net tangible book value on September 30, 2006 would have been \$335.2 million, or \$6.04 per share of common stock. 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 as described under "Use of Proceeds;" and

the addition of the number of shares offered by this prospectus supplement to the number of shares outstanding.

The following table illustrates the pro forma increase in net tangible book value of \$1.22 per share and the dilution (the difference between the offering price per share and net tangible book value per share) to new investors:

| | |
|---|----------|
| Assumed public offering price per share | \$ 14.13 |
| Net tangible book value per share as of September 30, 2006 | \$ 4.82 |
| Increase in net tangible book value per share attributable to offering | \$ 1.22 |
| Pro forma net tangible book value per share as of September 30, 2006, after giving effect to the offering | \$ 6.04 |
| Dilution per share to new investors in the offering | \$ 8.09 |

A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) our pro forma net tangible book value after giving effect to the offering by \$7.6 million, the pro forma net tangible book value per share after giving effect to the offering by approximately \$0.14 per share and the dilution per share to new investors in the offering by approximately \$0.86 per share.

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 the public offering price will be \$14.13 per share.

| | Shares Purchased | | Total Consideration | | Average Price Per Share |
|-----------------------|-------------------|---------------|-----------------------|---------------|----------------------------|
| | Number | Percent | Amount | Percent | |
| Existing stockholders | 47,449,825 | 85.6% | \$ 540,237,626 | 82.7% | \$ 11.39 |
| New investors | 8,000,000 | 14.4% | \$ 113,040,000 | 17.3% | \$ 14.13 |
| Total | 55,449,825 | 100.0% | \$ 653,277,626 | 100.0% | \$ 11.78 |

A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) both the total consideration by new investors and the total consideration by all stockholders by \$8.0 million and increase (decrease) the average price per share by all stockholders by \$0.14 per share.

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The above discussion and tables are based on 47,449,825 common shares outstanding at September 30, 2006, and does not include, as of that date:

5,213,978 shares of common stock issuable upon conversion of our Series B-1 Preferred at a conversion price of \$7.50 per share;

1,740,525 shares of common stock issuable upon conversion of our Series B-2 Preferred at a conversion price of \$7.00 per share;

1,106,344 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$10.00 per share;

829,856 shares of common stock issuable upon the exercise of outstanding warrants at an exercise price of \$15.49 per share;

4,541,207 shares of common stock issuable upon the exercise of outstanding options at a weighted-average exercise price of \$9.40 per share;

5,470,925 shares of common stock available for future issuance under our 2006 Long-Term Incentive Plan;

736,795 shares of common stock available for future issuance under our 2001 Employee Stock Purchase Plan, as amended; and

114,169 shares of common stock available for future issuance under our Deferred Compensation Plan.

Business

We are a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing oral drugs in four major therapeutic areas: cardiovascular, central nervous system, inflammatory and metabolic diseases. Our most advanced product candidate, lorcaserin hydrochloride, or lorcaserin, is being investigated in a Phase 3 clinical trial program for the treatment of obesity. Our broad pipeline of novel compounds targeting known and orphan G protein-coupled receptors, an important class of validated drug targets, includes compounds being evaluated independently and with our partners, Ortho-McNeil Pharmaceutical, Inc. and Merck & Co., Inc.

Lorcaserin is a selective 5-HT_{2C} serotonin receptor agonist under investigation for the treatment of obesity. We recently initiated the first of three planned Phase 3 pivotal trials evaluating the efficacy and safety of lorcaserin. This first trial, known as BLOOM (Behavioral modification and Lorcaserin for Overweight and Obesity Management), is a double-blinded, randomized and placebo-controlled trial that is expected to include approximately 100 centers in the United States and to enroll approximately 3,000 overweight and obese patients. A Phase 2b clinical trial demonstrated that treatment with lorcaserin produced a highly statistically significant, progressive and dose-dependent weight loss over a 12-week period. An assessment of echocardiograms for patients in this trial indicated that lorcaserin had no apparent effect on heart valves or pulmonary artery pressure.

We are developing APD125, a selective 5-HT_{2A} serotonin receptor inverse agonist for the treatment of insomnia. We have completed a Phase 1 clinical program of APD125 and expect to initiate a Phase 2 clinical trial of this drug candidate in the first half of 2007. We also expect to initiate a clinical trial for APD791, our drug candidate intended for the treatment and the prevention of arterial thromboembolic diseases such as acute coronary syndrome, in the first half of 2007.

In addition to our internal programs, we have active partnerships with two major pharmaceutical companies: Ortho-McNeil and Merck. Our Ortho-McNeil partnership is focused on diabetes, and our most advanced drug candidate in this partnership is APD668, an Arena-discovered, orally administered drug candidate that is in a Phase 1 clinical trial for the treatment of type 2 diabetes. Our Merck partnership is focused on niacin receptor agonists as treatments for atherosclerosis and other disorders, and several orally administered drug candidates are under evaluation.

Our goal is to discover, develop and commercialize novel, orally administered drugs that address major unmet medical needs by targeting GPCRs. GPCRs are a class of receptors that mediate the majority of cell-to-cell communication in humans. A high percentage of today's prescription drugs target one or more GPCRs, and we believe that approved GPCR-based drugs target about 60, or 30%, of the approximately 190 known non-sensory GPCRs. We believe our GPCR-focused technologies and integrated discovery and development capabilities will allow us to continue to build our pipeline of unique and selective drug candidates.

We intend to commercialize our drug candidates independently and with partners. We have not received regulatory approval for, or generated commercial revenues from, marketing or selling drugs.

Our Research & Development Programs

We have built a broad drug candidate pipeline that targets large and attractive market opportunities in several therapeutic areas. The following table summarizes our current independent and partnered development programs and selected research programs:

| Program (Indication) | Development Status | Next Potential Milestone | Commercial Rights |
|---|--------------------|----------------------------|-------------------|
| Lorcaserin (obesity) | Phase 3 | First DSMB review | Arena |
| APD125 (insomnia) | Phase 1 complete | Initiate Phase 2 | Arena |
| APD791 (arterial thrombosis) | Preclinical | Initiate Phase 1 | Arena |
| APD668 (diabetes) | Phase 1 | Initiate Phase 2 | Ortho-McNeil |
| MK-0354 (undisclosed)(1) | Preclinical | Reinitiate clinical trials | Merck |
| Niacin receptor agonist (atherosclerosis; raise HDL)(1) | Preclinical | Initiate Phase 1 | Merck |
| Type 2 diabetes & obesity | Research | | Arena |
| Wakefulness promoter | Research | | Arena |
| Cardioprotection | Research | | Arena |
| Cytokine & immune cell modulators | Research | | Arena |

Note: The table above does not list all of our research programs.

(1)

Merck discontinued development of MK-0354 for the treatment of atherosclerosis after a Phase 2 clinical trial completed in 2006, but is evaluating MK-0354 for continued development for an undisclosed indication under our partnership. Merck is also continuing to evaluate other niacin receptor agonists for the treatment of atherosclerosis and other disorders under our partnership.

Lorcaserin

Our most advanced drug candidate, lorcaserin, is being investigated in a Phase 3 clinical trial program for the treatment of obesity. Obesity affects tens of millions of adults and children in the United States and poses serious long-term threats to their health and welfare. Studies have shown that modest weight loss of as little as five percent of initial body weight can result in a meaningful reduction in the risks associated with obesity, such as diabetes. Currently, medical treatment options for obesity are limited.

Lorcaserin is a novel and selective 5-HT_{2C} serotonin receptor agonist. Two non-selective, serotonin-acting drugs, fenfluramine and dexfenfluramine (often used in combination with phentermine, the combination of which was commonly referred to as "fen-phen"), although efficacious as appetite suppressants and for treatment of obesity, were withdrawn from the market in 1997 after incidences of heart valve disease and pulmonary hypertension were associated with their usage. The fenfluramines release serotonin and have the potential to activate all 14 serotonin receptors, including the 5-HT_{2B} receptor. Stimulation of this receptor has been implicated in the heart valve abnormalities associated with these drugs. Based on our preclinical studies and clinical trial data to date, we believe that lorcaserin stimulates the 5-HT_{2C} serotonin receptor more selectively than fenfluramine and dexfenfluramine, and is therefore unlikely to cause the cardiovascular side effects associated with those drugs. This belief is supported by data from our 4- and 12-week clinical trials, in which no apparent effects of the drug were seen on heart valves or pulmonary arterial pressure. However, additional longer-term trials will be needed to confirm these results. This is part of the focus of our Phase 3 clinical trial program, which began with the BLOOM trial we initiated in September 2006.

Mechanism of Action. We believe lorcaserin selectively stimulates the 5-HT_{2C} serotonin receptor, a GPCR located in the hypothalamus. Stimulation of this hypothalamic receptor is strongly associated

with feeding behavior and satiety. We conducted preclinical studies examining the activity and 5-HT receptor subtype specificity of lorcaserin. In these studies, lorcaserin demonstrated a high affinity and specificity for the 5-HT_{2C} receptor, with approximately 15-fold and 100-fold selectivity over the 5-HT_{2A} and 5-HT_{2B} receptors, respectively, and no pharmacologic activity at other serotonin receptors.

Clinical Development. We have completed multiple Phase 1 and Phase 2 clinical trials of lorcaserin. The first Phase 2 trial included 352 obese patients dosed for 28 days, and the second included 469 obese patients dosed for 12 weeks. Highly statistically significant, clinically meaningful and progressive weight loss was observed in both Phase 2 trials, without evidence of any apparent drug effect on heart valves or pulmonary artery pressure, as assessed by serial echocardiograms. Lorcaserin was also generally well tolerated in both Phase 2 trials.

The randomized, double-blinded, multiple-dose, 28-day Phase 2a clinical trial of lorcaserin in obese patients compared doses of 1 mg, 5 mg and 15 mg to placebo. Over the 28-day treatment period there was a highly statistically significant ($p=0.0002$) mean weight loss of 2.9 pounds in patients taking the 15 mg dose of lorcaserin versus 0.9 pounds for the placebo group. Lorcaserin was generally well tolerated at all doses investigated in the trial. An assessment of follow-up echocardiograms taken at the end of dosing and approximately 90 days after patients received their first doses of lorcaserin in the Phase 2a clinical trial indicated no apparent drug effect on heart valves or pulmonary artery pressure.

A randomized, double-blinded, multiple-dose, 12-week Phase 2b clinical trial of lorcaserin in obese patients compared doses of 10 mg and 15 mg once daily and 20 mg (10 mg dosed twice daily) of lorcaserin to placebo. The primary endpoint of the trial, which excluded diet and exercise advice, was weight loss after administration of lorcaserin for 12 weeks. Patients completing the 12-week treatment period with lorcaserin achieved a highly statistically significant ($p<0.001$) mean weight loss of 4.0, 5.7 and 7.9 pounds at daily doses of 10 mg, 15 mg and 20 mg (10 mg dosed twice daily), respectively, compared to 0.7 pounds for the placebo group. Using an intent-to-treat, last-observation-carried-forward analysis, treatment with lorcaserin was also associated with a highly statistically significant ($p<0.001$) mean weight loss of 3.7, 4.8 and 6.8 pounds at daily doses of 10 mg, 15 mg and 20 mg (10 mg dosed twice daily), respectively, in patients taking lorcaserin compared to 0.4 pounds for the placebo group. The proportions of patients completing the 12-week treatment period with lorcaserin who achieved a 5% or greater weight loss from baseline were 13% ($p=0.015$), 20% ($p<0.001$) and 31% ($p<0.001$) at daily doses of 10 mg, 15 mg and 20 mg (10 mg dosed twice daily), respectively, compared to 2% in the placebo group. Lorcaserin was generally well tolerated at all doses investigated in the trial. Adverse events occurring in greater than 5% in any of the dosed groups were headache, nausea, dizziness, vomiting, dry mouth, nasopharyngitis, fatigue and urinary tract infection. As demonstrated by the graph below, average weight loss increased progressively at each time point measured throughout the trial for all lorcaserin dose groups, and was dose-dependent. As expected, after patients stopped taking lorcaserin, they started to regain weight.

Lorcaserin Phase 2b Clinical Trial: Weight Loss by Dose and Time

An assessment of echocardiograms at baseline and day 85 indicated no apparent lorcaserin effect on heart valves or pulmonary artery pressure. No changes in valvular regurgitation greater than one category, no significant differences between any treatment group and placebo in number of increases in valve regurgitation at any valve, and no significant increases in pulmonary artery pressure in any group were identified in the echocardiogram results. Valvular regurgitation was scored on a five-point scale (absent, trace, mild, moderate or severe) and is a measure of back flow or leakage of blood through heart valves, due to imperfect valve closing. FDA defined valvulopathy (mild or greater aortic valve regurgitation or moderate or greater mitral valve regurgitation) is one measure used in our Phase 3 program to assess potential effects of lorcaserin on heart valves. As demonstrated by the table below, the incidence of FDA-defined valvulopathy was greater in the placebo group versus the combined lorcaserin treated groups.

Lorcaserin Phase 2b Clinical Trial: Incidence of FDA-Defined Valvulopathy

| | Placebo | Lorcaserin | | |
|---------------------------------|---------|------------|-------|-------|
| | | 10 mg | 15 mg | 20 mg |
| Patients | 99 | 99A, 100M | 96 | 96 |
| Aortic (A) Regurgitation | 0 | 0 | 1 | 0 |
| Mitral (M) Regurgitation | 2 | 0 | 1 | 0 |
| Percent by Dose | 2.0% | 0.0% | 2.1% | 0.0% |
| Percent by Treatment | 2.0% | 0.7% | | |

Phase 3 Clinical Development. Following our discussions with the FDA, in September 2006 we initiated the first of three planned pivotal Phase 3 clinical trials to evaluate the safety and efficacy of lorcaserin for the treatment of obesity. The first trial, BLOOM, is double-blinded, randomized and placebo-controlled, and is expected to include approximately 100 centers in the United States and to enroll approximately 3,000 overweight and obese patients. The primary endpoint is the proportion of patients with a 5% or greater weight reduction from baseline at week 52 as compared to placebo.

The BLOOM trial will evaluate a 20 mg dose (10 mg dosed twice daily) of lorcaserin versus placebo over a two-year treatment period, as per the FDA guideline for the evaluation of weight-control drugs, in obese patients (Body Mass Index, or BMI, of 30 to 45) with or without co-morbid conditions and overweight patients (BMI of 27 to 30) with at least one co-morbid condition. All patients will receive echocardiograms at baseline and follow-up echocardiograms at 6, 12, 18 and 24 months after starting the trial. Echocardiograms will be reviewed by an independent Data and Safety Monitoring Board, or DSMB, at 6 and 12 months. Using predetermined safety criteria, the DSMB will review the echocardiographic data and make a judgment as to whether it is appropriate to continue the trial. We expect to complete enrollment in BLOOM around the end of 2006 and for the DSMB to perform its month six review of echocardiograms and make its judgment in the third quarter of 2007.

The complete lorcaserin Phase 3 program is designed to enroll a total of approximately 6,000 patients in three pivotal trials. Assuming a positive month six safety assessment from the DSMB for the BLOOM trial, we intend to initiate two additional Phase 3 trials enrolling a total of approximately 3,000 patients. In these pivotal trials, we plan to evaluate the 20 mg dose (10 mg dosed twice daily) and a 10 mg once-daily dose, each versus placebo over a one-year treatment period, and for one of the trials to enroll patients with type 2 diabetes. Diet and exercise advice will be part of each of the pivotal trials in accordance with the FDA guideline for evaluating weight loss drugs. In addition to the above planned pivotal trial program, we will conduct several other small trials, including drug interaction and abuse potential studies. Assuming we receive favorable results from the DSMB review and the Phase 3 program and other trials, we expect to file an NDA for lorcaserin in 2009.

Intellectual Property. As of October 31, 2006, we owned issued patents that cover compositions of matter for lorcaserin and related compounds and methods of treatment utilizing lorcaserin and related compounds in 35 jurisdictions including the United States, Germany, France, the United Kingdom, Italy and Spain, and applications pending in approximately 21 other jurisdictions including Japan, Canada and China. The patent on lorcaserin issued by the United States Patent and Trademark Office is serial number US 6,953,787 and the corresponding patent granted by the European Patent Office is serial number EP 1 411 881 B1. The earliest priority date for the patents on lorcaserin is 2002. Thus, the terms of these patents are capable of continuing into 2023 in most jurisdictions without taking into account any patent term extension regimes of any country.

APD125

Our lead drug candidate for the treatment of insomnia, APD125, is a novel and selective 5-HT_{2A} serotonin receptor inverse agonist that we expect to enter a Phase 2 clinical trial in the first half of 2007. The National Institutes of Health estimated in 2003 that between 30 to 40 percent of U.S. adults report some level of insomnia and that insomnia is a chronic problem for about 10 percent of the U.S. population. In these cases, the lack of restful sleep impairs the person's ability to carry out their daily responsibilities because they are too tired or have trouble concentrating. However, the great majority of insomnia patients do not seek treatment. Currently marketed therapies for insomnia include Ambien and Ambien CR, marketed by Sanofi-Aventis, Lunesta, marketed by Sepracor, Sonata, marketed by King Pharmaceuticals, Inc., Rozerem, a melatonin MT1 and MT2 agonist marketed by Takeda Pharmaceuticals North America, Inc., and various benzodiazepines, including Valium. With the exception of Rozerem, these therapies work by activating the GABA-A receptor in the brain, causing a general suppressive effect on the central nervous system, or CNS. The GABA-A drugs have side effects including the risk of developing tolerance to the drug and the potential for causing a sensation of dullness and lethargy upon awakening, often referred to as the "hangover effect." In addition, GABA-A drugs are DEA-scheduled controlled substances due to their potential for abuse. Despite these limitations, worldwide sales estimates for insomnia medications were \$3.7 billion in 2005.

Mechanism and Preclinical Data. APD125 acts through a different mechanism than currently marketed insomnia drugs. Based on our preclinical data, we believe that by selectively targeting the 5-HT_{2A} receptor, APD125 blocks one of several CNS-activating pathways, rather than initiating a general CNS-suppressive effect. Because of the different mechanism of action, APD125 may not have the side effects generally associated with currently marketed GABA-A drugs. Through this novel mechanism, APD125 has the potential to reduce insomnia symptoms and improve sleep maintenance by decreasing the number of awakenings during the night, decreasing the amount of wake time after initial sleep onset and increasing the total amount of time spent asleep, including time in deep sleep, or slow wave sleep (stage 3 and stage 4 sleep), the most restorative type of sleep.

Our preclinical studies have shown that, in animals, APD125 increases both the quality and total time of non-REM (rapid eye movement or dream) sleep, the most restorative phase of the sleep cycle in humans, while having no effect on REM sleep. The total increase in non-REM sleep time was manifested by fewer bouts of longer duration, indicating an increase in sleep consolidation. In addition, animals treated with APD125 showed during non-REM sleep an increase in delta power, a brain wave activity associated with increased sleep intensity. The improvements in non-REM duration and quality observed with APD125 administration were at least as robust as those observed with a prototypic GABA-A hypnotic control drug, Ambien. However, unlike Ambien, APD125 did not adversely affect REM sleep in these studies.

Clinical Development. In December 2004, we initiated our Phase 1 clinical trial program of APD125 in healthy volunteers. The Phase 1 program consisted of three randomized, double-blinded and placebo-controlled trials evaluating the single and multiple dose safety and pharmacokinetics of APD125 in normal volunteers. Additionally, the program evaluated the pharmacodynamics of nighttime dosing by assessing effects on sleep patterns in normal volunteers using polysomnography.

The results from the Phase 1 clinical trial program demonstrated that APD125 was well tolerated at single doses up to 160 mg and repeated doses up to 80 mg. At 40 mg, the maximum concentration in the body, or C_{max}, of APD125 plateaued; there were no significant differences in C_{max} among the 40 mg, 80 mg and 160 mg doses. At 80 mg, the total overall exposure, or area under the curve, of APD125 also plateaued; the pharmacokinetics at the 160 mg dose were generally similar to the 80 mg dose. At doses from 10-40 mg, APD125 caused a robust and highly statistically significant (p=0.0002) increase in the amount of deep, or slow wave, sleep in volunteers with normal sleep/wake patterns. In addition, other statistically significant signals indicative of improved sleep maintenance were seen, including statistically significant increases in stage 3 and stage 4 sleep, reductions in stage 1 sleep, reductions in the number of awakenings and an increase in delta power, the deepest form of slow wave sleep. Adverse events were infrequent and APD125 was well tolerated. Based on our Phase 1 results, we do not expect APD125 to be limited by next-day impairment of psychomotor skills or memory.

We believe that our clinical and preclinical data suggest that APD125 has the potential to improve the treatment of insomnia over GABA-A drugs.

Development Plan. The initiation of our Phase 2 clinical trial has been delayed pending further testing to characterize a degradation product identified in an accelerated stability evaluation. If the results of this testing are favorable and the FDA allows this trial to proceed, we plan to begin a Phase 2 clinical trial in the first half of 2007 in a three-way crossover, dose-ranging trial. We expect to enroll approximately 100 patients with insomnia, and measure a number of parameters, including primarily measures of sleep maintenance but also time to sleep onset. We expect results from this trial in the second half of 2007.

Intellectual Property. As of October 31, 2006, we owned issued patents that cover compositions of matter for APD125 and related compounds and methods of treatment utilizing APD125 and related compounds in 35 jurisdictions including Germany, France, the United Kingdom, Italy and Spain, and applications pending in approximately 38 other jurisdictions and international patent authorities including the United States, Japan, Canada and China. The patent on APD125 issued by the European Patent Office is serial number EP 1 558 582 B1. The earliest priority date for the patents on APD125 is 2003. Thus, the terms of these patents are capable of continuing into 2024 in most jurisdictions without taking into account any patent term extension regimes of any country.

APD791

Our lead anti-thrombotic drug candidate, APD791, a novel, orally available and selective inverse agonist of the 5-HT_{2A} serotonin receptor, is in preclinical development. APD791 is intended to lower the risk of arterial thrombosis by reducing the amplification of platelet aggregation, arterial constriction and intimal hyperplasia mediated by serotonin. Thrombosis is the formation of a clot, or thrombus, inside a blood vessel that restricts the flow of blood. The formation of a thrombus is often caused by an injury to the wall of the blood vessel. The injury to the blood vessel activates platelets, which then aggregate and adhere to one another as they start to release certain factors, including serotonin, that facilitate thrombosis. Thrombi that form in diseased atherosclerotic arteries of the heart may cause acute coronary syndrome or myocardial infarction, and thrombi that form in the vessels of the brain may cause stroke. The American Heart Association estimates that in the United States over 12 million people alive in 2003 had survived either a myocardial infarction or a stroke. To reduce the risk of future events, many patients receive daily anti-thrombotic therapy. Worldwide sales of Plavix®, a leading anti-thrombotic marketed by Bristol-Myers Squibb and Sanofi-Aventis, totaled \$5.9 billion in 2005, making it the second best selling drug in any therapeutic category.

Mechanism and Preclinical Data. APD791 is a novel, orally available and selective inverse agonist of the 5-HT_{2A} serotonin receptor. Serotonin activation of the 5-HT_{2A} receptor on platelets and vascular smooth muscle is thought to play an important role in the events leading to thrombosis, and elevated serotonin levels have been associated with increased cardiovascular risk. Normally, when a platelet is activated by one of a number of factors such as thrombin or collagen, the platelet releases serotonin, which, based on preclinical studies, promotes platelet aggregation, vasoconstriction and intimal hyperplasia, or thickening of the vessel wall. By blocking activation of the 5-HT_{2A} receptor on platelets and in other cardiovascular tissues, APD791 may curb platelet aggregation, vasoconstriction and intimal hyperplasia in the clinical setting, thereby reducing the risk of thrombosis. We believe APD791 represents a new approach to reducing the risk of arterial thrombo-embolic disease.

In a preclinical study, APD791 demonstrated improved coronary artery flow in a Folts model, an established model of acute coronary syndrome. In other preclinical studies, APD791 also demonstrated an improved separation of the dose needed for inhibition of thrombosis versus the dose that increased bleeding relative to existing therapies, suggesting that APD791 has the potential for improved safety relative to existing therapies. We believe these results are consistent with blocking the role of serotonin in the thrombosis process.

Development Plan. We advanced APD791 into preclinical development in December 2005 and plan to initiate clinical development in the first half of 2007.

Intellectual Property. As of October 31, 2006, we had patent applications covering compositions of matter for APD791 and related methods of treatment pending before the World Intellectual Property Organization, or WIPO (designating all contracting states), and in 20 additional jurisdictions that are not contracting states of the WIPO.

Ortho-McNeil Collaboration

In our partnership with Ortho-McNeil, we are developing compounds for the potential treatment of type 2 diabetes and other disorders by targeting an orphan GPCR, the Glucose-Dependent Insulinotropic receptor, or the GDIR. The GDIR is a novel receptor discovered by Arena that, in our preclinical models, demonstrated the ability to stimulate insulin production in response to increases in blood glucose. Under this partnership, Ortho-McNeil advanced APD668, a novel, orally administered drug candidate discovered by Arena, into a Phase 1 clinical trial in February 2006. Diabetes is a major worldwide disease. Based on 2003 data, the International Diabetes Foundation estimated that in 2005 there were 194 million adults with diabetes worldwide, an increase of over 40% since 1995. These figures included approximately 16 million in the United States and approximately 48 million in the European region. Approximately 90%, or 175 million, of diabetics worldwide suffer from type 2 diabetes, which is characterized by inadequate response to insulin and/or inadequate secretion of insulin as blood glucose levels rise. Therapies for type 2 diabetes are directed toward correcting the body's inadequate response with oral or injectable medications, or directly modifying insulin levels through injection of insulin or insulin analogs.

Oral medications for type 2 diabetes include insulin releasers such as glyburide, insulin sensitizers such as Actos and Avandia, inhibitors of glucose production by the liver such as metformin, DPP-IV inhibitors like Januvia, as well as Precose and Glyset, which slow the uptake of glucose from the intestine. The worldwide market for diabetes medications exceeded \$10.0 billion and oral anti-diabetes drugs exceeded \$6.0 billion in 2004. However, a significant portion of type 2 diabetics fail oral medication and require injected insulin therapy. Current oral medications for type 2 diabetes have a number of side effects, including hypoglycemia, weight gain and edema. Numerous pharmaceutical and biotechnology companies are seeking to develop insulin sensitizers, novel insulin formulations and other therapeutics to improve the treatment of diabetes.

Mechanism and Preclinical Data. We have found the GDIR to be expressed in beta cells, the cells in the pancreas responsible for producing insulin in response to increases in blood glucose. We believe the GDIR represents a novel mechanism for generating a new class of drugs for diabetes that may offer advantages over current approaches. Our preclinical results indicate that stimulating the GDIR allows beta cells to produce insulin more efficiently in response to changes in blood glucose levels. In addition, we have demonstrated in our preclinical studies that the GDIR stimulates incretin hormone release and thus may enhance glucose homeostasis by this additional mechanism. We have also found in these studies that stimulation of the GDIR leads to increased levels and activity of intracellular factors thought to be involved in the preservation of beta cells. Published research regarding the GLP-1 receptor suggests that it is not amenable to orally administered, small molecule drug development. On the other hand, our preclinical studies suggest that the GDIR receptor is amenable to such drug development. We have discovered potent, selective and orally available small molecule agonists of the GDIR that improve glucose tolerance and lower blood glucose levels in animal models of diabetes. The GDIR mechanism is glucose dependent, so that in our animal studies our compounds only lowered blood glucose when it rose above normal levels, such as after a meal. Our preclinical results indicate these compounds do not lower normal fasting baseline glucose levels in animal models and, therefore, do not cause hypoglycemia, unlike the glucose-insensitive sulphonylureas.

Development and Partnership Status. In December 2004, we entered into a collaboration and license agreement with Ortho-McNeil to further develop compounds for the potential treatment of type 2 diabetes and other disorders. In January 2005, we received a \$17.5 million upfront payment and two milestone payments of \$2.5 million each, and, in February 2006, we achieved a \$5.0 million milestone related to Ortho-McNeil's initiation of the Phase 1 clinical trial of APD668. In September 2006, Ortho-McNeil exercised its option to extend the research term of the agreement for one additional

year, committing to another year of annual research funding of \$2.4 million. We are eligible to receive a total of \$295.0 million in milestone payments for each compound, as well as royalty payments associated with Ortho-McNeil's commercialization of any products discovered under the agreement. These milestone payments include development and approval milestone payments of up to \$132.5 million for the first indication and \$62.5 million for the second indication for each compound, and up to \$100.0 million in sales milestone payments for each product resulting from the collaboration.

Merck Collaboration

In our partnership with Merck, we are collaborating on three GPCRs to develop therapeutics for atherosclerosis and other disorders. We believe one or more of these GPCRs plays a role in regulating plasma lipid profiles, including HDL cholesterol, the so-called "good cholesterol," and is responsible for the HDL-raising activity of niacin. There are very successful drugs available for lowering LDL cholesterol. However, development of novel, effective therapies to increase HDL cholesterol remains a major focus of research. We believe that such therapies may reduce the risk of atherosclerotic heart disease and compete in the large dyslipidemia market.

In September 2006, we announced that Merck completed a Phase 2 clinical trial of MK-0354, a niacin receptor agonist discovered by Arena and intended for the treatment of atherosclerosis and related disorders. Based on the results of this trial, Merck discontinued development of MK-0354 for atherosclerosis, but is evaluating the drug candidate for continued development under our partnership for an undisclosed indication. Merck also continues to evaluate other niacin receptor agonists under our partnership for atherosclerosis and related disorders.

As of September 30, 2006, we had received \$25.5 million from Merck in upfront and milestone payments and an equity investment. We may receive additional milestone payments of up to \$28.0 million for Merck's clinical and marketing achievements, as well as royalty payments associated with Merck's commercialization of any products discovered under the agreement. In addition, we have received research funding from Merck since the inception of our collaboration, and, under our agreement, Merck will pay us \$5.7 million per year for collaboration research through October 21, 2007.

Other Research and Development Programs

Cardiovascular. Acute myocardial infarction, which is commonly known as a heart attack, is often followed in survivors by heart failure. Myocardial infarction and heart failure are often a direct consequence of atherosclerosis, and both remain major causes of death. We have identified certain GPCRs that we believe play a role in the processes related to atherosclerosis and are seeking to identify small molecules directed at these GPCR targets that we believe could provide cardio-protection following myocardial infarction.

CNS Disorders. Many GPCRs are predominately found in the brain or the CNS, and, therefore, we believe targeting GPCRs provides an opportunity to selectively treat various CNS diseases. Many approved drugs for indications, ranging from insomnia and narcolepsy to depression, schizophrenia and Parkinson's disease, target GPCRs. Our discovery efforts in CNS disorders are focused on indications with large market opportunities where current therapies have significant limitations.

Inflammatory Disorders. We are developing small molecule therapeutics that target GPCRs involved in the inflammatory process. We have identified GPCRs that are found in specific immune cell types. We believe these GPCRs modulate the inflammatory process, and we are applying our screening technologies to these targets to identify small molecules that could activate or inhibit these GPCRs.

Some of the GPCRs we are targeting are expressed on T and B cells and macrophages, and could be important in the modulation of key cytokines that mediate inflammatory processes such as TNF-alpha.

Other Diabetes Programs. For metabolic diseases, we are working on a series of orphan GPCR targets in addition to the GDIR in order to develop orally available therapies to treat type 1 and type 2 diabetes. For example, we are conducting research with receptors that may act to regulate glucose uptake, glucose absorption, insulin sensitivity, insulin secretion, lipid levels and production of glucose in the liver. In order to treat general metabolic disease, we have prioritized GPCRs that have the potential to modulate blood glucose and lipid levels.

Other Obesity Programs. In addition to lorcaserin and other compounds that act on the 5-HT_{2C} serotonin receptor, we have discovery programs focused on several different GPCRs implicated in obesity. Our drug discovery efforts are directed at identifying novel drug candidates that target GPCRs in the CNS and peripheral tissues to reduce fat mass in humans. We have identified both known and orphan GPCRs expressed in the hypothalamus, an area of the brain known to be critical for regulating satiety and metabolism, that we believe regulate food intake and weight. We have also identified GPCRs in fat cells that may represent targets for obesity. We have identified early lead compounds for obesity targets other than the 5-HT_{2C} serotonin receptor, and are currently evaluating these compounds for their ability to reduce food intake and body weight.

Our Proprietary GPCR Technologies and Programs

Our drug candidates have resulted from our GPCR-focused drug discovery technologies and capabilities, including Constitutively Activated Receptor Technology, or CART, and our Melanophore technology, and our overall approach to drug discovery and development. GPCRs are categorized as "known" when their naturally occurring, or native, ligands have been identified. Scientists have used molecular cloning in combination with the sequencing of the human genome to identify both additional receptor subtypes of known GPCRs as well as hundreds of novel GPCRs. These novel GPCRs are categorized as "orphan" GPCRs because their native ligands have not been identified. We believe orphan GPCRs offer significant promise for the development of novel GPCR-based therapeutics, and, therefore, are an important focus of our discovery research.

Traditional ligand-based drug screening methods require the time-consuming identification and use of the receptor's native ligand to discover small molecule compounds that will bind at, or close to, the native ligand's binding site on the receptor. In contrast, we have developed technologies that do not require the use of the native ligand. Instead, we are able to activate a GPCR so that the G protein signals without the presence of the native ligand, by using CART and our other technologies. Applying our technologies to constitutively activate GPCRs assists in discovering drug-like compounds by stimulating the GPCR to mimic the biological response that occurs when the native ligand binds to the receptor. These technologies help avoid a major bottleneck in drug discovery efforts at orphan receptors by eliminating the step of first identifying the native ligand. We have found that our constitutive activation technologies can be applied broadly to GPCRs.

Our constitutive activation technologies allow us to simultaneously identify drug leads that act as receptor activators, or agonists, which increase the detected biological response, or act as receptor inhibitors, which decrease the detected response. We can also identify inverse agonists, which inhibit ligand-independent, as well as ligand-dependent, receptor activity.

We believe that our constitutive activation technologies offer several key advantages for drug discovery over traditional screening techniques that require the use of the native ligand including:

not requiring prior identification of the native ligand for an orphan receptor;

enhancing the detection of, and allowing us to simultaneously identify, both receptor inhibitor and receptor activator drug leads;

allowing for the identification of drug leads that inhibit both ligand-independent and ligand-dependent activity; and

providing the ability to discover novel and improved therapeutics directed at known receptors.

We use our constitutive activation technologies in combination with our patented Melanophore technology. Our Melanophore technology is a broadly applicable high-throughput screen for GPCRs. When a GPCR is activated (either by a ligand or independent of a ligand through constitutive activation), the GPCR couples to one or more G proteins, including those belonging to the Gs, Gq, and Gi/o classes. Melanophore technology can detect GPCRs that couple to major G protein classes. We believe our Melanophore technology is, therefore, also well-suited for studies of orphan receptors whose coupling parameters are unknown. We believe Melanophore technology provides us with a robust, reproducible, high-throughput and low-cost means for identifying and optimizing GPCR agonists, antagonists and inverse agonists, and is sensitive enough to detect the constitutive activity of many GPCRs.

Our Strategy

The key elements of our scientific and business strategy are to:

Advance our lead programs. We intend to continue to advance our current drug candidates, with a partner or independently, through clinical development and, if successful, to commercialization.

Discover and develop additional small molecule drug candidates targeting GPCRs. We intend to continue to discover and develop orally bio-available, small molecule compounds for GPCRs identified or validated through our research efforts.

Focus on attractive market opportunities. Obesity, insomnia, diabetes, atherosclerosis and arterial thrombosis each represent large market opportunities. We intend to continue to focus on these and other markets with attractive commercial potential.

Recognize significant economic value for our drug candidates under development. We intend to maximize the value of our drug candidates through both independent development and licensing and other partnership opportunities with pharmaceutical and larger biotechnology companies.

Continue to build our development capabilities. To capitalize on our discoveries, we plan to continue to expand our clinical development capabilities as our drug candidates enter into, and move through, clinical trials.

Maintain strong discovery research capabilities. Our proprietary technologies, our drug discovery infrastructure and the integrated approach to research used by our scientists, have allowed us to identify a number of GPCR targets and novel compounds. We believe these and other discoveries will continue to fuel our pipeline.

Competition

The biotechnology and pharmaceutical industries are highly competitive and are subject to rapid and significant change. We face significant competition from organizations that are pursuing the same or similar technologies. We also face significant competition from organizations that are pursuing drugs

that would compete with the drug candidates we are developing. We may not be able to compete successfully against these organizations, which include many large, well-financed and experienced pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies.

The focus of our scientific and business strategy is on GPCRs. We believe that many pharmaceutical and biotechnology companies and other organizations have internal drug discovery programs focused on GPCRs. In addition, other companies have attempted to overcome the problems associated with traditional drug screening by embarking on a variety of alternative strategies. Developments by others may render our drug candidates or technologies obsolete or noncompetitive.

Our present competitors with respect to lorcazerin include Abbott Laboratories, which markets Meridia, and Hoffman-La Roche, the U.S. prescription drug unit of the Roche Group, which markets Xenical, which may in the future be sold over-the-counter in the United States. A potential future competitor is Sanofi-Aventis, which is developing rimonabant, a cannabinoid-1 blocker. In addition, we believe that there are potentially competing 5-HT_{2C} programs that may be in development at various pharmaceutical and biotechnology companies, including Roche and GlaxoSmithKline, Inc.

In addition to the marketed compounds described above under the APD125 discussion, Neurocrine Biosciences and others are developing new GABA active compounds for the treatment of insomnia. We believe Sanofi-Aventis and Eli Lilly, and possibly other companies, are developing other potentially competing programs for insomnia, including programs targeting the 5-HT_{2A} receptor.

Many of our existing and potential competitors have substantially greater drug development capabilities and financial, scientific and marketing resources than we do. Additional consolidation in the pharmaceutical industry may result in even more resources being concentrated with our competitors. As a result, our competitors may be able to devote greater resources than we can to the research, development, marketing and promotion of drug discovery techniques or therapeutic products, or to adapt more readily to technological advances than we can. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval, or commercializing drugs before we do.

We expect to encounter significant competition for the principal drug candidates that we are developing. Companies that complete clinical trials, obtain regulatory approvals and commence commercial sales of their drug candidates before us may achieve a significant competitive advantage. Furthermore, we may be competing against companies with substantially greater manufacturing, marketing, distribution and selling capabilities, and any drug candidate that we successfully develop may compete with existing therapies that have long histories of safe and effective use.

We may rely on our collaborators for support of development programs and for the manufacturing and marketing of drug candidates. Our collaborators may be conducting multiple drug development efforts within the same disease areas that are the subject of their agreements with us, which may negatively impact the development of drugs that they discover that are subject to our agreements. Generally, our agreements with our collaborators do not preclude them from pursuing development efforts in one or more therapeutic areas of interest in which we have internal development efforts ongoing. In addition, we face and will continue to face intense competition from other companies for such collaborative arrangements, and technological and other developments by others may make it more difficult for us to establish such relationships.

Properties

We own approximately 110,000 square feet of research, development, warehouse and office space in San Diego, California. In addition, we lease from third parties approximately 132,000 square feet of research, development, warehouse and office space in the same business park. We have options to purchase two of the facilities that we lease, which consist of approximately 95,000 square feet. As a potential source of additional near-term liquidity, we are exploring the potential sale and leaseback of any or all of the facilities we own, as well as the assignment of our option to purchase one of the facilities we lease. As of September 30, 2006, the facilities we own had a carrying value of approximately \$28.6 million on our balance sheet, and we estimate the aggregate fair market value of these facilities to be in excess of their carrying value. We anticipate that a sale and leaseback involving these facilities, as well as the assignment of our option to purchase one of our leased facilities, would include a right by us to repurchase the facilities in the future and, therefore, be accounted for in a manner similar to the sale and leaseback of our facility at 6138-6150 Nancy Ridge Drive, which we completed in December 2003. For more information, please see Note 4 to the financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005. There is no assurance that we will be able to complete a sale and leaseback of any of our facilities or, if we do, that the terms will reflect our estimate of their value.

Employees

As of September 30, 2006, we had 349 employees, including 291 in research and development and 58 employees in administration, which includes finance, legal, facilities and other general support areas. None of our employees is covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

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Underwriting

We have entered into an underwriting agreement with the underwriters named below. CIBC World Markets Corp. is acting as representative of the underwriters.

The underwriting agreement provides for the purchase of a specific number of shares of common stock by each of the underwriters. The underwriters' obligations are several, which means that each underwriter is required to purchase a specified number of shares, but is not responsible for the commitment of any other underwriter to purchase shares. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase the number of shares of common stock set forth opposite its name below:

| Underwriter | Number of Shares |
|--------------------------|---------------------|
| CIBC World Markets Corp. | |
| Cowen and Company, LLC | |
| Piper Jaffray & Co. | |
| Needham & Company, LLC | |
| Leerink Swann & Co., Inc | |
| Fortis Securities LLC | |
| Morgan Joseph & Co. Inc. | |
| Oppenheimer & Co. Inc. | |
| Total | 8,000,000 |

The underwriters have agreed to purchase all of the shares offered by this prospectus supplement (other than those covered by the over-allotment option described below) if any are purchased. Under the underwriting agreement, if an underwriter defaults in its commitment to purchase shares, the commitments of non-defaulting underwriters may be increased or the underwriting agreement may be terminated, depending on the circumstances.

The shares should be ready for delivery on or about _____, 2006 against payment in immediately available funds. The underwriters are offering the shares subject to various conditions and may reject all or part of any order. The representative had advised us that the underwriters propose to offer the shares directly to the public at the public offering price that appears on the cover page of this prospectus supplement. In addition, the representative may offer some of the shares to other securities dealers at such price less a concession of \$ _____ per share. The underwriters may also allow, and such dealers may reallow, a concession not in excess of \$ _____ per share to other dealers. After the shares are released for sale to the public, the representative may change the offering price and other selling terms at various times.

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to 30 days after the date of this prospectus supplement, permits the underwriters to purchase a maximum of 1,200,000 additional shares from us to cover over-allotments. If the underwriters exercise all or part of this option, they will purchase shares covered by the option at the public offering price that appears on the cover page of this prospectus supplement, less the underwriting discount. If this option is exercised in full, the total price to public will be \$ _____ and the total proceeds to us will be \$ _____. The underwriters have severally agreed that, to the extent the over-allotment option is exercised, they will each purchase a number of additional shares proportionate to the underwriter's initial amount reflected in the foregoing table.

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The following table provides information regarding the amount of the discount to be paid to the underwriters by us:

| | Per Share | Total Without Exercise of Over-Allotment Option | Total with Full Exercise of Over-Allotment Option |
|-----------------------------|------------------|--|--|
| Arena Pharmaceuticals, Inc. | \$ | \$ | \$ |

A \$1.00 increase (decrease) in the assumed public offering price of \$14.13 per share would increase (decrease) the underwriting discount by \$0.0525 per share and the total without the exercise of the over-allotment option by approximately \$0.4 million and the total with the full exercise of the over-allotment option by approximately \$0.5 million.

We estimate that our total expenses of this offering, excluding the underwriting discount, will be approximately \$435,100.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

We, our officers and directors have agreed to a 90-day "lock up" with respect to shares of common that they beneficially own, including securities that are convertible into shares of common stock and securities that are exchangeable or exercisable for shares of common stock. This means that, subject to certain exceptions, for a period of 90 days following the date of this prospectus supplement, we and such persons may not offer, sell, pledge or otherwise dispose of these securities without the prior written consent of CIBC World Markets Corp.

The representatives have informed us that they do not expect discretionary sales by the underwriters to exceed five percent of the shares offered by this prospectus supplement.

Rules of the Securities and Exchange Commission may limit the ability of the underwriters to bid for or purchase shares before the distribution of the shares is completed. However, the underwriters may engage in the following activities in accordance with the rules:

Stabilizing transactions The representative may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

Over-allotments and syndicate covering transactions The underwriters may sell more shares of our common stock in connection with this offering than the number of shares than they have committed to purchase. This over-allotment creates a short position for the underwriters. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares in this offering described above. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing shares in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market, as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the shares that could adversely affect investors who purchase shares in this offering.

Penalty bids If the representative purchases shares in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering.

Passive market making Market makers in the shares who are underwriters or prospective underwriters may make bids for or purchases of shares, subject to limitations, until the time, if ever, at which a stabilizing bid is made.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales or to stabilize the market price of our common stock may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our common stock. As a result, the price of the shares of our common stock may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

Neither we nor the underwriters makes any representation or prediction as to the effect that the transactions described above may have on the price of the shares. These transactions may occur on the Nasdaq Global Market or otherwise. If such transactions are commenced, they may be discontinued without notice at any time.

Notice to Non-U.S. Investors

The offering is exclusively conducted under applicable private placement exemptions and therefore it has not been and will not be notified to, and this document or any other offering material relating to the shares has not been and will not be approved by, the Belgian Banking, Finance and Insurance Commission ("Commission bancaire, financière et des assurances/Commissie voor het Bank, Financie en Assurantiewezen"). Any representation to the contrary is unlawful.

Each underwriter has undertaken not to offer sell, resell, transfer or deliver, or to take any steps thereto, directly or indirectly, any shares, and not to distribute or publish this document or any other material relating to the shares or to the offering in a manner which would be construed as: (a) a public offering under the Belgian Royal Decree of 7 July 1999 on the public character of financial transactions; or (b) an offering of securities to the public under Directive 2003/71/EC which triggers an obligation to publish a prospectus in Belgium. Any action contrary to these restrictions will cause the recipient and us to be in violation of the Belgian securities laws.

Neither this prospectus nor any other offering material relating to the shares has been submitted to the clearance procedures of the *Autorité des marchés financiers* in France. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be: (a) released, issued, distributed or caused to be released, issued or distributed to the public in France; or (b) used in connection with any offer for subscription or sale of the shares to the public in France. Such offers, sales and distributions will be made in France only: (i) to qualified investors, or *investisseurs qualifiés*, and/or to a restricted circle of investors, or *cercle restreint d'investisseurs*, in each case investing for their own account, all as defined in and in accordance with Articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*; (ii) to investment services providers authorised to engage in portfolio management on behalf of third parties; or (iii) in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations, or *Règlement Général* of the *Autorité des marchés financiers*, does not constitute a public offer, or *appel public à l'épargne*. Such shares may be resold only in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, which we refer to each as a Relevant Member State, an offer to the public of any shares which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) by the underwriters to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of CIBC World Markets Corp. for any such offer; or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each underwriter has represented, warranted and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000, or FSMA) received by it in connection with the issue or sale of any shares in circumstances in which section 21(1) of the FSMA does not apply to us; and
- (b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

In the State of Israel, the shares offered hereby may not be offered to any person or entity other than the following:

- (a) a fund for joint investments in trust (i.e., mutual fund), as such term is defined in the Law for Joint Investments in Trust, 5754-1994, or a management company of such a fund;
- (b) a provident fund as defined in Section 47(a)(2) of the Income Tax Ordinance of the State of Israel, or a management company of such a fund;
- (c) an insurer, as defined in the Law for Oversight of Insurance Transactions, 5741-1981;

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- (d) a banking entity or satellite entity, as such terms are defined in the Banking Law (Licensing), 5741-1981, other than a joint services company, acting for their own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (e) a company that is licensed as a portfolio manager, as such term is defined in Section 8(b) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (f) a company that is licensed as an investment advisor, as such term is defined in Section 7(c) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account;
- (g) a company that is a member of the Tel Aviv Stock Exchange, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (h) an underwriter fulfilling the conditions of Section 56(c) of the Securities Law, 5728-1968;
- (i) a venture capital fund (defined as an entity primarily involved in investments in companies which, at the time of investment, (i) are primarily engaged in research and development or manufacture of new technological products or processes and (ii) involve above-average risk);
- (j) an entity primarily engaged in capital markets activities in which all of the equity owners meet one or more of the above criteria; and
- (k) an entity, other than an entity formed for the purpose of purchasing shares in this offering, in which the shareholders equity (including pursuant to foreign accounting rules, international accounting regulations and U.S. generally accepted accounting rules, as defined in the Securities Law Regulations (Preparation of Annual Financial Statements), 1993) is in excess of NIS 250 million.

Any offeree of the shares offered hereby in the State of Israel shall be required to submit written confirmation that it falls within the scope of one of the above criteria. This prospectus will not be distributed or directed to investors in the State of Israel who do not fall within one of the above criteria.

The shares offered pursuant to this prospectus will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to art. 652a or art. 1156 of the Swiss Federal Code of Obligations. We have not applied for a listing of the shares being offered pursuant to this prospectus on the SWX Swiss Exchange or on any other regulated securities market, and consequently, the information presented in this prospectus does not necessarily comply with the information standards set out in the relevant listing rules. The shares being offered pursuant to this prospectus have not been registered with the Swiss Federal Banking Commission as foreign investment funds, and the investor protection afforded to acquirers of investment fund certificates does not extend to acquirers of securities.

Investors are advised to contact their legal, financial or tax advisers to obtain an independent assessment of the financial and tax consequences of an investment in the shares.

Legal Matters

Selected legal matters with respect to the validity of common stock offered by this prospectus supplement will be passed upon for us by Cooley Godward Kronish LLP, San Diego, California. Certain legal matters in connection with the common stock offered in this prospectus supplement will be passed upon for the underwriters by Latham & Watkins LLP, Menlo Park, California.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2005, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Where You Can Find More Information

We 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. This prospectus supplement and the 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, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. We also file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other material we file with the SEC, at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information on the Public Reference Room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including Arena. The SEC's Internet site can be found at <http://www.sec.gov>.

Important Information Incorporated By Reference

The SEC allows us to "incorporate by reference" into this prospectus supplement the information we file with it, which means that we can disclose important information to you by referring you to those documents. Information incorporated by reference is part of this prospectus supplement. Later information filed with the SEC will update and supersede this information. The SEC's Internet site can be found at <http://www.sec.gov>.

We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until this offering is completed:

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 (other than information furnished rather than filed), filed with the SEC on January 24, 2006, January 27, 2006, February 3, 2006, March 20, 2006, March 29, 2006, April 19, 2006, May 18, 2006, June 13, 2006, June 16, 2006, July 6, 2006, July 25, 2006, August 1, 2006, August 14, 2006, September 12, 2006, September 25, 2006, September 27, 2006 and November 16, 2006;

the description of our Rights Agreement contained in our registration statement on Form 8-A filed on November 15, 2002, as amended on December 30, 2003 and November 16, 2006, including any amendments or reports filed for the purposes of updating this description; and

the description of our common stock contained in our registration statement on Form 8-A filed on July 26, 2000, including any amendments or reports filed for the purposes of updating this description.

You may request a copy of these filings, at no cost, by contacting us at:

Arena Pharmaceuticals, Inc.
Attention: Investor Relations
6166 Nancy Ridge Drive
San Diego, CA 92121
Telephone number: (858) 453-7200

In accordance with Section 412 of the Exchange Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

PROSPECTUS

Arena Pharmaceuticals, Inc.

Common Stock

Our common stock is listed on the NASDAQ Global Market under the symbol "ARNA." On September 8, 2006, the last reported sale price of our common stock on the NASDAQ Global Market was \$11.42 per share.

This prospectus and the accompanying prospectus supplement will allow us to sell up to 12,500,000 shares of our common stock over time in one or more offerings. Each time we offer shares, we will provide you with a supplement to this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus and any prospectus supplement carefully before you invest.

Investing in our common stock involves a high degree of risk. See "Risk Factors" on page 2 of this prospectus and as updated in our future filings made with the Securities and Exchange Commission, which are incorporated by reference in this prospectus.

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

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

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

The date of this prospectus is September 12, 2006.

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We are not making an offer to sell or seeking an offer to buy shares of our common stock under this prospectus or any applicable prospectus supplement in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, any applicable prospectus supplement and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus or any sale of a security.

About This Prospectus

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process. Under this shelf registration statement, we may sell up to 12,500,000 shares of our common stock in one or more offerings. Each time we sell any of our common stock under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also add, update or change in a prospectus supplement any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus, together with any applicable prospectus supplement and the documents incorporated by reference into this prospectus, include all material information relating to this offering. You should carefully read both this prospectus and any applicable prospectus supplement together with the additional information described under "Where You Can Find More Information" before buying common stock in this offering.

Summary

Arena Pharmaceuticals, Inc.

We are a clinical-stage biopharmaceutical company focusing our research and development efforts on small molecule drugs in four major therapeutic areas: metabolic, central nervous system, cardiovascular and inflammatory diseases. We are developing a broad pipeline of compounds targeting an important class of drug targets called G protein-coupled receptors, or GPCRs, using our knowledge of GPCRs and our technologies, including CART and Melanophore. We have four internally discovered, clinical-stage drug candidates for major diseases. Our most advanced unpartnered drug candidates are lorcaserin hydrochloride, which is under investigation for the treatment of obesity, and APD125, which is under investigation for the treatment of insomnia. We also have two clinical-stage collaborations with major pharmaceutical companies: Merck & Co., Inc. and Ortho-McNeil, Inc.

The pharmaceutical marketplace in which we operate includes many large, well-established companies competing with us to develop or market treatments for the same diseases and disorders. See "Risk Factors".

Arena Pharmaceuticals® and Arena® are registered service marks of Arena. CART is an unregistered service mark of Arena. "APD" is an abbreviation for Arena Pharmaceuticals Development.

We incorporated in the state of Delaware in April 1997. Our corporate offices are located at 6166 Nancy Ridge Drive, San Diego, California 92121. Our telephone number is (858) 453-7200. Our website address is www.arenapharm.com. Information contained in our website does not constitute part of this prospectus.

Unless otherwise specified or required by context, references in this prospectus to "we," "us," "our" and "Arena" refer to Arena Pharmaceuticals, Inc. and our subsidiaries on a consolidated basis.

Risk Factors

An investment in our common stock involves a high degree of risk. Before you make a decision to invest in our common stock, you should consider carefully the risks described in the section entitled "Risk Factors" contained in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2006, as filed with the SEC on August 4, 2006, which is incorporated herein by reference in its entirety, as well as any amendment or update thereto reflected in subsequent filings with the SEC. If any of these risks actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose part or all of your investment. Moreover, the risks described are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, operating results, prospects or financial condition.

Forward-Looking Statements

This prospectus, including the documents that we incorporate by reference herein, contains, and any applicable prospectus supplement including the documents we incorporate by reference therein may contain, "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements can generally be identified as such because the context of the statement will include words such as "may," "will," "intends," "plans," "believes," "anticipates," "expects," "estimates," "predicts," "potential," "continue," or "opportunity," the negative of these words or words of similar import. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals or prospects are also forward-looking statements. Discussions containing these forward-looking statements may be found, among other places, in "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q for the quarters ended subsequent to our filing of such Annual Report on Form 10-K with the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC. These forward-looking statements are or will be, as applicable, based largely on our expectations and projections about future events and future trends affecting our business, and so are or will be, as applicable, subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. The risks and uncertainties include, among others, those referenced in "Risk Factors" above and in any applicable prospectus supplement and any documents incorporated by reference herein or therein.

In addition, past financial or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the date of this prospectus or the prospectus supplement or the date of documents incorporated by reference in this prospectus that include forward-looking statements.

Use of Proceeds

Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of our common stock under this prospectus for the clinical and preclinical development of our internally discovered drug candidates, for discovery research for new drug candidates, and for general corporate purposes, including working capital.

Description of Capital Stock

As of the date of this prospectus, our amended and restated certificate of incorporation, as amended, authorizes us to issue 142,500,000 shares of common stock, par value \$.0001 per share, and 7,500,000 shares of preferred stock, par value \$.0001 per share. As of August 29, 2006, there were 47,359,765 shares of common stock outstanding. To date, our board of directors has designated 350,000 of the authorized shares of preferred stock as Series A Junior Participating Preferred Stock (the "Series A Preferred Stock"), which series is described in greater detail below under "Share Purchase Rights Plan," and 4,650 of the authorized shares of preferred stock as Series B Convertible Preferred Stock as described in greater detail below under "Series B Preferred Stock." As of August 29, 2006, no shares of Series A Preferred Stock and 4,650 shares of Series B Convertible Preferred Stock were outstanding.

The following summary describes the material terms of our capital stock and stockholder rights plan. The description of capital stock and stockholder rights plan is qualified by reference to our amended and restated certificate of incorporation, our bylaws, the certificate of designations of our Series A Preferred Stock and our Series B Convertible Preferred Stock, and our stockholder rights plan, which are incorporated by reference as exhibits into the registration statement of which this prospectus is a part.

Common Stock

Voting. Common stockholders are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval.

Dividends and Other Distributions. Holders of our common stock are entitled to share in an equal amount per share in any dividends declared by our board of directors on the common stock and paid out of legally available assets.

Distribution on Dissolution. Subject to any preferential rights of any outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any outstanding preferred stock.

Other Rights. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

Preferred Stock

Under our amended and restated certificate of incorporation, as amended, our board of directors has the authority, without further action by stockholders, to designate up to 7,500,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock. To date, our board of directors has designated 350,000 of the authorized shares of preferred stock as the Series A Preferred Stock, which series is described in greater detail below under "Share Purchase Rights Plan," and 4,650 of the authorized shares of preferred stock as Series B Convertible Preferred Stock as described in greater detail below under "Series B Preferred Stock."

The issuance of additional preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. The issuance could have the effect of decreasing the market price of the

common stock. The issuance of preferred stock also could have the effect of delaying, deterring or preventing a change in control of us.

Share Purchase Rights Plan. Each outstanding share of our common stock has attached to it one preferred share purchase right, which we refer to as a Right. Each Right entitles the registered holder to purchase from us one one-hundredth of a share of Series A Preferred Stock at a price of \$36 (the "Purchase Price"), subject to adjustment. The description and terms of the Rights are set forth in a Rights Agreement dated as of October 30, 2002, as amended, between us and Computershare Trust Company, Inc. as Rights Agent, which is incorporated by reference as an exhibit into the registration statement of which this prospectus is a part.

Until the earlier to occur of (i) 10 days following a public announcement that a person or group of affiliated or associated persons (an "Acquiring Person") have acquired beneficial ownership of 10% or more of our outstanding common stock or (ii) 10 business days (or such later date as may be determined by action of our board of directors prior to such time as any person or group of affiliated persons becomes an Acquiring Person) following the commencement of, or announcement of an intention to make, a tender offer or exchange offer the consummation of which would result in the beneficial ownership by a person or group of 10% or more of our outstanding common stock (the earlier of such dates being called the "Distribution Date"), the Rights will be evidenced, with respect to any of our common stock certificates outstanding as of November 13, 2002, by such common stock certificate with a copy of the Summary of Rights in the form attached as Exhibit C to the Rights Agreement.

The Rights Agreement provides that none of our directors or officers shall be deemed to beneficially own any of our common stock owned by any other director or officer by virtue of such persons acting in their capacities as such, including, without limitation, in connection with any formulation and publication of our board of directors' recommendation of its position, and any actions taken in furtherance thereof, with respect to any acquisition proposal relating to Arena, a tender or exchange offer for any of our common stock or any solicitation of proxies with respect to any of our common stock.

The Rights Agreement provides that, until the Distribution Date (or earlier redemption or expiration of the Rights), the Rights will be transferred with and only with our common stock. Until the Distribution Date (or earlier redemption or expiration of the Rights), new common stock certificates issued after November 13, 2002, upon transfer or new issuance of our common stock will contain a notation incorporating the Rights Agreement by reference. Until the Distribution Date (or earlier redemption or expiration of the Rights), the surrender for transfer of any certificates for our common stock outstanding as of November 13, 2002, even without such notation or a copy of the Summary of Rights attached thereto, will also constitute the transfer of the Rights associated with our common stock represented by such certificate. As soon as practicable following the Distribution Date, separate certificates evidencing the Rights ("Right Certificates") will be mailed to holders of record of our common stock as of the close of business on the Distribution Date and such separate Right Certificates alone will evidence the Rights.

The Rights are not exercisable until the Distribution Date. The Rights will expire on October 30, 2012, (the "Final Expiration Date"), unless the Final Expiration Date is extended or the Rights are earlier redeemed or exchanged by us, in each case, as described below.

The Purchase Price payable, and the number of shares of the Series A Preferred Stock or other securities or property issuable, upon exercise of the Rights are subject to adjustment from time to time to prevent dilution (i) in the event of a stock dividend on, or a subdivision, combination or reclassification of, the Series A Preferred Stock, (ii) upon the grant to holders of the Series A Preferred Stock of certain rights or warrants to subscribe for or purchase Series A Preferred Stock at a price, or securities convertible into Series A Preferred Stock with a conversion price, less than the then

current market price of the Series A Preferred Stock or (iii) upon the distribution to holders of the Series A Preferred Stock of evidences of indebtedness or assets (excluding regular periodic cash dividends paid out of earnings or retained earnings or dividends payable in Series A Preferred Stock) or of subscription rights or warrants (other than those referred to above).

The number of outstanding Rights and the number of one one-hundredths of a share of Series A Preferred Stock issuable upon exercise of each Right are also subject to adjustment in the event of a stock split of our common stock or a stock dividend on our common stock payable in our common stock or subdivisions, consolidations or combinations of our common stock occurring, in any such case, prior to the Distribution Date.

Series A Preferred Stock purchasable upon exercise of the Rights will not be redeemable. Once issued upon exercise of Rights, each share of Series A Preferred Stock will be entitled to a minimum preferential quarterly dividend payment of \$1 per share but will be entitled to an aggregate dividend of 100 times the dividend declared per share of our common stock. In the event of liquidation, the holders of outstanding shares of Series A Preferred Stock will be entitled to a minimum preferential liquidation payment of \$100 per share but will be entitled to an aggregate payment of 100 times the payment made per share of our common stock. Each outstanding share of Series A Preferred Stock will have 100 votes, voting together with our common stock. Finally, in the event of any merger, consolidation or other transaction in which our common stock is exchanged, each outstanding share of Series A Preferred Stock will be entitled to receive 100 times the amount received per share of our common stock. These rights are protected by customary antidilution provisions.

Because of the nature of the Series A Preferred Stock's dividend, liquidation and voting rights, the value of the one one-hundredth interest in a share of Series A Preferred Stock purchasable upon exercise of each Right should approximate the value of one share of our common stock.

In the event that any person or group of affiliated or associated persons becomes an Acquiring Person, the Rights Agreement provides that proper provision shall be made so that each holder of a Right, other than Rights beneficially owned by the Acquiring Person (which will thereafter be void), will thereafter have the right to receive (subject to adjustment) upon exercise thereof at the then current Purchase Price, that number of shares of our common stock having a market value of two times the Purchase Price. At any time after any person or group becomes an Acquiring Person and prior to the acquisition by such person or group of 50% or more of our outstanding common stock, our board of directors may exchange the Rights (other than Rights owned by such person or group, which will have become void), in whole or in part, at an exchange ratio of one share of our common stock, or one one-hundredth of a share of Series A Preferred Stock (or of a share of a class or series of our preferred stock having equivalent rights, preferences and privileges), per Right (subject to adjustment).

In the event that we are acquired in a merger or other business combination transaction or 50% or more of our consolidated assets or earning power are sold after a person or group has become an Acquiring Person, proper provision will be made so that each holder of a Right will thereafter have the right to receive, upon the exercise thereof at the then current Purchase Price, that number of shares of common stock of the acquiring company which at the time of such transaction will have a market value of two times the Purchase Price.

With certain exceptions, no adjustment in the Purchase Price will be required until cumulative adjustments require an adjustment of at least 1% in the Purchase Price. No fractional shares of Series A Preferred Stock will be issued (other than fractions which are integral multiples of one one-hundredth of a share of Series A Preferred Stock, which may, at our election, be evidenced by depositary receipts) and in lieu thereof, an adjustment in cash will be made based on the market price of the Series A Preferred Stock on the last trading day prior to the date of exercise.

At any time prior to the acquisition by a person or group of affiliated or associated persons of beneficial ownership of 10% or more of our outstanding common stock, our board of directors may redeem the Rights in whole, but not in part, at a price of \$.01 per Right (the "Redemption Price"). The redemption of the Rights may be made effective at such time on such basis with such conditions as our board of directors in its sole discretion may establish.

The terms of the Rights may be amended by our board of directors without the consent of the holders of the Rights, including an amendment to (i) fix a Final Expiration Date later than October 30, 2012, (ii) reduce the Redemption Price or (iii) increase the Purchase Price, except that from and after such time as any person or group of affiliated or associated persons becomes an Acquiring Person no such amendment may adversely affect the interests of the holders of the Rights (other than the Acquiring Person and its affiliates and associates).

Until a Right is exercised, the holder thereof, as such, will have no rights as a stockholder of Arena, including, without limitation, the right to vote or to receive dividends.

Series B Preferred Stock. On December 24, 2003, we completed the private placement of \$35 million of Series B-1 Convertible Preferred Stock to two institutional investors (the "Investors") pursuant to a Securities Purchase Agreement (the "Securities Purchase Agreement"). We issued an aggregate of 3,500 shares of Series B-1 Convertible Preferred Stock in such transaction.

The Series B-1 Convertible Preferred Stock is convertible into our common stock at a fixed conversion price of \$7.50 per share. If not previously converted, we must redeem the Series B-1 Convertible Preferred Stock five years from the original issue date or following request by the holders of the Series B-1 Convertible Preferred Stock to redeem some or all of such shares. We may make any such redemption in cash or, if certain conditions have been met, in shares of our common stock. Dividends on the Series B-1 Convertible Preferred Stock are payable at a rate of 4% per annum either in kind or in shares of our common stock.

In connection with the sale of the Series B-1 Convertible Preferred Stock, we issued to the Investors seven-year Warrants to purchase up to 1,486,200 shares of our common stock at an exercise price of \$10.00 per share. We also issued to the Investors Unit Warrants giving such Investors the right to purchase from us for a period of approximately 16 months from December 24, 2003, at their option, up to \$11.5 million of Series B-2 Convertible Preferred Stock and additional seven-year Warrants to purchase shares of our common stock. On April 22, 2005, the Investors exercised their Unit Warrants in full and received (i) an aggregate of 1,150 shares of our Series B-2 Convertible Preferred Stock and (ii) seven-year Warrants to purchase an aggregate of 450,000 shares of common stock at an exercise price of \$10.00 per share (subject to weighted-average adjustment in certain circumstances).

On March 31, 2006, following our call notice to one of the Investors, Smithfield Fiduciary LLC, such holder exercised its warrants to purchase 829,856 shares of our common stock. In connection with this exercise in full of its warrants, Smithfield claimed that it was entitled to receive exchange warrants that would include a provision that could require us to issue additional exchange warrants in the future. We disagreed with this interpretation and, on June 30, 2006, entered into a Settlement Agreement and Release with Smithfield. As part of the Settlement Agreement and Release we issued Smithfield a new seven-year warrant to purchase 829,856 shares of our common stock at an initial exercise price of \$15.49 per share. The new warrant does not contain any right for us, or for the holder to require us, to call the warrant, nor does it provide the holder the right to receive any exchange warrants in the future.

If not previously converted, we must redeem the Series B-2 Convertible Preferred Stock in five years from April 22, 2005, or earlier under certain circumstances, at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties. We may make any such redemption in cash or, subject to certain conditions, in shares of common stock. The

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Series B-2 Convertible Preferred Stock is convertible into common stock at a fixed conversion price of \$7.00 per share. Otherwise, the Series B-2 Convertible Preferred Stock has substantially identical terms as the Series B-1 Convertible Preferred Stock, as more fully described in the Certificate of Designations relating to the Series B Convertible Preferred Stock (the "Certificate of Designations").

So long as any shares of Series B Convertible Preferred Stock are outstanding, we cannot, directly or indirectly, (i) incur or guarantee, assume or suffer to exist any debt other than permitted debt, as more fully described in the Securities Purchase Agreement, or (ii) allow or suffer to exist any lien other than permitted liens, as more fully described in the Securities Purchase Agreement.

From the end of the Blockout Period (as defined in the Securities Purchase Agreement) and for so long as an Investor holds 20% of the shares of Series B Convertible Preferred Stock originally purchased by such Investor, we have agreed that we will not, directly or indirectly, effect any Subsequent Placement (as defined in the Securities Purchase Agreement), unless, among other things, we have delivered to each Investor a written notice of any proposed or intended issuance or sale or exchange of the securities being offered in such Subsequent Placement offering to issue and sell to or exchange with each Investor a pro rata portion of fifty percent (50%) of the offered securities, based on such Investor's pro rata portion of the aggregate purchase price paid by the Investors for all of the shares of Series B Convertible Preferred Stock purchased under the Securities Purchase Agreement.

Each share of Series B Convertible Preferred Stock is entitled to a number of votes equal to the number of shares of our common stock into which it is convertible. Each Investor agrees that for so long as it holds Series B Convertible Preferred Stock, it shall vote its shares of Series B Convertible Preferred Stock and our common stock on all matters in which such Investor is entitled to vote and on which holders of common stock have the right to vote, in the manner recommended by our board of directors to all of our shareholders unless our board of directors elects to permit the Investors to vote such shares in their own discretion.

If a Change of Control (as defined in the Certificate of Designations) occurs before the two-year anniversary of the original issue date of the Series B Convertible Preferred Stock, we can repurchase the Series B Convertible Preferred Stock at a price equal to the greater of 125% of the stated value or the market value (as calculated in the Certificate of Designations) of such shares of Series B Convertible Preferred Stock plus all accrued but unpaid dividends thereon to the date of payment. If such Change of Control occurs following the two-year anniversary of the original issue date of the Series B Convertible Preferred Stock, we can repurchase the Series B Convertible Preferred Stock at a price equal to the greater of 115% of the stated value or the market value (as calculated in the Certificate of Designations) of such shares of Series B Convertible Preferred Stock plus all accrued but unpaid dividends thereon to the date of payment. We can elect to pay any such redemption in shares of our common stock, if certain conditions have been met.

The holders of our Series B-1 Convertible Preferred Stock can require us to redeem all or some of their shares of Series B-1 Convertible Preferred Stock at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties. The stated value is the original holder's investment plus any dividends settled by increasing the stated value at the time the dividend is payable.

The holders of our Series B-2 Convertible Preferred Stock will be entitled to require us to redeem their shares of Series B-2 Convertible Preferred Stock at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties, if, following the 21st month anniversary of the original issue date of the Series B-2 Convertible Preferred Stock, the average of the closing prices of our common stock for any 30 consecutive trading days is below \$7.00, which is the conversion price for the Series B-2 Convertible Preferred Stock. Also, the holders of the Series B-2 Convertible Preferred Stock may require us to redeem their shares if we issue common stock or common stock equivalents for an effective net price to us per share less than approximately \$5.33

(excluding, among other things, certain common stock and common stock equivalents issued or issuable (i) to our officers, directors, employees or consultants, (ii) in connection with certain strategic partnerships or joint ventures, and (iii) in connection with certain mergers and acquisitions). We can elect to pay any such redemption in shares of our common stock, if certain conditions have been met.

In addition to the foregoing redemption rights, at any time following the occurrence of a "Triggering Event," a holder of the Series B Convertible Preferred Stock may require us to repurchase all or any portion of the Series B Convertible Preferred Stock then held by such holder at a price per share equal to the greater of 115% of the stated value or the market value (as calculated in the Certificate of Designations) of such shares of Series B Convertible Preferred Stock plus all accrued but unpaid dividends thereon to the date of payment. We can elect to pay such redemption price in shares of our common stock under certain circumstances. "Triggering Event" is specifically defined in the Certificate of Designations, and includes any of the following events: (i) immediately prior to a bankruptcy event; (ii) we fail for any reason to timely deliver a certificate evidencing any securities to a purchaser or the exercise or conversion rights of the holders are otherwise suspended for other than a permissible reason; (iii) any of certain events of default (as set forth in the Registration Rights Agreement with the Series B Convertible Preferred Stock holders) occur and remain uncured for 60 days; (iv) we fail to make any cash payment required under the Series B Convertible Preferred Stock transaction documents and such failure is not timely cured; (v) the issuance of a going concern opinion by our independent registered public accounting firm that is not timely cured; (vi) we breach a section of the Securities Purchase Agreement relating to indebtedness and subordination; or (vii) we default in the timely performance of any other obligation under the Series B Convertible Preferred Stock transaction documents and such default is not timely cured.

Our Stockholders Rights Plan has been amended to provide, among other things, that the Investors will not become "Acquiring Persons" solely by virtue of such purchases and issuances of our common stock in connection therewith.

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 publicly held 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 before the date that the person became an "interested stockholder," our board of directors approved either the "business combination" or the transaction which makes the person an "interested stockholder," or after the date that the person became an "interested stockholder," the business combination is approved by our board of directors and the vote of at least 66²/₃% of our outstanding voting stock that is not owned by the "interested stockholder." Generally, a "business combination" includes a merger, asset sale or other transaction resulting in a financial benefit to the stockholder. An "interested stockholder" is a person who either owns 15% or more of our outstanding voting stock or, together with affiliates and associates, owns or, within three prior years, did own, 15% or more of our outstanding voting stock. The statute could have the effect of delaying, deferring or preventing a change in our control.

Bylaw and Certificate of Incorporation Provisions. Our bylaws provide that special meetings of our stockholders may be called by our board of directors or President. Our amended and restated certificate of incorporation (i) specifies that the authorized number of directors shall be fixed by our board of directors in the manner provided by our bylaws, which provide that the number of directors constituting our board of directors shall be fixed from time to time by resolution passed by a majority of our board of directors and (ii) 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 and restated certificate of incorporation and bylaws could delay or discourage

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.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, Inc.

Listing on the NASDAQ Global Market

Our common stock is listed on the NASDAQ Global Market under the symbol "ARNA."

Plan of Distribution

We may sell our common stock covered by this prospectus in any of three ways (or in any combination):

to or through underwriters or dealers;

directly to one or more purchasers; or

through agents.

We may distribute the common stock:

from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to the prevailing market prices; or

at negotiated prices.

The prospectus supplement or supplements will describe the method of distribution and set forth the terms of the offering of our common stock covered by this prospectus, including:

the name or names of any underwriters, dealers or agents;

the amounts of securities underwritten or purchased by each of them;

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

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

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

the public offering price of the common stock;

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

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

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Any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time. We may determine the price or other terms of the common stock offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the obligations of the underwriter, dealer or agent in the applicable prospectus supplement.

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

We may sell the common stock through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the common stock and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment. We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the common stock from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, dealers and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, or to contribution with respect to payments which the agents, dealers or underwriters may be required to make in respect thereof. Agents, dealers and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act of 1934. Over-allotment involves sales in excess of the offering size, which create a short position. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares in this offering described above. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing shares in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market, as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the shares that could adversely affect investors who purchase shares in this offering. Stabilizing transactions permit bids to purchase the underlying security for the purpose of fixing the price of the security so long as the stabilizing bids do not exceed a specified maximum. 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.

Similar to other purchase transactions, an underwriter's purchase to cover the syndicate short sales or to stabilize the market price of our common stock may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our common stock. As a result, the price of the shares of our common stock may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

Neither we nor the underwriters makes any representation or prediction as to the effect that the transactions described above may have on the price of the shares. If such transactions are commenced, they may be discontinued without notice at any time.

Legal Matters

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

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2005, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Where You Can Find More Information

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C., 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. Our SEC filings are also available to the public at the SEC's website at <http://www.sec.gov>.

Incorporation of Certain Information by Reference

The SEC allows us to "incorporate by reference" the information we file with them, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference 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 of 1934 after the date of this prospectus until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

our annual report on Form 10-K for the year ended December 31, 2005 (filed on March 7, 2006);

our quarterly reports on Form 10-Q for the quarterly periods ended March 31, 2006 (filed on May 10, 2006) and June 30, 2006 (filed on August 4, 2006);

our current reports on Form 8-K filed on January 24, 2006, January 27, 2006, February 3, 2006, March 20, 2006, March 29, 2006, April 19, 2006, May 18, 2006, June 13, 2006, June 16, 2006, July 6, 2006, July 25, 2006, August 1, 2006, August 14, 2006 and September 12, 2006;

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the description of our Stockholders Rights Plan contained in our registration statement on Form 8-A filed on November 15, 2002, as amended on December 30, 2003, including any amendments or reports filed for the purposes of updating such description; and

the description of our common stock contained in our registration statement on Form 8-A, filed on July 26, 2000, including any amendment or reports filed for the purpose of updating such description.

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

Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, California 92121
(858) 453-7200
Attn: Investor Relations

This prospectus is part of a registration statement we filed with the SEC. That registration statement and the exhibits filed along with the registration statement contain more information about us and the shares in this offering. Because information about documents referred to in this prospectus is not always complete, you should read the full documents which are filed as exhibits to the registration statement. You may read and copy the full registration statement and its exhibits at the SEC's public reference rooms or their website.

8,000,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

, 2006

CIBC World Markets

Sole Book-Running Manager

Cowen and Company

Piper Jaffray

Co-Lead Managers

Needham & Company, LLC

Leerink Swann & Company

Fortis Securities

Morgan Joseph

Oppenheimer & Co.

You should rely only on the information contained or incorporated by reference in this prospectus supplement. No dealer, salesperson or other person is authorized to give information that is not contained or incorporated by reference in this prospectus supplement. This prospectus supplement is not an offer to sell nor is it seeking an offer to buy these securities in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus supplement is correct only as of the date of this prospectus supplement, regardless of the time of the delivery of this prospectus supplement or any sale of these securities.

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