

ARENA PHARMACEUTICALS INC
Form 424B3
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Registration No. 333-136023

PROSPECTUS

Arena Pharmaceuticals, Inc.

**UP TO 829,856 SHARES OF
COMMON STOCK**

Our common stock is traded on the NASDAQ Global Market under the symbol ARNA . On August 3, 2006, the closing price of our common stock was \$10.50.

This prospectus relates to the resale, from time to time, of up to 829,856 shares of our common stock by the selling stockholder named in this prospectus. See Selling Stockholder beginning on page 20. We will not receive any of the proceeds from the sale of these shares.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE RISK FACTORS BEGINNING ON PAGE 3 AND AS UPDATED IN ANY FUTURE FILINGS MADE WITH THE SECURITIES AND EXCHANGE COMMISSION THAT ARE INCORPORATED BY REFERENCE IN THIS PROSPECTUS.

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

The date of this prospectus is August 4, 2006

PROSPECTUS SUMMARY

The following summary highlights information contained elsewhere in this prospectus or incorporated by reference herein. While we have included what we believe to be the most important information about the company and this offering, the following summary may not contain all the information that may be important to you. You should read this entire prospectus carefully, including the risks of investing discussed under Risk Factors beginning on page 3, the financial statements and related notes, and the information to which we refer you and the information incorporated into this prospectus by reference, for a complete understanding of our business and this offering. Unless otherwise specified or required by context, references in this prospectus to we , us , our and Arena refer to Arena Pharmaceuticals, Inc. and its subsidiaries on a consolidated basis. References to the selling stockholder or Smithfield in this prospectus refer to Smithfield Fiduciary LLC, who may sell shares from time to time as described in this prospectus.

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. The most advanced, lorcaserin, is under investigation for the treatment of obesity. Our lead drug candidate for the treatment of insomnia, APD125, is a compound with a novel mechanism of action. 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 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.

RISK FACTORS

An investment in our stock involves a high degree of risk. You should consider carefully the risks described below, together with other information in this prospectus and the information incorporated by reference herein, before making a decision to invest in our common stock. If any of the risks described below 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 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, operating results, prospects or financial condition.

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 \$31.7 million for the six months ended June 30, 2006, and we had an accumulated deficit of \$277.6 million from our inception in April 1997 through June 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 commercial 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 our how we decide to 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 been discussing with the FDA a Phase 3 clinical trial program for our obesity drug candidate, lorcaserin hydrochloride (previously referred to by us as APD356), and expect to announce the commencement of this Phase 3 program in the second half of 2006. The final program may not meet analysts' and investors' expectations or may be perceived negatively, including due to clinical trial design or cost (which may change significantly depending on our clinical results), and we may not be successful in commencing these clinical trials on our projected

timetable, if at all.

We need to address manufacturing and formulation issues relating to our planned Phase 2 trial for APD125 that we believe may be resolvable using data available to us, but we or the FDA may determine that additional data need to be generated before we can initiate the Phase 2 trial. We expect to be able to start the Phase 2 trial in the second half of 2006, but we cannot be sure when, if ever, the trial will proceed.

Failure to initiate or delays in our clinical trials of lorcaserin hydrochloride, APD125 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 and time consuming, and their progress may be interrupted and their outcome is uncertain.

Clinical trials are very expensive, difficult to design and implement, and can be more expensive than originally anticipated. The clinical trial process is also time consuming. Assuming favorable results, we estimate that the clinical trials of our most advanced drug candidates will continue for several years and may take significantly longer to complete. Before we can obtain regulatory approval for the commercial sale of any drug candidate that we wish to develop, we are required to complete extensive clinical trials

in humans to demonstrate its safety and efficacy for treatment of specific indications and monitor safety throughout the clinical development process. All of our drug candidates are prone to the risks of failure inherent in drug development. 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 approval. Administering any of our drug candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our drug candidate for any or all of the targeted indications. The FDA, other regulatory authorities, our collaborators, or we may suspend or terminate clinical trials at any time. Any failure or significant delay in completing clinical trials for our drug candidates, or in receiving regulatory approval for the sale of any drugs resulting from our drug candidates, may severely harm our business and reputation. The timing of the commencement, continuation and completion of clinical trials may be subject to significant delays relating to various causes, including:

lack of effectiveness during the clinical trials;

side effects experienced by study participants or other safety issues;

slower than expected rates of patient recruitment and enrollment;

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

our manufacturing process or compound formulation, including changes in such process or 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;

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;

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.

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

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 and by comparable governmental authorities in foreign markets. Neither our collaborators nor we are permitted to market our potential drugs 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. The process of obtaining regulatory approval is expensive, often takes many years, and can vary substantially based upon the type, complexity and novelty of the drug candidate involved. 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. Clinical trials may commence only after the IND application becomes effective. A New Drug Application, or NDA, must be supported by extensive clinical and preclinical data regarding manufacturing, process and controls to demonstrate the safety and effectiveness of the drug candidate. Approval policies or regulations may change. Moreover, failure to comply with the FDA and other applicable foreign and United States regulatory requirements may subject us to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure and detention, product recalls, total or partial suspension of production, and refusal to approve pending NDAs, or supplements to approved NDAs.

We have not previously filed NDAs with the FDA, nor have we previously conducted large scale Phase 3 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. Despite the time and expense invested, regulatory approval is very uncertain and never

guaranteed and we could encounter problems that cause us to abandon clinical trials or to repeat or perform additional preclinical testing and clinical trials. The FDA has substantial discretion in the drug approval process. The number of preclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. The FDA can delay, limit or deny approval of a drug candidate for many reasons, including:

not finding a drug candidate sufficiently safe and/or effective;

not finding the data from preclinical testing and clinical trials sufficient to prove safety or efficacy;

not approving of our or a third-party manufacturer's processes or facilities; or

changes in its approval policies or the adoption of new regulations.

Because, in part, of the early stage of our drug candidate research and development process, we cannot predict whether or not regulatory approval will be obtained for any drug we develop. Two of our internally discovered drug candidates, lorcaserin hydrochloride and APD125, are under clinical development by us, and two of our internally discovered drug candidates are under clinical development by our partners, Ortho-McNeil and Merck. Compounds developed by us or our partners may not prove to be safe and effective in clinical trials and may not meet all of the applicable regulatory requirements needed to receive marketing approval. Administering any of our drug candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory authorities denying approval of our drug candidates for any or all of the targeted indications. If regulatory approval of a drug candidate is granted, the approval will be limited to those disease states and conditions for which the drug candidate is demonstrated through clinical trials to be sufficiently safe and effective. Failure to obtain regulatory approval will delay or prevent us from commercializing drugs. These risks also apply to the development activities of our collaborators, and we do not expect any drugs resulting from our collaborators research and development efforts to be commercially available for many years, if ever. The FDA, other regulatory authorities, our collaborators or we may suspend or terminate clinical trials at any time. Any failure or significant delay in completing clinical trials for our drug candidates, or in receiving regulatory approval for the sale of any drugs resulting from our drug candidates, may severely harm our business and reputation.

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. Success in preclinical studies or completed clinical trials does not ensure that later studies or trials, including continuing preclinical studies and large-scale clinical trials, will be successful nor does it necessarily predict future results. Favorable results in early studies or trials may not be repeated in later studies or trials, and drug candidates in later stage trials may fail to show desired safety and efficacy despite having progressed through initial-stage trials. Unfavorable results from ongoing preclinical studies or clinical trials could result in delays, modifications or abandonment of ongoing or future clinical trials. In addition, we may report top-line data from time to time. Top-line data is based on preliminary analysis of key efficacy and safety data, and is subject to change.

A number of companies in the biotechnology industry have suffered significant setbacks in advanced clinical trials, even after promising results in earlier 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, failure to construct appropriate clinical trial protocols could result in the test or control group experiencing a disproportionate number of adverse events and could cause a clinical trial to be delayed, repeated or terminated.

Our most advanced drug candidates, lorcaserin hydrochloride and APD125, have not completed the large, pivotal Phase 3 trials for efficacy and safety that are required for FDA approval. Preclinical data and the limited clinical results that we have obtained for lorcaserin hydrochloride 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 hydrochloride or APD125 to achieve or sustain the desired effects in the intended population or to do so safely. In addition, in December 2005 we announced the commencement of preclinical studies with our anti-platelet compound, APD791, under investigation for the potential prevention of thromboembolic diseases, such as heart attacks and strokes. We cannot be certain that results sufficiently favorable to justify commencement of Phase 1 studies will be obtained in these preclinical investigations.

We have developed lorcaserin hydrochloride to more selectively stimulate the 5-HT_{2C} serotonin receptor because we believe this selectivity 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 hydrochloride's selectivity profile may not avoid the undesired side effects. Moreover, the potential relationship between the activity of lorcaserin hydrochloride and the activity of fenfluramine and dexfenfluramine may result in increased FDA regulatory scrutiny of the safety of lorcaserin hydrochloride and may raise potential adverse publicity in the marketplace, which could affect clinical enrollment or ultimately sales if lorcaserin hydrochloride is approved for sale.

We have developed APD125 to selectively inhibit the 5-HT_{2A} serotonin receptor because we believe this mechanism may be better tolerated and improve sleep quality and maintenance as compared to existing sleep therapies. Preclinical data and the results from our Phase 1 clinical trial in subjects with normal sleep patterns may not predict APD125's effects on sleep quality, sleep maintenance or sleep onset latency in patients with insomnia.

We will be required to demonstrate through larger-scale clinical trials that our drug candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. There is typically a high rate of attrition from the failure of drug candidates proceeding through clinical trials. To date, long-term safety and efficacy have not yet been demonstrated in clinical trials for any of our drug candidates. If lorcaserin hydrochloride or APD125 fails to demonstrate sufficient safety and efficacy in any clinical trial, we will experience potentially significant delays in, or decide to abandon development of, that drug candidate. If we abandon or are delayed in our development efforts related to lorcaserin hydrochloride, APD125, 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.

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. 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.

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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 advancing our lead programs, we may have to curtail some of our activities.

If we are not successful in achieving additional milestones under our cardiovascular collaboration with Merck or our diabetes collaboration with Ortho-McNeil, or developing or partnering lorcasein hydrochloride 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 \$21.5 million for the six months ended June 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 milestones. 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 six months ended June 30, 2006, 100% of our revenues were from our collaborations with Merck and Ortho-McNeil. Absent any new collaborators, we expect substantially 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 three years from October 21, 2004. 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 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 initial term of the research program under our agreement with Ortho-McNeil is until December 20, 2006, unless extended for an additional year by Ortho-McNeil or as we may otherwise agree. 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 any future revenues.

Setbacks in the pharmaceutical and biotechnology industries, such as those caused by safety concerns relating to high-profile drugs like Vioxx, competition from generic drugs and 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 hydrochloride 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 a manufacturing failure that could delay the clinical development or regulatory approval of our drug candidates, or their ultimate commercial production if approved.

Any performance failure on the part of us or a third-party manufacturer could delay clinical development or regulatory approval of our drug candidates. Manufacturers often encounter difficulties involving production yields, regulatory compliance, quality control and quality assurance, as well as shortages of qualified personnel. We or a third-party manufacturer may encounter such difficulties. The manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration of the U.S. Department of Justice and corresponding state agencies 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, 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, the scale-up and production of intermediates and other compounds for research and development purposes, and the 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 hazardous 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:

an 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 and our insurance coverage for those claims may be inadequate.

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human 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;

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 office 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-marketing 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 safety reporting requirements, and 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, and could include withdrawal of the drug from the market. Failure to comply with applicable regulatory requirements may result in:

issuance of warning letters by the FDA;

finances 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.

In order to market any drugs outside of the United States, we and our collaborators must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks 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.

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 have a negative impact on 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.

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 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 legal issues. Consequently, the analysis of our patent applications will be 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.

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 in our patents' coverage.

As of June 30, 2006, we owned, in part or in whole, or had exclusively licensed the following patents: 17 in the United States, 139 in European countries, eight in New Zealand, six in Australia, six in Lebanon, three in Hong Kong, two in Singapore, and one in each of Japan, China, Israel and Taiwan. In addition, as of June 30, 2006, we had approximately 665 patent applications before the United States Patent and Trademark Office, foreign patent offices and international patent authorities. These patents and patent applications are divided into 88 distinct families of related patents that are directed to CART, Melanophore technology, other novel screening methods, chemical compositions of matter, methods of treatment using chemical compositions, or GPCR genes. One of our patent families was exclusively in-licensed and contains a single issued patent. Eighty of our patent families, which include a total of 144 patents and 563 patent applications, were invented solely by our employees. The remaining 7 of our patent families, which include a total of eight patents and 102 patent applications, were the subject of joint inventions by our employees and the employees of other entities. 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 drug or method.

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. 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 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 inadvertently 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 throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs. 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 June 30, 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 our clinical trials;

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

entering into a new collaboration or modifying or terminating an existing collaboration;

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

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

others introducing new drug discovery techniques or introducing or withdrawing drugs 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 June 30, 2006, was approximately \$38.7 million, and accrues interest at four percent 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 June 30, 2006, was approximately \$12.1 million, and accrues interest at four percent 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;

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; 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 47,345,325 shares of our common stock outstanding as of June 30, 2006. The outstanding shares of our Series B-1 Preferred are convertible into up to 5,161,677 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 1,723,066 shares of common stock at \$7.00 per share of common stock. Holders of Series B Preferred are entitled to receive a four percent 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 June 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 (the selling stockholder in this offering), 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 agreed to file 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 June 30, 2006, there were 4,026,086 options to purchase shares of our common stock issued and outstanding under our equity compensation plans at a weighted average exercise price of \$9.21, 6,004,974 additional shares of common stock issuable under our 2006 Long-Term Incentive Plan, 822,367 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 the 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 plan, dated as of October 30, 2002, between us and Computershare Trust Company, Inc., as Rights Agent, as amended on December 24, 2003. The rights plan 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 by-laws 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.

FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference herein, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. 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 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 noted in Risk Factors above and any documents incorporated by reference herein.

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 date of documents incorporated by reference in this prospectus that include forward-looking statements.

USE OF PROCEEDS

The proceeds from the sale of the common stock under this prospectus will belong to the selling stockholder. We will not receive any proceeds from this offering.

SELLING STOCKHOLDER

Pursuant to the Settlement Agreement and Release we entered into with Smithfield Fiduciary LLC on June 30, 2006, we have filed a registration statement, of which this prospectus forms a part, in order to permit Smithfield Fiduciary LLC to resell to the public the shares of our common stock issuable upon exercise of its warrant. For additional information regarding the warrant, see Risk Factors Risks Relating to Our Securities. 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.

The selling stockholder may sell up to 829,856 shares of our common stock pursuant to this prospectus. The shares of our common stock covered by this prospectus may be issued to the selling stockholder pursuant to the warrant described above. The selling stockholder has not held any position or office, nor has it had any material relationship, except as set forth in the financing transaction documents and Settlement Agreement and Release, with us or our predecessors or affiliates within the past three years.

The following table sets forth information regarding beneficial ownership of our common stock by the selling stockholder as of July 14, 2006. There were 47,345,763 shares of our common stock outstanding as of July 14, 2006.

| Name | Shares of Common Stock Beneficially Owned Before Offering | | Number of Shares of Common Stock Offered Hereby | Shares of Common Stock Beneficially Owned Following the Offering(2) | |
|-----------------------------|--|---------------|---|--|------------|
| | Number | % of Class(1) | | Number | % of Class |
| Smithfield Fiduciary LLC(3) | 3,780,674(4) | 7.4%(4) | 829,856 | 2,950,818 | 5.8% |

(1) For the purposes of calculating the percent of class beneficially owned by a holder, shares of common stock which may be issued to that holder within 60 days of July 14, 2006, are deemed to be outstanding.

(2) We do not know when or in what amounts the selling stockholder may offer shares for sale. The selling stockholder may choose not to sell any of the shares offered by this prospectus. This table assumes the sale by the selling stockholder of all of the shares of common stock available for resale under this prospectus.

(3) Highbridge Capital Management, LLC, is the trading manager of Smithfield Fiduciary LLC and consequently has voting control and investment discretion over securities held by Smithfield Fiduciary LLC. Glenn Dubin and Henry Swieca control Highbridge Capital Management, LLC. Each of Highbridge Capital Management, LLC, Glenn Dubin and Henry Swieca disclaims beneficial ownership of the securities held by Smithfield Fiduciary LLC.

(4) The selling stockholder disclaims beneficial ownership of our common stock that exceeds 4.999% of our outstanding common stock. Under the terms of our Series B Convertible Preferred Stock and the warrant held by the selling stockholder, the number of shares of our common stock that may be acquired by the selling stockholder upon any conversion of the preferred stock or exercise of the warrant is limited to the extent necessary to ensure that, following such conversion or exercise, as applicable, the total number of shares of our common stock then beneficially owned by the selling stockholder and its affiliates and any other persons whose beneficial ownership of our common stock would be aggregated with the selling stockholder for purposes of Section 13(d) of the Exchange Act does not exceed 4.999% of our common stock (including shares

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of our common stock issuable upon such conversion). The selling stockholder can waive this provision or increase (but not to more than 9.999%) or decrease this percentage by giving us written notice, but (i) any such waiver or increase will not be effective until the 61st day after such notice is delivered to the us, and (ii) any such waiver or increase or decrease will apply only to such holder. The 4.999% limitation is disregarded for purposes of this table, and the numbers of shares of common stock beneficially owned and percentages of class listed in the table do not reflect this limitation.

PLAN OF DISTRIBUTION

The selling stockholder may, from time to time, sell any or all of its shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholder may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

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

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholder may also sell shares under Rule 144 under the Securities Act or pursuant to other available exemptions from the registration requirements of the Securities Act, if available, rather than under this prospectus.

The selling stockholder may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of our securities and may sell or deliver shares in connection with these trades.

Broker-dealers engaged by the selling stockholder may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by the selling stockholder. The selling stockholder may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling stockholder may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by it and, if it defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholder also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholder and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares of common stock to the selling stockholder, other than the fees and disbursements of counsel, brokerage fees or underwriting fees. We have agreed to indemnify the

selling stockholder against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The selling stockholder has advised us that it has not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by the selling stockholder. If we are notified by the selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling stockholder uses this prospectus for any sale of the shares of common stock, it will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of our common stock and activities of the selling stockholder.

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, an 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

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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

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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 after the date of this prospectus until the termination of the offering of the shares covered by this prospectus (in each case, other than information furnished under Form 8-K):

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

our quarterly report on Form 10-Q for the quarterly period ended March 31, 2006 (filed on May 10, 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 and August 1, 2006;

the description 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.

No one has been authorized to give any information or to make any representations other than contained or incorporated by reference in this prospectus, and if given or made, such information or representations must not be relied upon as having been authorized by us. This prospectus does not constitute an offer or solicitation by anyone in any jurisdiction in which such offer or solicitation is not authorized or in which the person making such offer is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation. Neither the delivery of this prospectus nor any sale made hereunder shall, under any circumstance, create any implication that there has not been any change in our affairs since the date hereof.