ARENA PHARMACEUTICALS INC
Form S-3
July 25, 2006

As filed with the Securities and Exchange Commission on July 25, 2006

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

ARENA PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**23-2908305**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

6166 Nancy Ridge Drive

San Diego, California 92121

(858) 453-7200

(Address, Including Zip Code and Telephone Number, Including

Area Code, of Registrant s Principal Executive Offices)

Steven W. Spector, Esq.

Senior Vice President, General Counsel and Secretary

6166 Nancy Ridge Drive

San Diego, California 92121

(858) 453-7200

(Name, Address, Including Zip Code and Telephone Number, Including

Area Code, of Agent for Service)

Copies to:

Steven M. Przesmicki, Esq.

Cooley Godward LLP

4401 Eastgate Mall

San Diego, CA 92121

(858) 550-6000

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Class of Securities to be Registered	Number of Shares to be Registered(1)	Proposed Maximum Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value $.0001 per share, issuable upon exercise of warrant, including related rights to purchase Series A Junior Participating Preferred Stock	829,856	$ 9.37	$ 7,775,750.72	$ 832.01

(1) Pursuant to Rule 416 under the Securities Act of 1933, the shares being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the amount of the registration pursuant to Rule 457(c) under the Securities Act of 1933, based upon the average of the high and low prices for the common stock on July 21, 2006, as reported by the NASDAQ Global Market.

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

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

Subject to Completion, dated July 25, 2006

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 July 21, 2006, the closing price of our common stock was $9.23.

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 , 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-HT2C 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-HT2A 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.

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 lorcaserin 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;

fines and other civil penalties;

criminal prosecutions;

injunctions, suspensions or revocations of marketing licenses;

suspension of any ongoing clinical trials;

suspension of manufacturing;

delays in commercialization;

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

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

restrictions on operations, including costly new manufacturing requirements; and

product recalls or seizures.

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

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