

ARENA PHARMACEUTICALS INC

Form S-3

November 07, 2005

As filed with the Securities and Exchange Commission on November 7, 2005

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 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

(State or Other Jurisdiction of Incorporation or Organization)

23-2908305

(I.R.S. Employer Identification Number)

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 the effective date of this Registration Statement.

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

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.

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.

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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.

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

| Title of Class of Securities to be Registered | Number of Shares to be Registered(3) | Proposed Maximum Offering Price Per Share(2) | Proposed Maximum Aggregate Offering Price | Amount of Registration Fee |
|--|---|---|--|-----------------------------------|
| Common Stock, par value \$.0001 per share, including related rights to purchase Series A Junior Participating Preferred Stock(1) | 10,000,000 | \$ 10.27 | \$ 102,700,000 | 12,087.79 |

(1) Pursuant to Rule 416 under the Securities Act, 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 November 1, 2005, as reported by the Nasdaq National Market.

(3) The aggregate amount of the registrant's common stock registered hereunder that may be sold in at the market offerings for the account of the registrant is limited to that which is permissible under Rule 415(a)(4) under the Securities Act of 1933, as amended.

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 November 7, 2005

PROSPECTUS

Arena Pharmaceuticals, Inc.

Common Stock

Our common stock is listed on the Nasdaq National Market under the symbol ARNA. On November 1, 2005, the last reported sale price of our common stock on the Nasdaq National Market was \$10.21 per share.

This prospectus and the accompanying prospectus supplement will allow us to sell up to 10,000,000 shares of our common stock over time in one or more offerings. Each time we offer shares, we will provide you with a supplement to this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus and any prospectus supplement carefully before you invest.

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

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

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any

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applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement. This prospectus may not be used to sell any of the common stock unless accompanied by a prospectus supplement.

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

The date of this prospectus is _____, 2005.

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

About This Prospectus

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This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration statement, we may sell up to 10,000,000 shares of our common stock in one or more offerings. Each time we sell any of our common stock under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also add, update or change in a prospectus supplement any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus, together with any applicable prospectus supplement and the documents incorporated by reference into this prospectus, include all material information relating to this offering. You should carefully read both this prospectus and any applicable prospectus supplement together with the additional information described under **Where You Can Find More Information** before buying common stock in this offering.

Summary

Arena Pharmaceuticals, Inc.

We are a clinical-stage biopharmaceutical company focusing on the discovery, development and commercialization of small molecule drugs in four major therapeutic areas: metabolic, cardiovascular, inflammatory and central nervous system diseases. We are developing a broad pipeline of compounds that act on an important class of drug targets called G protein-coupled receptors, or GPCRs, using our knowledge of GPCRs and our technologies, including CART (Constitutively Activated Receptor Technology) and Melanophore. We have three internally discovered, clinical-stage product candidates. Our most advanced clinical compound, APD356, a selective 5-HT_{2C} serotonin receptor agonist for the treatment of obesity, is in a Phase 2b clinical trial. Our lead product candidate for the treatment of insomnia, APD125, a compound with a novel mechanism of action (a selective 5-HT_{2A} receptor inverse agonist), is scheduled to begin a Phase 2 clinical trial by the end of 2005. As part of our collaboration with Merck & Co., Inc., our product candidate for the treatment of atherosclerosis and related disorders is in a Phase 1 clinical trial. We also have an active collaboration with Ortho-McNeil, Inc., a Johnson & Johnson company, for the treatment of type 2 diabetes.

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

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

Risk Factors

An investment in our common stock involves a high degree of risk. You should consider carefully the risks described below, together with other information in this prospectus, any applicable prospectus supplement and the information incorporated by reference herein and therein, before you make 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 all or part of your investment. Moreover, the risks described below are not the only ones that we face. Additional risks not currently 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 \$57.5 million for the nine months ended September 30, 2005, and we had an accumulated deficit of \$226.3 million from our inception in April 1997 through September 30, 2005. 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 products. 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 will 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 our clinical trials.

We expect to announce results from our Phase 2b clinical trial of our most advanced product candidate, APD356 for obesity, around the end of the year. In addition, we also expect to announce additional safety results from our recent Phase 1 clinical trial for our second most advanced product candidate, APD125 for insomnia. These results may not be favorable or viewed favorably by us or third parties, including investors, analysts and potential collaborators. Biotechnology company stock prices have declined significantly where clinical results were not favorable, were perceived negatively or otherwise did not meet expectations. Failure to initiate or delays in our clinical trials of APD356, APD125 or of any of our other product candidates, or unfavorable results or negative perceptions regarding any of such trials, could cause our stock price to decline significantly.

Clinical trials for our product candidates are expensive, time consuming, may be interrupted and their outcome is uncertain.

Clinical trials are very expensive and difficult to design and implement. The clinical trial process is also time consuming. Assuming favorable results, we estimate that the clinical trials of our most advanced product candidates will continue for several years. Before we can obtain regulatory approval for the commercial sale of any product candidate that we wish to develop, we are required to complete extensive clinical trials in humans to demonstrate its safety and efficacy. 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;

unforeseen or serious 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;

delays in obtaining regulatory approvals to commence a study or clinical holds or other 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;

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.

The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and our current product 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 product candidate, but rather to test safety, to study pharmacokinetics and pharmacodynamics, and to understand the product candidate's side effects at various doses and schedules. Success in preclinical or completed clinical trials does not ensure that later large-scale trials will be successful nor does it necessarily predict future results. Favorable results in early trials may not be repeated in later trials.

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.

Clinical trials of our most advanced product candidates, APD356 and ADP125, have been conducted only in small numbers of subjects. Preclinical data and the limited clinical results we have obtained for APD356 and APD125 may not predict results from studies in larger numbers of subjects drawn from more diverse populations treated for longer periods of time or, in the case with APD125, when patients with insomnia are studied rather than normal volunteers, and also may not predict the ability of APD356 or APD125 to achieve or sustain the desired effects in the intended population or to do so safely.

We have developed APD356 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 APD356's selectivity profile may not avoid the undesired side effects. Moreover, the potential relationship between the activity of APD356 and fenfluramine and dexfenfluramine may result in increased FDA regulatory scrutiny of the safety of APD356 and may raise potential adverse publicity in the marketplace. In response to our Investigational New Drug submission for APD356, the FDA recommended we assess the abuse potential and requested that we provide our plans for cardiac valve monitoring during Phase 2 and Phase 3 clinical trials. We have submitted to the FDA our plan for cardiac valve monitoring and our communication with the FDA on these issues is expected to be on-going.

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 these product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. To date, long-term safety and efficacy have not yet been demonstrated in clinical trials for any of our product candidates. If APD356 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 product candidate. If we abandon or are delayed in our development efforts related to APD356 or APD125, or any other product candidate, we may not be able to generate sufficient revenues to continue our operations at the current level or become profitable, our reputation in the industry and in the investment community would likely be significantly damaged, it may not be possible to complete financings, and our stock price would likely decrease significantly.

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

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 product 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 products.

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 approaches that 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 product 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.

Our product 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 commercialize products.

The clinical development, manufacturing, labeling, packaging, storage, record-keeping, advertising, promotion, export, marketing, and distribution of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable governmental authorities in foreign markets. Neither we nor our collaborators are permitted to market our potential products in the United States until we receive regulatory approval from the FDA. Neither we nor our collaborators have received marketing approval for any of our product 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 product involved. 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 product 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.

In addition, we have not previously filed NDAs with the FDA. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for our product 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 product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. The FDA can delay, limit or deny approval of a product candidate for many reasons, including:

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

not finding the data from preclinical testing and clinical trials sufficient;

not approving of our or a third-party manufacturers processes or facilities; or

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

Because, in part, of the early stage of our product candidate research and development process, we cannot predict whether or not regulatory approval will be obtained for any product we develop. Only two of our product candidates, APD356 and APD125, are undergoing clinical trials by us, and only one of our product candidates is undergoing clinical trials by a partner, Merck. Compounds developed by us, alone or with other parties, 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 product candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory authorities denying approval of our product candidates for any or all of the targeted indications. If regulatory approval of a product is granted, the approval will be limited to those disease states and conditions for which the product is demonstrated through clinical trials to be sufficiently safe and effective. Failure to obtain regulatory approval will delay

or prevent us from commercializing products. 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 product candidates, or in receiving regulatory approval for the sale of any drugs resulting from our product candidates, may severely harm our business and reputation.

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 APD356 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 opportunity for success.

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

Our revenues were \$13.7 million and \$12.8 million for the years ended December 31, 2004 and 2003, respectively, and were \$17.4 million for the nine months ended September 30, 2005. 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, and we are not entitled to the more significant milestone payments under our agreements until our collaborators have advanced compounds in clinical testing. Only one of our partners, Merck, has advanced one of our compounds into clinical testing and paid us the applicable milestone. We cannot guarantee that any of the other development, approval or sales milestones in our existing or future collaborations will be satisfied, or that we will receive any payments for the achievement of those other milestones.

For the year ended December 31, 2004, revenues recognized under our collaboration with Merck represented approximately 95% of our total revenues. For the nine months ended September 30, 2005, 100% of our revenues were from our collaborations with Merck and Ortho-McNeil. We expect substantially all of our revenues for the remaining three months of 2005 will 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 products; 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 product 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.

Our agreement with Ortho-McNeil will continue until the expiration of Ortho-McNeil's payment obligations for research funding, milestone payments and royalties, unless the agreement is terminated earlier by either party. 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 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 collaborators that could delay or prevent the development or commercialization of our product candidates.

We may have conflicts with our collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, or the ownership of intellectual property developed during the collaboration. If any conflicts arise with Ortho-McNeil, Merck or any other 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 product 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 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 product 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 product candidates, our commercial opportunity 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 we or our collaborators 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 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.

Consolidation and setbacks in our industry and our or our collaborator's inability to obtain acceptable prices for drugs could make partnering more difficult and diminish our revenues.

Consolidation in the pharmaceutical and biotechnology industry, setbacks caused by safety concerns relating to high-profile drugs like Vioxx and Celebrex, competition from generic drugs and litigation may have an adverse effect on us. In addition, 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, if their therapeutic areas of focus change following a merger, or if they have reduced research budgets as a result of some financial setback.

Our and our collaborators' ability to commercialize future drugs will depend in part on government regulation and the reimbursement policies of government authorities, private health insurers and other third-party payers. 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 product candidates in the future by reducing the potential revenues that we and our collaborators could generate 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, we may not be able to advance our product candidates 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 are relying on contract clinical sites to conduct our clinical trials for APD356 and APD125. Clinical research organizations will 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 expect any drugs resulting from our collaborators' research and development efforts to be commercially available for many years, if ever.

Any performance failure on the part of a third-party manufacturer could delay clinical development or regulatory approval of our product candidates. Third-party manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. 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 third-party manufacturers' compliance with these regulations and standards. If one of our manufacturers fails to maintain compliance, the production of our product 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

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

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials, and will face an even greater risk if we sell our product candidates commercially. An individual may bring a liability claim against us if one of our product candidates 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 product candidates;

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 product candidates.

We have limited product liability insurance that covers our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for any of our product 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.

We may incur increased costs as a result of recently enacted changes in laws and regulations relating to corporate governance matters.

Changes in the 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 and by the Nasdaq National 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.

All of our laboratories and offices are in a single location in San Diego. We depend on our laboratories and other 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 product candidates receives regulatory approval, our product candidates will still be subject to extensive post-market regulation.

If we or our collaborators receive regulatory approval for our product 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 our products.

If any of our product candidates receive United States regulatory approval, the FDA may still impose significant restrictions on the indicated uses for which such products may be marketed or impose ongoing requirements for potentially costly post-approval studies. In addition, regulatory agencies subject a product, its manufacturer and the manufacturer's facilities to continual review and inspections. The subsequent discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, may result in restrictions on the marketing of that product, and could include withdrawal of the product 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 products 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 product 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 products 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 product 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 product 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 will be effective in our first quarter of 2006, will change how we account for share-based compensation, and may have a significant impact on our future results of operations.

We currently account for share-based payments to employees and directors using the intrinsic value method. Under this method, we generally do not recognize any compensation related to stock option grants we issue under our stock option plans or the discounts we provide under our employee stock purchase plan.

SFAS No. 123R will require us to recognize share-based compensation as compensation expense in the statement of operations based on the fair values of such equity on the date of the grant, with the compensation expense recognized over the period in which the recipient is required to provide service in exchange for the equity award. This statement will also require us to adopt a fair value-based method for measuring the compensation expense related to share-based compensation. We have begun, but have not completed, evaluating the impact of the adoption of SFAS 123R on our results of operations. Historically, we have used the Black-Scholes option pricing model, which is widely used to estimate the value of traded options that have no vesting restrictions and are fully transferable, which are significantly different characteristics from our employee stock options. In connection with evaluating the impact of SFAS 123R, we are considering the potential implementation of different valuation methods to determine the fair value of share-based compensation. We believe the adoption of SFAS 123R will have a material impact on our results of operations, regardless of the valuation method used. SFAS 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. This requirement will reduce our net operating cash flows and increase our net financing cash flows in periods after adoption. SFAS 123R may also delay when we may become profitable.

Future changes in generally accepted accounting principles, including pronouncements relating to revenue recognition, may 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 product 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 U.S. 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 and 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 October 31, 2005, we owned, in part or in whole, or had exclusively licensed the following patents: 17 in the United States, 63 in European countries, eight in New Zealand, six in Australia, four in Lebanon, one in Japan, one in Singapore, one in Hong Kong and one in Israel. In addition, as of October 31, 2005, we had approximately 344 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 80 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. Seven of our patent families containing a total of nine patents and 57 patent applications were the subject of joint inventions by our employees and the employees of other entities. The remaining 72 patent families containing a total of 92 patents and 287 patent applications were invented solely by our employees. There is no assurance that any of these patent applications will issue, or that any of the patents will be enforceable or will cover a drug product or other commercially significant product 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 drug products that modulate a particular drug target or GPCR, regardless of whether the infringing drug product 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 highly controversial and the subject of intense 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 trade secrets to protect our technologies. However, trade secrets are difficult to protect. We require our employees to contractually agree not to improperly use our trade secrets or disclose them 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 require collaborators, service providers and consultants to enter into confidentiality agreements, 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, manufacture, market and sell our product candidates and conduct our research and development activities without infringing or misappropriating the proprietary rights of other entities. 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 other entities based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of GPCRs, some of which purport to allow the patent holder to control the use of all drug products that modulate a particular drug target or GPCR, regardless of whether the infringing drug product bears any structural resemblance to a chemical compound known to the patent holder at the time of patent filing. Numerous U.S. and foreign issued patents and pending patent applications owned by others also exist in the therapeutic areas in which we are developing products. These could materially affect our ability to develop our product candidates or sell our products, 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 product candidates or technologies may infringe. There also may be existing patents, of which we are not aware, that our product 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 other entities 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, other entities 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 other entities.

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 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 products, 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 product 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 drug products. These products may compete with our products 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 product 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, 2003, to October 31, 2005, the market price of our stock was as low as \$3.48 per share and as high as \$10.54 per share.

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

our success or failure in clinical trials;

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

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

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 the private placement to two institutional investors of (i) an aggregate of 3,500 shares of our Series B-1 Preferred, (ii) seven-year Warrants to purchase up to an aggregate of 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 for a period of approximately 16 months from December 24, 2003, up to \$11.5 million of our Series B-2 Preferred and

additional seven-year Warrants to purchase up to 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 to redeem all or some of their shares of Series B-1 Preferred at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties. The stated value is the original holder's investment plus any dividends settled by increasing the stated value at the time the dividend is payable. The aggregate redemption price of our Series B-1 Preferred at September 30, 2005, was approximately \$37.6 million, and accrues interest at 4.0% annually.

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

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.

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 Events include 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 Event (as defined in the Registration Rights Agreement with the Series B Preferred holders) occurs and remains 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. Triggering Event is specifically defined in the Certificate of Designations for the Series B-1 Preferred and the Series B-2 Preferred.

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 other 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 National Market or other eligible market;

the shares to be issued can be issued without violating the rules of the Nasdaq National 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 35,387,800 shares of our common stock outstanding as of October 31, 2005. The outstanding shares of our Series B-1 Preferred are convertible into up to 5,009,546 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 1,672,282 shares of common stock at \$7.00 per share of common stock. Holders of Series B Preferred are entitled to receive a 4.0% annual dividend that is payable by issuing common stock or by increasing the amount of common stock that is issuable upon conversion of the Series B Preferred. In addition, holders of our Series B Preferred own Warrants to acquire common stock, which, if exercised and converted, would obligate us to issue up to 1,936,200 additional shares of common stock at an exercise price of \$10.00 per share. In addition, as of October 31, 2005, there were 3,639,732 common stock options issued and outstanding under our equity compensation plans at a weighted average exercise price of \$8.00, 636,961 additional shares of common stock issuable under our equity compensation plans, 554,976 shares of common stock reserved for issuance under our 2001 Employee Stock Purchase Plan and 134,169 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. In addition, the average number of shares of our stock that trade each day is generally low. As a result, 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.

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.

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

We intend to use the net proceeds from this offering:

for the clinical and preclinical development of our internally discovered product candidates;

for discovery research for new product candidates; and

for general corporate purposes, including working capital.

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

Forward-Looking Statements

This prospectus including the documents that we incorporate by reference herein contains, and any applicable prospectus supplement including the documents we incorporate by reference therein may contain, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, 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 opportunity, the negative of these words, or 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 in any applicable prospectus supplement and any documents incorporated by reference herein or therein.

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

Use of Proceeds

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

Description of Capital Stock

As of the date of this prospectus, our amended and restated certificate of incorporation authorizes us to issue 67,500,000 shares of common stock, par value \$.0001 per share, and 7,500,000 shares of preferred stock, par value \$.0001 per share. As of October 31, 2005, approximately 35.4 million shares of common stock were outstanding. To date, our board of directors has designated 350,000 of the authorized shares of preferred stock as Series A Junior Participating Preferred Stock (the Series A Preferred Stock), which series is described in greater detail below under Share Purchase Rights Plan, and 4,650 of the authorized shares of preferred stock as Series B Convertible Preferred Stock as described in greater detail below under Series B Preferred Stock. As of October 31, 2005, 4,650 shares of Series B Preferred Stock were outstanding.

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

Common Stock

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

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

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

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

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by stockholders, to designate up to 7,500,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, qualifications and

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restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock. To date, our board of directors has designated 350,000 of the authorized shares of preferred stock as the Series A Preferred Stock, which series is described in greater detail below under *Share Purchase Rights Plan*, and 4,650 of the authorized shares of preferred stock as Series B Convertible Preferred Stock as described in greater detail below under *Series B Preferred Stock*.

The issuance of additional preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. The issuance could have the effect of decreasing the market price of the common stock. The issuance of preferred stock also could have the effect of delaying, deterring or preventing a change in control of us.

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

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

respect to any of our common stock certificates outstanding as of November 13, 2002, by such common stock certificate with a copy of the Summary of Rights in the form attached as Exhibit C to the Rights Agreement.

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

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

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

The Purchase Price payable, and the number of shares of the Series A Preferred Stock or other securities or property issuable, upon exercise of the Rights are subject to adjustment from time to time to prevent dilution (i) in the event of a stock dividend on, or a subdivision, combination or reclassification of, the Series A Preferred Stock, (ii) upon the grant to holders of the Series A Preferred Stock of certain rights or warrants to subscribe for or purchase Series A Preferred Stock at a price, or securities convertible into Series A Preferred Stock with a conversion price, less than the then-current market price of the Series A Preferred Stock or (iii) upon the distribution to holders of the Series A Preferred Stock of evidences of indebtedness or assets (excluding regular periodic cash dividends paid out of earnings or retained earnings or dividends payable in Series A Preferred Stock) or of subscription rights or warrants (other than those referred to above).

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

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

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

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

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

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

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

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

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

Series B Preferred Stock. On December 24, 2003, we completed the private placement of \$35 million of Series B-1 Convertible Preferred Stock to two institutional investors (the Investors) pursuant to a Securities Purchase Agreement (the Securities Purchase Agreement).

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

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

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If not previously converted, the Company must redeem the Series B-2 Convertible Preferred Stock in five years from April 22, 2005, or earlier under certain circumstances, at such shares' stated value, plus accrued but unpaid dividends thereon to the date of payment and any applicable penalties. Any such redemption may be made by the Company in cash or, subject to certain conditions, in shares of common stock. The Series B-2 Convertible Preferred Stock is convertible into common stock at a fixed conversion price of \$7.00 per share. Otherwise, the Series B-2 Convertible Preferred Stock has substantially identical terms as the Series B-1 Convertible Preferred Stock, as more fully described in the Certificate of Designations relating to the Series B Convertible Preferred Stock (the "Certificate of Designations").

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

In addition, so long as shares of Series B Convertible Preferred Stock are outstanding, we cannot, directly or indirectly, allow or suffer to exist any lien other than permitted liens, as more fully described in the Securities Purchase Agreement.

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

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

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

The holders of our Series B-1 Preferred can require us 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 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, which is the conversion price for the Series B-2 Preferred. 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). We can elect to pay any such redemption in shares of our common stock, if certain conditions have been met.

At any time following the occurrence of a Triggering Event (as defined in the Certificate of Designations), a holder of the Series B Convertible Preferred Stock may require us to repurchase all or any portion of the Series B Convertible Preferred Stock then held by such holder at a price per share equal to the greater of 115% of the stated value or the market value (as calculated in the Certificate of Designations) of such shares of Series B Convertible Preferred Stock plus all accrued but unpaid dividends thereon to the date of payment. We can elect to pay such redemption price in shares of our common stock under certain circumstances.

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

Anti-Takeover Provisions

Delaware Law. We are governed by the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless before the date that the person became an interested stockholder, our board of directors approved either the business combination or the transaction which makes the person an interested stockholder, or after the date that the person became an interested stockholder, the business combination is approved by our board of directors and the vote of at least 66 2/3% of our outstanding voting stock that is not owned by the interested stockholder. Generally, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the stockholder. An interested stockholder is a person who either owns 15% or more of our outstanding voting stock or, together with affiliates and associates, owns or, within three prior years, did own, 15% or more of our outstanding voting stock. The statute could have the effect of delaying, deferring or preventing a change in our control.

Bylaw and Certificate of Incorporation Provisions. Our bylaws provide that special meetings of our stockholders may be called only by the Chairman of the board of directors, our Chief Executive Officer, our President, or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors. Our amended and restated certificate of incorporation also specifies that the authorized number of directors may be changed only by resolution of the board of directors and does not include a provision for cumulative voting for directors. Under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares may be able to ensure the election of one or more directors. These and other provisions contained in our amended and restated certificate of incorporation and bylaws could delay or discourage transactions involving an actual or potential change in control of us or our management, including transactions in which stockholders might otherwise receive a premium for their shares over then current prices. Such provisions could also limit the ability of stockholders to remove current management or approve transactions that stockholders may deem to be in their best interests and could adversely affect the price of our common stock.

Transfer Agent And Registrar

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

Listing on the Nasdaq National Market

Our common stock is listed on the Nasdaq National Market under the symbol ARNA.

PLAN OF DISTRIBUTION

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

to or through underwriters or dealers;

directly to one or more purchasers; or

through agents.

We may distribute the common stock:

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

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

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

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

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

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

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

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

the public offering price of the common stock;

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

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

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

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

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

contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

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

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

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

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

Legal Matters

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

Experts

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Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2004, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004, 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 Securities Exchange Act of 1934 after the date of this prospectus until the

termination of the offering of the shares covered by this prospectus (other than information furnished under Items 2.02 or Item 7.01 of Form 8-K):

our annual report on Form 10-K for the fiscal year ended December 31, 2004 (filed on March 2, 2005);

our quarterly reports on Form 10-Q for the quarterly periods ended March 31, 2005 (filed on May 5, 2005), June 30, 2005 (filed on August 4, 2005) and September 30, 2005 (filed on November 7, 2005);

our proxy for our annual meeting of stockholders on June 13, 2005 (filed on April 22, 2005);

our current reports on Form 8-K filed on January 13, 2005, January 21, 2005, February 1, 2005, February 9, 2005, April 25, 2005, May 5, 2005, May 11, 2005, June 7, 2005, June 30, 2005, August 26, 2005 and October 11, 2005;

a description of the amendment to our Stockholders Rights Plan on Form 8-A/A filed on December 30, 2003;

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; and

all filings we make with the SEC pursuant to the Securities Exchange Act of 1934 after the date of the initial registration statement, of which this prospectus is a part, and prior to the effectiveness of the registration statement.

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

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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.

ARENA PHARMACEUTICALS, INC.

PROSPECTUS

, 2005

PART II**INFORMATION NOT REQUIRED IN THE PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

The following sets forth the estimated costs and expenses, all of which shall be borne by the Registrant, in connection with the offering of the securities pursuant to this Registration Statement:

| | | |
|-------------------------|----|-------------|
| Registration Fee | \$ | 12,087.79* |
| Legal Fees and Expenses | \$ | 125,000* |
| Accounting Fees | \$ | 75,000* |
| Printer Fees | \$ | 50,000* |
| Total | \$ | 262,087.79* |

* Estimated

Item 15. Indemnification of Directors and Officers.

The By-laws of the Registrant provide for indemnification of the Registrant's directors and officers to the fullest extent permitted by law. Insofar as indemnification for liabilities under the Securities Act may be permitted to directors, officers or controlling persons of the Registrant pursuant to the Registrant's Certificate of Incorporation, By-laws and the Delaware General Corporation Law (the "DGCL"), the Registrant has been informed that in the opinion of the SEC such indemnification is against public policy as expressed in such Act and is therefore unenforceable.

Section 102(b)(7) of the DGCL provides that a certificate of incorporation may include a provision which eliminates or limits the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the company or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, relating to prohibited dividends or distributions or the repurchase or redemption of stock or (iv) for any transaction from which the director derives an improper personal benefit. The Registrant's Certificate of Incorporation includes such a provision. As a result of this provision, the Registrant and its stockholders may be unable to obtain monetary damages from a director for breach of his or her duty of care.

Item 16. Exhibits.

| Exhibits: | Description |
|-----------|-------------|
|-----------|-------------|

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- 1.1 Form of Underwriting Agreement (to be filed by amendment or as an exhibit to a current report of the registrant on Form 8-K and incorporated herein by reference).
- 3.1 Fifth Amended and Restated Certificate of Incorporation of the registrant (incorporated by reference to Exhibit 3.1 to the registrant's quarterly report on Form 10-Q for the period ended June 30, 2002, filed with the Securities and Exchange Commission on August 14, 2002, Commission File No. 000-31161).
- 3.2 Amended and Restated By-Laws of the registrant (incorporated by reference to Exhibit 3.2 to the registrant's current report on Form 8-K filed with the Securities and Exchange Commission on January 21, 2003, Commission File No. 000-31161).
- 3.3 Certificate of Designations of the Series A Junior Participating Preferred Stock of the registrant (incorporated by reference to Exhibit 3.3 to the registrant's quarterly report on Form 10-Q for the period ended September 30, 2002, filed with the Securities and Exchange Commission on November 15, 2002, Commission File No. 000-31161).
- 3.4 Certificate of Designations of the Series B-1 Convertible Preferred Stock and Series B-2 Convertible Preferred Stock of the registrant (incorporated by reference to Exhibit 3.1 to the registrant's current report on Form 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161).
- 4.1 Rights Agreement, dated October 30, 2002, between the registrant and Computershare Trust Company, Inc. (incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed with the Securities and Exchange Commission on November 1, 2002, Commission File No. 000-31161).
- 4.2 Amendment No. 1, December 24, 2003, to Rights Agreement dated October 30, 2002, between the registrant and Computershare Trust Company, Inc. (incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161).
- 4.3 Form of common stock certificate (incorporated by reference to Exhibit 4.2 to the registrant's registration statement)

on Form S-1, as amended, filed with the Securities and Exchange Commission on July 19, 2000, Commission File No. 333-3594).

- 5.1 Opinion of Cooley Godward LLP.
- 23.1 Consent of Cooley Godward LLP (included as Exhibit 5.1 to this filing).
- 23.2 Consent of Ernst & Young LLP, independent registered public accounting firm.
- 24.1 Power of Attorney (included on the signature page hereto).

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i) and (1)(ii) do not apply if the registration statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each post-effective amendment

shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of the securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered that remain unsold at the termination of this offering.

(4) That: (i) for purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of the registration statement as of the time it was declared effective; and (ii) for the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(5) That, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC this form of indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against these liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by a director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction

the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of this issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on November 4, 2005.

ARENA PHARMACEUTICALS, INC.

By: /s/ JACK LIEF
Jack Lief, President and Chief Executive Officer

POWER OF ATTORNEY

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KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Jack Lief and Steven W. Spector, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments, exhibits thereto and other documents in connection therewith) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith (including any registration statement relating to this Registration Statement and filed pursuant to Rule 462(b) of the Securities Act of 1933, as amended), with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite the name.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

| Signatures | Date |
|---|------------------|
| By: /s/ JACK LIEF Jack Lief, President, Chief Executive Officer and Director (Principal Executive Officer) | November 4, 2005 |
| By: /s/ ROBERT E. HOFFMAN Robert E. Hoffman, CPA, Vice President, Finance and Chief Accounting Officer (Principal Financial and Accounting Officer) | November 4, 2005 |
| By: /s/ DOMINIC P. BEHAN Dominic P. Behan, Ph.D., Director | November 4, 2005 |
| By: /s/ DONALD D. BELCHER Donald D. Belcher, Director | November 4, 2005 |
| By: /s/ SCOTT H. BICE Scott H. Bice, J.D., Director | November 4, 2005 |
| By: /s/ HARRY F. HIXSON, JR. Harry F. Hixson, Jr., Ph.D., Director | November 4, 2005 |
| By: /s/ J. CLAYBURN LA FORCE, JR. J. Clayburn La Force, Jr., Ph.D., Director | November 4, 2005 |

By: /s/ LOUIS J. LAVIGNE, JR.
Louis J. Lavigne, Jr., Director

November 4, 2005

By: /s/ TINA S. NOVA
Tina S. Nova, Ph.D., Director

November 4, 2005

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EXHIBIT INDEX

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