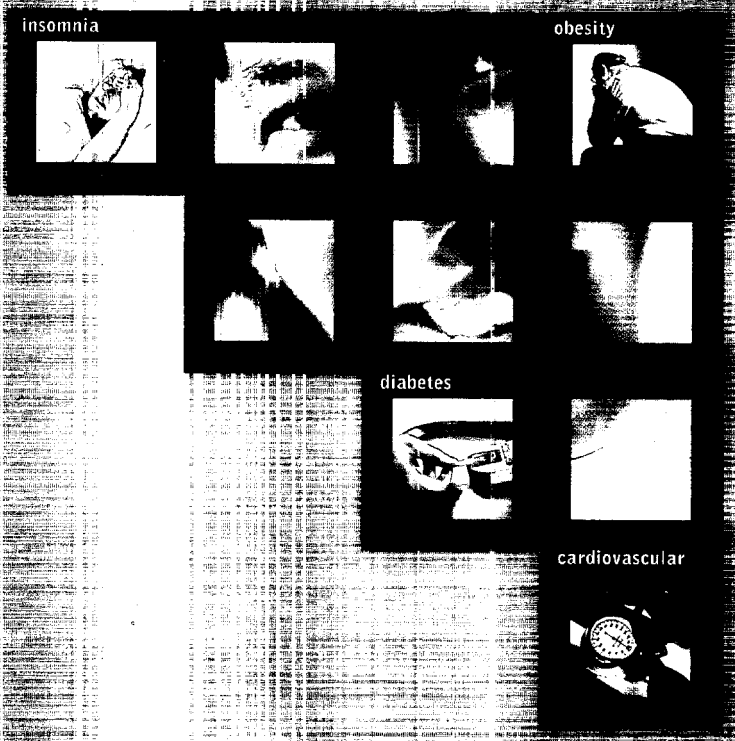
Arena Pharmaceuticals, Inc.



2004 ANNUAL REPORT

Arena

Further validation of our GPCR technology platform comes through our major collaborations with two large pharmaceutical companies. Our cardiovascular collaboration with Merck & Co. involves developing compounds that target a GPCR that we believe is responsible for the HDL-raising activity of niacin, with one goal being to discover a drug with improved characteristics over today's treatments. HDL is the so-called "good cholesterol." Throughout 2004, we announced the receipt of a number of milestone payments from Merck, the most recent of which was for Merck's selection of an Arena-discovered compound for advancement into preclinical development. In addition, in October we extended and expanded our collaboration for three additional years and, at the same time, Merck made a $7.5 million equity investment in Arena at approximately a 70% premium to the then-current market price. In total, through the end of last year, we have received $33.4 million from Merck since our collaboration started in October 2002, including $20.4 million received this past year. We believe this is substantial progress in only two years, and I expect to report continued progress regarding this collaboration.

In December, we signed a collaboration with Ortho-McNeil Pharmaceutical, Inc., a Johnson & Johnson company, focused on one of our programs for type 2 diabetes and other disorders, and have already advanced two compounds into preclinical development. We believe this is one of the largest and most favorable preclinical partnerships in biotechnology history, with financial terms approaching what is generally seen in partnerships with human clinical data. Under this collaboration, we have already received $22.5 million in upfront and milestone payments and are eligible to receive up to $295 million in development and commercialization milestone payments for each compound selected by Ortho-McNeil. We are also eligible to receive royalties starting in the low double-digits, which will increase as product sales increase.

In addition to the tremendous progress in our clinical-stage and partnered programs, we also continued to advance our GPCR drug discovery and research, including moving additional compounds into the lead optimization stage. By applying our CART and Melanophore screening technologies to GPCRs, we have identified and are developing compounds that indicate early promise of addressing future disease conditions, such as diabetes, metabolic syndrome, acute coronary syndrome and rheumatoid arthritis.

Arena has exciting clinical programs, validating partnerships, first-rate GPCR drug discovery and development capabilities, multiple research programs and an experienced and dedicated team. I firmly believe that our deep understanding of GPCR research, the proprietary tools and methods we employ, our proven ability to advance projects into clinical testing and partner with pharmaceutical companies and our financial resources will allow us to achieve our goal of becoming the scientific and commercial leader in GPCR-based drug discovery and development.

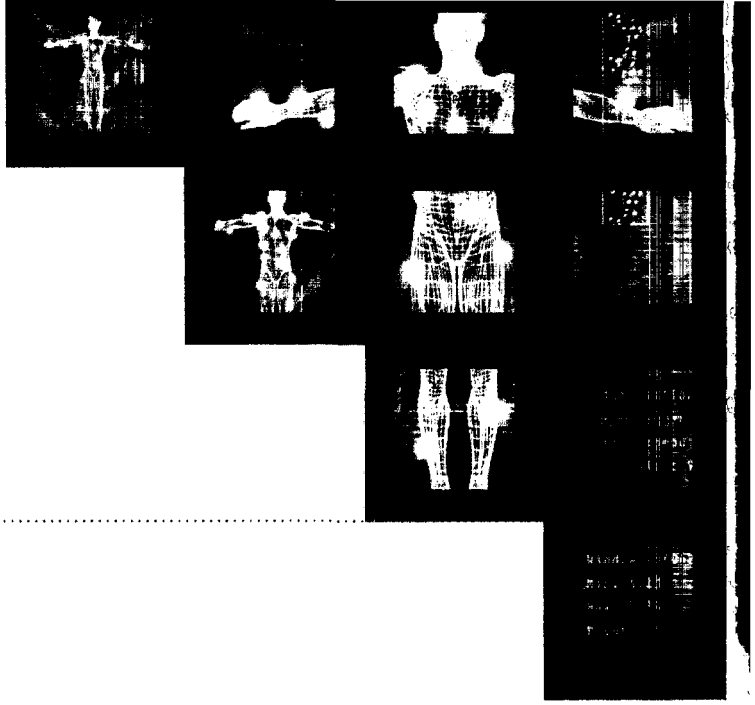
Our team remains committed to discovering and developing safer and more effective therapeutics and to building significant value for our stockholders. I expect 2005 to be even more meaningful than 2004 in these respects, and I look forward to updating you on our progress.

Sincerely,

Jack Lief

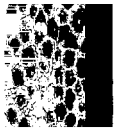
Jack Lief
President and Chief Executive Officer
March 31, 2005

letter



dear stockholders

Since Arena's inception, we have been working diligently with our world class G protein-coupled receptor (GPCR) technologies to develop compounds to address large unmet medical needs that could have blockbuster commercial potential. We have had much success in our short eight-year history, and 2004 included some of our most significant accomplishments yet. Most notably, we initiated clinical trials on two distinct, internally discovered compounds (one for obesity and one for insomnia), made excellent progress with new and existing collaborations, advanced the development of numerous earlier stage programs and strengthened our board of directors by adding experienced and successful biotechnology leaders. Importantly, in 2004 we accomplished key goals and milestones that we believe will better position us to achieve our objective of developing and bringing to market new drugs.

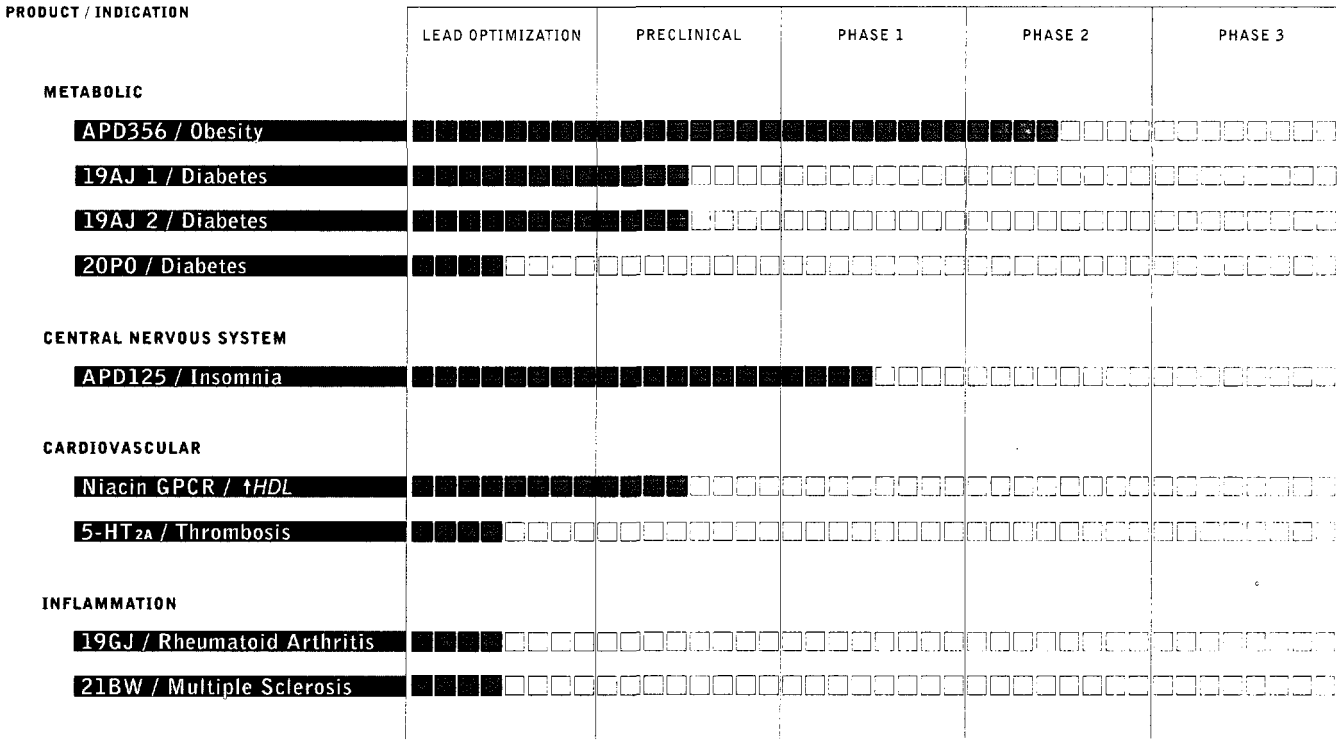


I continue to be very proud of the progress of our programs, including two we moved into the clinic in 2004. In February 2004, we initiated our first clinical trial on an internally discovered compound, APD356 for obesity. This study and a subsequent safety study paved the way for initiating in December a Phase 2 clinical study of 400 obese patients to evaluate the ability of APD356 to promote weight loss over one month. We expect to complete this study in the second quarter of this year. Obesity has reached epidemic proportions in the United States; almost two out of every three Americans are overweight and almost one in three is obese. Furthermore, the annual mortality attributed to excess weight is approaching that attributed to smoking, and the total medical cost of obesity in the United States is now almost $75 billion annually. However, there is still no effective treatment for obesity on the market that does not cause significant side effects.

In November, we advanced a second internally discovered compound into the clinic by initiating a Phase 1 safety study for APD125 for insomnia. APD125 has the potential to improve sleep quality by promoting deeper, more restful sleep, while eliminating the undesirable features associated with conventional hypnotics. We expect to complete this Phase 1 safety study by the middle of this year, and, if the results are favorable, anticipate advancing APD125 into a Phase 2 clinical trial later in 2005. Although over half of adults experience symptoms of insomnia a few nights or more per week, many do not seek treatment. The hypnotic drugs currently on the market impair functioning when at therapeutic blood levels, are DEA-scheduled and have the potential for "hangover" or residual effects. APD125 works on a novel mechanism that could potentially introduce a new non-GABA class of insomnia drugs without or with a reduced level of these negative attributes. This, we believe, holds a significant competitive advantage and could possibly allow for fewer prescribing restrictions than today's leading insomnia drugs.

pipeline

As of March 31, 2005



UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2004

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

COMMISSION FILE NUMBER 000-31161

ARENA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**23-2908305**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
6166 Nancy Ridge Drive, San Diego, CA	**92121**
(Address of principal executive offices)	(Zip Code)

(858) 453-7200

(Registrant's telephone number, including area code)

Securities registered pursuant to 12(b) of the Act: **None**

Securities registered pursuant to 12(g) of the Act:

Common Stock, $0.0001 par value
(Title of Class)

Preferred Stock Purchase Rights
(Title of Class)

ndicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities :xchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), ınd (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

ndicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) is ıot contained herein, and will not be contained, to the best of the registrant's knowledge, in the definitive proxy or information :tatements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

ndicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 under the Securities Exchange Act of 1934). Yes ☒ No ☐

The approximate aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was :pproximately $102.8 million as of June 30, 2004, based on the closing price of the Common Stock as reported on the NASDAQ National Market on such date. For purposes of this calculation, shares of Common Stock held by directors and officers and :tockholders whose beneficial ownership in the registrant is known by the registrant to exceed 10% have been excluded. This number s provided only for purposes of this report and does not represent an admission by either the registrant or any such person as to the :tatus of such person.

As of February 15, 2005, there were 35,205,869 shares of the registrant's Common Stock outstanding.

)OCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of this Annual Report on Form 10-K is incorporated by reference from the registrant's definitive proxy statement for the annual meeting of stockholders to be held in June 2005, which will be filed with the Securities and Exchange Commission within 120 days after the close of the registrant's fiscal year ended December 31, 2004.

ARENA PHARMACEUTICALS, INC.

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INFORMATION RELATING TO FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K includes forward-looking statements. These forward-looking statements involve a number of risks and uncertainties. Such forward-looking statements include statements about our strategies, intentions, expectations, goals, objectives, discoveries, collaborations, preclinical and clinical programs, and our future achievements. These forward-looking statements can generally be identified as such because the context of the statement will include words such as "may," "will," "intends," "plans," "believes," "anticipates," "expects," "estimates," "predicts," "potential," "continue," or "opportunity," the negative of these words or words of similar import. For such statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this Annual Report on Form 10-K are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they are made. These forward-looking statements are based largely on our expectations and projections about future events and future trends affecting our business, and are subject to risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Important factors that could cause actual results to differ materially from those in these forward-looking statements are disclosed in this Annual Report on Form 10-K, including, without limitation, those discussions under "RISK FACTORS" in "Item 1. Business" and in "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations." In addition, past financial and/or operating performance is not necessarily a reliable indicator of future performance and you should not use our historical performance to anticipate results or future period trends. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our results of operations and financial condition. Except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances that arise after the filing of this Form 10-K or documents incorporated by reference herein that include forward-looking statements.

Arena Pharmaceuticals®, Arena® and our corporate logo are registered service marks of Arena. CART™ and BRL Screening™ are unregistered service marks of Arena.

In this Annual Report on Form 10-K, "Arena Pharmaceuticals," "Arena," "we," "us" and "our" refer to Arena Pharmaceuticals, Inc. and our wholly owned subsidiary, BRL Screening, Inc., unless the context otherwise provides.

PART I

Item 1. Business.

We are a biopharmaceutical company with a pipeline of internally discovered, small-molecule product candidates that target G protein-coupled receptors, or GPCRs. Our product candidates act on or through known and orphan GPCRs, and have been discovered using our GPCR-focused drug discovery technologies and capabilities. Two of our product candidates are in clinical trials: APD356 for the treatment of obesity is in a Phase 2 clinical trial; and APD125 for the treatment of insomnia is in a Phase 1 clinical trial. We also have active collaborations with two major pharmaceutical companies, Ortho-McNeil Pharmaceutical, Inc., a Johnson & Johnson company, for the treatment of type 2 diabetes, and Merck & Co., Inc., for the treatment of atherosclerosis and related disorders. We incorporated in April 1997.

Our goal is to discover, develop, and commercialize novel, orally available drugs that address major unmet medical needs by targeting GPCRs. GPCRs are a class of receptors that mediate the majority of cell-to-cell communication within humans, and a high percentage of today's prescription drugs target one or more GPCRs. We believe that approved GPCR-based drugs target about 60, or 30%, of the approximately 190 known GPCRs, predominantly in the biogenic amine family, a sub-family of class I GPCRs. GPCRs are categorized as "known" when their naturally occurring, or native, ligands have been identified. Scientists have used molecular cloning in combination with the sequencing of the human genome to identify both additional receptor subtypes of known GPCRs as well as hundreds of novel GPCRs. These novel GPCRs are categorized as "orphan" GPCRs because their native ligands have not been identified. We believe orphan GPCRs offer promise for the development of novel GPCR-based therapeutics, and, therefore, are a major focus of our discovery research.

We focus on four therapeutic areas: metabolic, central nervous system (or CNS), cardiovascular and inflammatory diseases. We believe our technologies and integrated discovery and development capabilities will allow us to continue to build our pipeline of unique and selective product candidates.

We intend to commercialize our product candidates independently and with partners. We have retained commercial rights for our most advanced development programs, except for our diabetes partnership with Ortho-McNeil and our cardiovascular collaboration with Merck. We have not received regulatory approval for, or generated commercial revenues from, marketing or selling drugs.

In 2004, we made significant progress, including:

- announcing results for single and multiple dose Phase 1 clinical trials of our product candidate for obesity, APD356;
- initiating a Phase 2 study of APD356;
- initiating a Phase 1 clinical trial of our product candidate for insomnia, APD125;
- announcing a two-year extension and expansion of our cardiovascular collaboration with Merck and receiving three milestone payments and an equity investment totaling $15.5 million; and
- establishing a world-wide partnership with Ortho-McNeil for our diabetes program, 19AJ, under which we received an upfront payment of $17.5 million and two milestone payments totaling $5.0 million in January 2005.

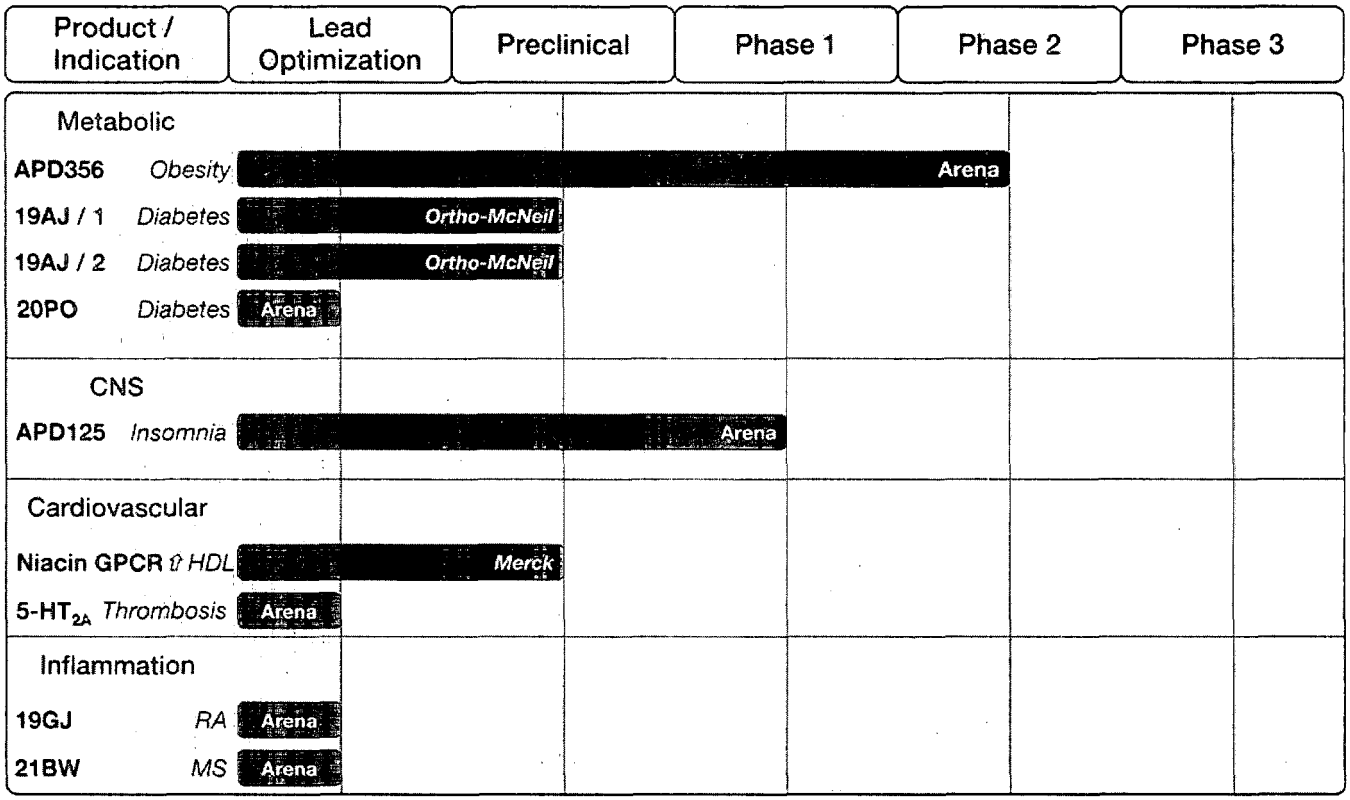
Our Strategy

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

- *Continue to advance our lead programs.* We intend to advance our current product candidates, either alone or in conjunction with pharmaceutical and biotechnology companies, through clinical development and, if successful, commercialization.
- *Discover and develop additional small molecule product candidates targeting GPCRs.* We intend to continue to develop orally available, small molecule compounds for GPCRs identified or validated by our research efforts.
- *Focus on attractive market opportunities.* Obesity, insomnia, diabetes and thrombosis each represent multi-billion dollar market opportunities. We intend to continue to focus on these and other programs with attractive commercial potential.
- *Retain significant commercial rights and/or economic value for our product candidates.* We intend to maximize the value of our product candidates through either internal development or commercial partnerships in which we retain significant economic value and/or targeted copromotion rights.
- *Continue to build our development capabilities.* To capitalize on our discoveries, we plan to continue to expand our clinical development capabilities as our product candidates enter into, and move through, clinical trials.
- *Maintain strong research discovery capabilities.* Our proprietary technologies, including CART and Melanophore, and our drug discovery infrastructure, have allowed us to identify a number of GPCR targets and novel compounds. We believe these and other discoveries will continue to fuel our pipeline.

Our Research & Development Programs

Our product candidates range from being in a Phase 2 clinical trial to the early stages of drug research. The following table summarizes our most advanced internal and partnered research and development programs:



APD356

Our most advanced product candidate, which we call APD356, is a novel and selective 5-HT_{2C} receptor agonist for the treatment of obesity. In animal studies, stimulation of this hypothalamic receptor has resulted in decreased food intake and weight loss. Obesity and a related condition known as metabolic syndrome affect tens of millions of adults and children in the United States and pose a serious long-term threat to their health and welfare. Medical treatment options for obesity and metabolic syndrome are currently very limited.

Our preclinical studies show APD356 stimulates the 5-HT_{2C} serotonin receptor more selectively than fenfluramine and dexfenfluramine. Based on these studies, we believe that APD356 is less likely to cause the cardiovascular side effects associated with fenfluramine and dexfenfluramine. Until 1997, Wyeth marketed fenfluramine and dexfenfluramine, serotonin-releasing agents and non-selective serotonin receptor agonists, which were often used in combination withphentermine for the treatment of obesity. The combination of fenfluramine or dexfenfluramine with phentermine is commonly referred to as fen-phen. Despite their efficacy as appetite suppressants, both fenfluramine and dexfenfluramine were withdrawn from the market in 1997 after reported incidences of heart valve disease and pulmonary hypertension associated with their usage.

Mechanism and Preclinical Data. APD356 selectively stimulates the 5-HT_{2C} serotonin receptor, a GPCR located in the hypothalamus. We have conducted preclinical studies examining the activity and 5-HT receptor subtype specificity of APD356. In these studies, APD356 demonstrated a high affinity and specificity for the 5-HT_{2C} receptor, with approximately 15-fold and 100-fold selectivity over the 5-HT_{2A} and 5-HT_{2B} receptors, respectively, and no pharmacologic activity at other serotonin receptors. In addition, in these studies, APD356 did not release serotonin. The fenfluramines release serotonin, and their primary metabolite, norfenfluramine, also has activity at the 5-HT_{2B} receptor, stimulation of which has been implicated in the heart valve abnormalities associated with these drugs. Because of its selectivity, we believe that APD356 is less likely to cause the cardiovascular side effects associated with fenfluramine and dexfenfluramine.

In a free-fed animal model, APD356 reduced total food intake in a dose-dependent manner. APD356 dosed once, orally at 6 mg/kg, 12 mg/kg and 24 mg/kg reduced food intake approximately 12% to 25% over 22 hours compared to a saline control. In the same model, dexfenfluramine dosed once, orally at 0.3 mg/kg, 1 mg/kg, and 3 mg/kg reduced food intake approximately 10% to 30% over the same time period.

In an obese animal model, APD356 caused dose-dependent reductions in body weight after 14 days of oral administration. APD356 dosed at 4.5 mg/kg, 9 mg/kg, 18 mg/kg twice-daily, and 36 mg/kg once-daily reduced bodyweight by approximately 3%, 6%, 11%, and 12%, respectively. We believe this compares favorably to Meridia, a drug marketed by Abbott Laboratories, which reduced bodyweight by approximately 12% when dosed at 6 mg/kg once-daily in the same model. The reductions in bodyweight caused by APD356 appeared to be due to lowered body fat, as lean body mass in the obese animals was unaffected at all APD356 doses.

Clinical Development. In July 2004, we announced results from a three-part Phase 1a study of APD356. In part A, safety was assessed in 45 subjects who received single doses of APD356. We began dose escalation at 10 mg and ended at 40 mg due to CNS-related side effects, including nausea, dizziness, headache and disorientation. Doses of 10 mg and 20 mg were well tolerated. In part B, we evaluated the effect of food consumption on APD356 absorption and pharmacokinetics in 12 volunteers, and found that APD356 was well-tolerated with food, and that food neither reduced maximum concentrations of the drug reached in the blood nor the amount of the drug absorbed. Finally, in part C, we evaluated the effect of single doses of APD356 on food intake in 20 subjects in a four-period crossover study. Each subject received single doses of placebo and 0.1 mg, 1 mg, or 10 mg doses of APD356 in random order over four successive weeks, and two hours after each dosing was offered a standard test meal in a controlled setting. In this way, subjects acted as their own control. At the 10 mg dose, average food intake declined 6.5% versus the placebo period, which is not statistically significant. Excluding a single outlier, who ate more than twice as much during period one (which also was the period in which he received the highest dose) as during each of the other three periods, average food intake declined 10.7%, which would be statistically significant. We believe this effect is a clinically meaningful signal of pharmacology.

In November 2004, we announced results from a Phase 1b clinical safety trial of APD356 in obese volunteers. In this trial, 27 subjects (15 males and 12 females) with an average body mass index, or BMI, of 31, and a BMI range of 25 to 58, were enrolled. Participants were administered 3 mg, 10 mg and 20 mg doses of APD356 or placebo daily for 14 days in successive cohorts of nine subjects (six received APD356 and three received placebo) and remained within a Phase 1 unit throughout the dosing period. Participants were instructed to maintain their usual exercise patterns, and were offered sufficient food to maintain their desired intake levels. APD356 was well tolerated; there were no severe or serious adverse events reported, no withdrawals due to an adverse event, and no reports of euphoria, dysphoria, or disorientation. The most common side effects, occurring primarily at the 20 mg dosage level, were headache and nausea, sometimes with vomiting. These side effects were occasional and generally mild in nature. APD356 continued to demonstrate very predictable pharmacokinetic behavior, similar to that found in its Phase 1a trial. The maximum plasma concentration and exposures increased in proportion with increasing doses of APD356, and there were no apparent gender differences in pharmacokinetic parameters. Based on a comparison of echocardiograms taken at screening with those taken at the end of treatment and two and three months thereafter, there was no apparent drug effect on heart valves or pulmonary artery pressure. This Phase 1b study was neither designed nor powered to detect significant weight change between treatment groups. When compared with placebo, none of the mean changes in weight in the groups that received APD356 were statistically significant.

Based on these results, in December 2004 we began a randomized, double-blinded, multiple-dose, 28-day Phase 2 clinical trial of APD356 in obese subjects. We expect that the trial will compare doses of 1 mg, 5 mg and 15 mg of APD356 toplacebo, evaluating weight loss after administration once daily for 28 days. We expect to announce initial results from this trial in the second quarter of 2005.

Intellectual Property. We have patent applications covering compositions of matter for APD356 and related compounds, and related methods of treatment, pending in 26 countries including the United States and Japan, and before the European Patent Office, or EPO. In addition, we have a pending patent application covering the synthetic route for APD356 before the World Intellectual Property Organization, or WIPO, designating all contracting states. We also have a patent application that covers the particular hydrate and crystal form of APD356 that we intend to use in late-phase clinical trials and perhaps commercially.

APD125

Our lead product candidate for insomnia, which we call APD125, is a novel and selective 5-HT_{2A} receptor inverse agonist that is presently in a Phase 1 clinical trial. According to the National Institutes of Health, as many as 25% of Americans report occasional sleeping problems, and insomnia is a chronic problem for about 10% of the population. In these cases, the lack of restful sleep impairs the person's ability to carry out daily responsibilities because they are too tired or have trouble concentrating. However, only a fraction of those suffering from insomnia seek medical treatment, as fewer than 10% of adults with this disorder report using medication for treatment. Currently marketed therapies include Ambien, marketed by sanofi-aventis, zaleplon, an off-patent compound, and various benzodiazepines, including Valium. These therapies generally work by activating the GABA-A receptor in the brain, and cause a general CNS-suppressive effect. While these drugs are effective at initiating sleep, they have side effects including the risk of developing tolerance to the drug and the potential for causing a sensation of dullness and lethargy upon awakening, often referred to as the "hangover effect." In addition, these drugs are DEA-scheduled controlled substances due to their potential for abuse. Despite these limitations, current medications for insomnia are expected to have worldwide sales in excess of $2 billion in 2005.

Mechanism and Preclinical Data. APD125 is our lead compound in a series we have discovered that selectively inhibits the 5-HT_{2A} receptor. APD125 acts through a different mechanism than currently marketed insomnia drugs, and we believe that because of this APD125 may not have the side effects associated with such drugs. Rather than activating a general CNS-suppressive system (GABA), APD125 inhibits a CNS activating system mediated through 5-HT_{2A} receptors. In our animal studies, we have demonstrated that APD125 increases both the quality and total time of non-REM sleep, the most restorative phase of the sleep cycle in humans, while having no effect on REM (rapid eye movement or dream) sleep. In addition, APD125 appeared to promote sleep onset. The total increase in non-REM sleep time was manifested by fewer bouts of longer duration, indicating an increase in sleep consolidation. In addition, animals treated with APD125 showed an increase in delta power during non-REM sleep, a brain wave activity associated with increased sleep intensity. The improvements in non-REM duration and quality observed with APD125 administration were at least as robust as those observed with a prototypic GABA-A hypnotic control drug, Ambien. However, unlike Ambien, APD125 did not adversely affect REM sleep in these studies. We believe these animal data suggest that APD125 has the potential to improve the treatment of insomnia over GABA-A hypnotics.

Clinical Development. In December 2004, we initiated a Phase 1 clinical trial of APD125 in healthy volunteers. This dose-ranging study will evaluate the safety, tolerability and pharmacokinetics of single doses of APD125. We expect to announce results from this trial in the middle of 2005. Depending on the results of this trial, we intend to initiate multiple-dose tolerability and single-dose pharmacology trials.

Intellectual Property. We have patent applications covering compositions of matter for APD125, and related methods of treatment, pending in the United States, in 12 additional jurisdictions that are not contracting states of the WIPO, and before the EPO and the WIPO, designating all contracting states. We also have two separate pending patent applications covering the synthetic route for APD125, one of which is before the WIPO, designating all contracting states.

19AJ / Ortho-McNeil Collaboration

Our lead product candidate for diabetes targets an orphan GPCR, which we call 19AJ, found in the pancreas. Our two lead compounds for this target are currently in preclinical development in partnership with Ortho-McNeil. Diabetes is a major worldwide disease. The International Diabetes Foundation has estimated that in 2001 there were 177 million adults with diabetes worldwide, an increase of 17% over the number in 2000. This estimate includes 21.4 million in the United States and 32.2 million in the European Union. Approximately 90%, or 160 million, of diabetics suffer from type 2 diabetes, the adult-onset form of the disease. Type 2 diabetes is characterized by inadequate response to insulin and/or inadequate secretion of insulin as blood glucose levels rise. Therapies for type 2 diabetes are directed toward correcting the body's inadequate response with oral medications, or directly modifying insulin levels through direct injection of insulin or insulin analogs.

Oral medications for type 2 diabetes include insulin releasers such as Glyburide, insulin sensitizers such as Actos and Avandia and agents which slow the uptake of glucose into the bloodstream such as Precose and Glyset. The worldwide market for oral diabetes medications was expected to exceed $10 billion in 2004. However, a significant portion of type 2 diabetics fail oral medication and require injected insulin therapy. Current oral medications for type 2 diabetes have a number of side effects, including hypoglycemia, weight gain and edema. Numerous pharmaceutical and biotechnology companies are seeking to develop insulin sensitizers, novel insulin formulations and other therapeutics to improve the treatment of diabetes.

Mechanism and Preclinical Data. 19AJ is a receptor that we have found to be preferentially expressed in beta cells, the cells in the pancreas responsible for producing insulin in response to increases in blood glucose. The pharmaceutical industry has discovered three main mechanisms that have resulted in beta-cell therapeutics: GLP-1 receptor peptide agonists, DPP-IV inhibitors and sulphonylureas. We believe 19AJ represents a novel mechanism for generating a new class of drugs for diabetes that may offer advantages over current approaches. Our preclinical results indicate that stimulating the 19AJ receptor allows beta cells to produce insulin more efficiently in response to changes in blood glucose levels. In addition, we have found in these studies that stimulation of the 19AJ receptor leads to increased levels and activity of intracellular factors thought to be involved in the preservation of beta cells. Unlike the GLP-1 receptor, we have found that the 19AJ receptor is amenable to small molecule drug development. We have discovered potent, selective and orally available small molecule agonists of the receptor that improve glucose tolerance and lower blood glucose levels in animal models of diabetes. The 19AJ mechanism is glucose dependent, so that in our animal studies our compounds only lowered blood glucose when it rose above normal levels, such as after a meal. Our preclinical results indicate these compounds do not lower normal fasting baseline glucose levels in animal models and, therefore, do not cause hypoglycemia, unlike the glucose-insensitive sulphonylureas.

Development Plans and Partnership Status. In December 2004, we entered into a collaboration and license agreement with Ortho-McNeil to further develop compounds for the potential treatment of type 2 diabetes and other disorders. Our two lead compounds are currently in preclinical development with Ortho-McNeil. In January 2005, we received a $17.5 million upfront payment, and two milestones payments of $2.5 million each. We are eligible to receive up to $295.0 million in milestone payments for each compound, as well as royalty payments associated with Ortho-McNeil's commercialization of any drugs discovered under the agreement. These milestone payments include development and approval milestone payments of up to $132.5 million for the first indication and $62.5 million for the second indication for each compound, and up to $100.0 million in sales milestone payments for each product resulting from the collaboration.

Merck Cardiovascular Collaboration

In October 2002, we entered into a research and licensing agreement with Merck to collaborate on three GPCRs to develop therapeutics for atherosclerosis and related disorders. We believe one or more of these GPCRs plays a role in regulating plasma lipid profiles, including HDL cholesterol, the so-called "good cholesterol," and is responsible for the HDL-raising activity of niacin. In October 2004, we extended and expanded our collaboration with Merck and Merck selected one of our compounds for preclinical development. As of December 31, 2004, we had received $19.5 million from Merck in upfront and milestone payments and an equity investment. We may receive additional milestone payments of up to $34.0 million for Merck's clinical and marketing achievements, as well as royalty payments associated with Merck's commercialization of any drugs discovered under the agreement. In addition, we have received research funding from Merck since the inception of our collaboration, and, under our agreement, Merck will pay us $5.7 million a year for collaboration research through October 19, 2007.

There are very successful drugs available for lowering LDL cholesterol. However, development of novel, effective therapies to increase HDL cholesterol remains a major focus of research. We believe that such therapies may reduce the risk of atherosclerotic heart disease and compete in the large anti-hyperlipidemic market.

Other Research and Development Programs

Cardiovascular. In addition to our Merck collaboration, our programs in the cardiovascular area include ones directed toward the prevention of thrombosis and cardiac reperfusion injury. The American Heart Association estimates that in the United States alone over 12 million people alive in 2001 have survived either a myocardial infarction or a stroke. To reduce the risk of future events, many subjects receive daily anti-platelet therapy. In 2003, worldwide sales of Plavix, a leading antithrombotic marketed by Bristol-Myers Squibb, exceeded $2.4 billion.

Platelet aggregation results in the formation of a blood clot and vessel occlusion leading to cardiovascular disease such as myocardial infarction and stroke. There are several important signals that increase the platelet aggregation response, such as thrombin, ADP, epinephrine, prostaglandins and collagen. Activated platelets are a rich source of a secondary signal, serotonin, that when released into the blood acts to amplify the aggregation response produced by the various primary signals. This serotonin-induced amplification process is mediated through 5-HT_{2A} receptors present on platelets. We have developed potent and selective small molecule inhibitors of the 5-HT_{2A} receptor that can block the serotonin-amplified aggregation response and have antithrombotic activity in animal models.

In contrast to our 5-HT_{2A} lead compounds for insomnia which distributes significantly to the CNS, we have designed our lead antithrombotic compounds to have limited exposure to the brain through the blood-brain barrier. Moreover, in animal models, these compounds demonstrate a better therapeutic index due to a separation of antithrombotic activity from the increased bleeding that may be seen as a treatment effect of currently marketed products. Acute myocardial infarction, which is commonly known as a heart attack, is often followed by heart failure in survivors. Myocardial infarction, and often heart failure, are direct consequences of atherosclerosis, and both remain major causes of death. We have identified certain GPCRs that we believe play a role in these processes and are seeking to identify small molecules directed at these GPCR targets that we believe could provide cardio-protection following myocardial infarction.

Inflammatory Disorders. We are developing small molecule therapeutics that target GPCRs involved in the inflammatory process. TNF-α is an important pro-inflammatory mediator in diseases such as rheumatoid arthritis. Biologic therapeutics, such as Enbrel, Remicade and Humira, function to inhibit the activity of TNF-α. In 2003, worldwide sales of these three drugs exceeded $3.3 billion. However, biologic treatments are expensive and restricted to intravenous or subcutaneous administration. We have discovered small molecule compounds which can be orally administered and that in preclinical studies act to target GPCRs in the immune system to inhibit the production of TNF-α. We plan to continue to test the efficacy of these molecules in animal models of inflammatory diseases, such as arthritis, in 2005.

Diseases such as inflammatory bowel disease, which includes Crohn's disease and ulcerative colitis, and asthma, are initiated and exacerbated by an aberrant inflammatory response. Immune cells such as monocytes, dendritic cells, eosinophils, neutrophils, mast cells and specific T cell subsets play a role in these diseases. We have identified GPCRs that are found in specific immune cell types. We believe these GPCRs modulate the inflammatory process, and we are applying our screening technologies to these targets to identify small molecules that could activate or inhibit these GPCRs.

CNS Disorders. Many GPCRs are found predominately in the brain or the CNS, and, therefore, we believe targeting GPCRs provides an opportunity to selectively treat various CNS diseases. Many approved drugs for indications ranging from insomnia and narcolepsy to depression, schizophrenia, and Parkinson's disease target GPCRs. Our discovery efforts in CNS disorders are focused on indications with large market opportunities where current therapies have significant limitations. For example, we are developing small molecules targeting a GPCR through a different mechanism than serotonin or norepinephrine, and have confirmed that inhibitors of this GPCR show activity in animal models of depression and anxiety. We intend to continue our research and development of these compounds.

Other Diabetes Programs. For metabolic diseases, we are working on a series of orphan GPCR targets other than 19AJ in order to develop orally available therapies to treat type 1 and type 2 diabetes. We are focusing our discovery efforts on approximately 10 known and orphan GPCR targets that we believe regulate important mechanisms involved in glucose control. For example, we are conducting research with receptors that may act to regulate glucose uptake, glucose absorption, insulin sensitivity, insulin secretion, lipid levels and production of glucose in the liver. In order to treat general metabolic disease, we have prioritized GPCRs that have the potential to modulate blood glucose and lipid levels. We have identified selective small molecule agonists to an orphan receptor we call 20PO. In preclinical studies, oral administration of these compounds improved glucose tolerance in a standard glucose tolerance test and lowered free fatty acids *in vivo*. We believe that agonists to the 20PO receptor have potential for the treatment of diabetes and lipid disorders.

Other Obesity Programs. In addition to APD356 and other compounds that act on the 5-HT_{2C} serotonin receptor, we have discovery programs focused on several different GPCRs implicated in obesity. Our drug discovery efforts are directed at identifying novel product candidates that target GPCRs in the CNS and peripheral tissues to reduce fat mass in people. We have identified both known and orphan GPCRs expressed in the hypothalamus, an area of the brain known to be critical for regulating satiety and metabolism, that we believe regulate food intake and weight. We have also identified targets in fat cells that may represent targets for obesity. We have identified early lead compounds for obesity targets other than the 5-HT_{2C} serotonin receptor, and are currently evaluating these compounds for their ability to reduce food intake and body weight.

Our Proprietary GPCR Technologies and Programs

Our product candidates have resulted from our GPCR-focused drug discovery technologies, capabilities and programs, including Constitutively Activated Receptor Technology, or CART, our Melanophore technology and Project Genesis. Our integrated drug discovery platform allows us to determine GPCR function, tissue and cell distribution, and potential relation to disease.

CART

Traditional ligand-based drug screening methods require the time-consuming identification and use of the receptor's native ligand to discover small molecule compounds that will bind at, or close to, the native ligand's binding site on the receptor. In contrast, we have developed technologies that do not require the use of the native ligand. Instead, we are able to activate the GPCR so that the G protein signals without the presence of the native ligand. We call this Constitutively Activated Receptor Technology, or CART. CART allows us to discover drug-like compounds by activating the GPCR to mimic the biological response that occurs when the native ligand binds to the receptor. Therefore, CART avoids a major bottleneck in drug discovery efforts at orphan receptors by eliminating the step of first identifying the native ligand. We have found that CART can be applied broadly to GPCRs.

Screening using CART allows us to simultaneously identify drug leads that act as receptor activators, or agonists, which increase the detected biological response, or act as receptor inhibitors, which decrease the detected response. We can also identify inverse agonists, which inhibit ligand-independent, as well as ligand-dependent, receptor activity.

We believe that CART offers several key advantages for drug discovery over traditional screening techniques that require the use of the native ligand including:

- not requiring prior identification of the native ligand for an orphan receptor;
- enhancing the detection of, and allowing us to simultaneously identify, both receptor inhibitor and receptor activator drug leads;
- allowing for the identification of drug leads that inhibit both ligand-independent and ligand-dependent activity; and
- providing the ability to discover novel and improved therapeutics directed at known receptors.

Melanophore Technology

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

Project Genesis

We have substantially completed our efforts under Project Genesis, a program to identify human GPCRs, determine where these GPCRs are expressed in normal and diseased tissues, and utilize our CART and Melanophore technologies to screen against our chemical libraries.

Through Project Genesis, we have learned, among other things, where and how GPCRs function in the body and how they interact with the small molecule chemicals that modulate their activity. We believe that this knowledge will allow us to more efficiently advance our therapeutic programs. We are applying medicinal chemistry to further develop the small molecule leads identified through screening.

Research and Development Expenses

Research and development activities are the primary source of our expenses, which include personnel costs, research supplies, facility and equipment costs and preclinical study fees. Research expenses related to the development and improvement of our technology and product candidates totaled $57.7 million for the year ended December 31, 2004, $50.9 million for the year ended December 31, 2003, and $44.4 million for the year ended December 31, 2002. Included in these expenses is research that was sponsored by our collaborators. We estimate that research expenses incurred on projects sponsored by our collaborators totaled $3.4 million for the year ended December 31, 2004, $5.8 million for the year ended December 31, 2003 and $5.9 million for the year ended December 31, 2002.

Corporate Collaborations

In addition to Ortho-McNeil and Merck, we have entered into strategic collaborations with other pharmaceutical and biotechnology companies to discover and develop novel drug leads using our GPCR technologies. We intend to continue to pursue collaborations in an effort to access our partners' research, drug development, manufacturing, marketing and financial resources. Ninety-five percent of our revenues during the year ended December 31, 2004, were from our collaboration with Merck, which included research funding, milestone achievements and technology access and development fees. Please see "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" for a more detailed discussion of our collaborations, including financial information, activities being conducted and termination provisions.

Intellectual Property

Our success depends in large part on our ability to protect our proprietary technology, compounds and information, and to operate without infringing the proprietary rights of third parties. We rely on a combination of patent, trade secret, copyright, and trademark laws, as well as confidentiality agreements, licensing agreements, and other agreements, to establish and protect our proprietary rights.

As of January 31, 2005, we owned or had exclusively licensed the following patents: 15 in the United States, 11 in European countries, six in Australia, five in New Zealand, one in Japan, one in Singapore, and one in Israel. In addition, as of January 31, 2005, we had approximately 273 patent applications before the United States Patent and Trademark Office, foreign patent offices and international patent authorities. These patents and patent applications are directed to 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. These patents and patent applications are divided into 76 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. Eight of our patent families containing a total of seven patents and 23 patent applications were the subject of joint inventions by our employees and the employees of other entities. The remaining 67 patent families containing a total of 32 patents and 250 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 cover a drug product or other commercially significant product or method. Except for the U.S. patents relating to our Melanophore technology, the term of all of our other current patents commenced, and our future patents, if any, will commence, on the date of issuance and terminate 20 years from the earliest effective filing date of the patent application. Since our U.S. Melanophore patents were issued under now superceded rules that provided a patent term of 17 years from the date of issuance, the term of these patents are scheduled to end in 2012. Because the time from filing to issuance of biotechnology patent applications is often more than three years, the resulting term of our pending patent applications, if any, on our products and technologies may be substantially less than 20 years. In the United States, patent term extensions are available for certain delays in patent office proceedings and United States Food and Drug Administration, or FDA, approval. However, due to the specific requirements for obtaining these extensions, there is no assurance that our patents will be afforded extensions even if we encounter significant delays in patent office proceedings or FDA approval.

We seek patent protection for our key inventions, including clinical candidates and product candidates we identify, routes for chemical synthesis, CART, new receptors that we discover, and genetically altered receptors. It has generally been possible to obtain broad composition of matter patents on novel chemical compounds. It has also generally been possible to obtain broad method patents for techniques and procedures for screening and drug-identification technologies. It has generally been more difficult to obtain broad composition of matter patents for nucleic acid and amino acid sequences. However, it has been possible to obtain patents that protect specific sequences and functional equivalents of those sequences. Furthermore, intellectual property law allows for separate and distinct patents for novel, altered genetic sequences that have improved properties over previously disclosed sequences. We believe that we can obtain patents on certain of our CART-activated receptor sequences because they are not functional equivalents of the natural version of the receptor. We expect to continue to develop other means of activating GPCRs for drug screening and to file patent applications with respect thereto.

In March 2003, we became aware that the Japanese Patent Office had issued a Notification of Reasons for Revocation of our Japanese patent. In December 2004, we succeeded in having our Japanese patent on our Melanophore technology reinstated with a narrower claim scope, which we do not believe materially impacts our ability to utilize the Melanophore technology.

In addition to patent protection, we rely on trade secrets, proprietary know-how, and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of our trade secrets and proprietary information, all of our employees are required to enter into and adhere to an employee confidentiality and invention assignment agreement, laboratory notebook policy, and invention disclosure protocol, as a condition of employment. Additionally, our employee confidentiality and invention assignment agreement requires that our employees not bring to us, or use without proper authorization, any third-party proprietary technology. We also require our consultants and collaborators that have access to proprietary property and information to execute confidentiality and invention rights agreements in our favor before beginning their relationship with us. While such arrangements are intended to enable us to better control the use and disclosure of our proprietary property and provide for our ownership of proprietary technology developed on our behalf, they may not provide us with meaningful protection for such property and technology in the event of unauthorized use or disclosure.

Competition

The biotechnology and pharmaceutical industries are highly competitive and are subject to rapid and significant change. We face significant competition from organizations that are pursuing the same or similar technologies. We also face significant competition from organizations that are pursuing drugs that would compete with the product candidates we are developing. We may not be able to compete successfully against these organizations, which include many large and well-financed and experienced pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies.

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

Our present competitors with respect to APD356 include Abbott, which markets Meridia, and Roche, which markets Xenical. A potential future competitor is sanofi-aventis, which is developing rimonabant, a cannabinoid-1 blocker. In addition, we are aware of potentially competing 5-HT_{2C} programs at Roche and GlaxoSmithKline.

In addition to the marketed compounds described above under the APD125 discussion, Pfizer/Neurocrine have submitted an NDA for Indiplon, and Sepracor has recently received FDA approval for Lunesta, formally called Estorra. We believe sanofi-aventis and Eli Lilly have been developing potentially competing 5-HT_{2A} programs for insomnia.

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

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

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

Government Regulation

We plan to develop and commercialize selected drug candidates by ourselves and license other candidates to partners for further development and commercialization. Our and our collaborator's on-going drug development activities are subject to the laws and regulations of governmental authorities in the United States and other countries in which these products may be tested or marketed. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy and uncertain. Before marketing in the United States, any pharmaceutical or therapeutic product must undergo rigorous preclinical testing and clinical trials and an extensive regulatory approval process implemented by the FDA under the federal Food, Drug and Cosmetic Act. Moreover, the FDA imposes substantial requirements on new product research and the clinical development, manufacture and marketing of pharmaceutical products, including testing and clinical trials to establish the safety and effectiveness of these products. In the United States, we are also subject to other federal, state and local environmental and safety laws and regulations, including regulation of the use and care of laboratory animals. In addition, the state of California imposes licensing requirements on facilities manufacturing drugs for clinical trials or for commercial marketing.

Governments in other countries have similar requirements for testing, approval and marketing, including in the European Union (the "EU"). Before commencing clinical trial investigations in humans in Europe, we and/or our collaborators must submit the appropriate applications to applicable authorities in member countries.

Before commencing clinical investigations in humans in the United States, we and/or our collaborators must submit an investigational new drug, or IND, application to the FDA. Clinical trials are typically conducted in three sequential phases, although the phases may overlap or be combined. Phase 1 represents the initial administration of the drug to a small group of humans, either healthy volunteers or patients, to test for safety, dosage tolerance, absorption, metabolism, excretion and clinical pharmacology. Phase 2 involves studies in patients to begin to assess the effectiveness of the product, to ascertain dose tolerance and the optimal dose range and to gather additional data relating to safety and potential adverse effects. Once a drug is found to have some effectiveness and an acceptable safety profile in the targeted patient population, Phase 3 studies are initiated to establish safety and effectiveness in an expanded patient population and at multiple clinical study sites. The FDA may require further post-marketing studies, referred to as Phase 4 studies. The FDA reviews both the clinical plans and the results of the trials and we, our collaborators or the FDA may decide that clinical trials should be discontinued at any time if any significant safety issues are identified. Clinical testing must meet requirements for institutional review board or ethics committee oversight, informed consent, good clinical practices and other FDA or other regulatory authority oversight.

The length of time necessary to complete clinical trials varies significantly and is difficult to predict. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Additional factors that may cause delay, termination or increased cost of our or our collaborators' clinical trials include, among other factors:

- slow patient enrollment;
- the eligibility criteria for the study;
- competition with clinical trials for other drug candidates;
- lack of sufficient clinical supplies of the product candidate;
- lack of effectiveness of the product being tested;
- adverse medical effects or side effects in treated patients;
- inadequately trained or insufficient personnel at a study site to assist in overseeing and monitoring the clinical trial;
- delays in approval from a study site's institutional review board; and
- longer treatment time required to demonstrate effectiveness or to determine the appropriate product dose.

If preclinical and clinical studies are successful, the results, together with other information about the product and its manufacture, are submitted to the FDA in the form of a New Drug Application, or NDA, to request marketing approval. Before receiving FDA approval to market a product, we or our collaborators must demonstrate that the product is safe and effective through clinical trials in the patient population that will be treated. The approval process is likely to require substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all.

Additional animal studies or clinical trials may be requested during the FDA review period that may delay marketing approval. As part of the approval process, each manufacturing facility must be inspected by the FDA. Among the conditions of approval is the requirement that a manufacturer's quality control and manufacturing procedures conform with federally mandated current good manufacturing practices, or cGMPs. Both before and after approval, manufacturers must expend time, money and effort to ensure compliance with cGMPs, and the FDA conducts periodic inspections to certify such compliance. Violations may result in the issuance of warning letters, restrictions on the product or manufacturer, including costly recalls or withdrawal of the product from the market, or other enforcement action.

If regulatory approval of a product is granted by the FDA, this approval will be limited to those specific conditions for which the product, as demonstrated through clinical studies, has an appropriate safety and efficacy balance. After FDA approval for the initial indications, further clinical trials will be necessary to gain approval for the use of the product for additional indications. Marketing or promoting a drug for an unapproved indication is prohibited. The FDA requires that adverse effects be reported to the FDA and may also require post-marketing testing to monitor for adverse effects, which can involve significant expense. Even after FDA approvals are obtained, a marketed product is subject to continual review. Later discovery of previously unknown information or failure to comply with the applicable regulatory requirements may result in restriction on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Furthermore, failure to obtain reimbursement coverage from governmental or third-party insurers may adversely impact successful commercialization.

We have a chemical development facility that we are using 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 human clinical trials. California law prohibits the shipment of product from a manufacturing facility in California for any clinical testing or commercial use prior to satisfaction of drug manufacturing licensing requirements. The facility was inspected and licensed by the California Department of Health Services and is in compliance with state regulatory requirements for the manufacture and distribution of active pharmaceutical ingredients.

Sources and Availability of Raw Materials and Clinical Supplies

In general, we purchase raw materials and supplies on the open market. Substantially all such materials are obtainable from a number of sources so that the loss of any one source of supply would not have a material adverse effect on us. However, we currently only have two sources of supply for the active pharmaceutical ingredient for our lead development projects. The loss of that supply would temporarily delay our lead development projects, APD356 and APD125.

Compliance with Environmental Regulations

We are subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, the Controlled Substances Act and other present and potential future federal, state or local regulations. Our research and development programs involve the controlled use of hazardous materials, chemicals, biological materials and various radioactive compounds.

Although we believe that our operations comply in all material respects with the applicable environmental laws and regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result, and the extent of that liability could exceed our resources. Our compliance with these laws and regulations did not, and is not expected to, have a material effect upon our capital expenditures, earnings or competitive position.

Employees

As of February 1, 2005, we had 291 employees, including 243 in research and development and 48 employees in administration, which includes finance, legal, facilities and other general support areas. None of our employees is covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Available Information

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 are available free of charge on our website (www.arenapharm.com) as soon as reasonably practicable after they are filed with, or furnished to, the Securities and Exchange Commission.

Risk Factors

An investment in our stock involves a high degree of risk. You should consider carefully the risks described below, together with other information in this Form 10-K, before making investment decisions regarding our stock. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Relating to Our Business

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

We had losses of $61.3 million for the year ended December 31, 2004, and we had an accumulated deficit of $168.8 million from our inception in April 1997 through December 31, 2004. 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 compounds that could become marketed drugs.

We expect 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 compounds discovered using our technologies.

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 financing may not be available to us or may not be available on terms that you or we believe are favorable.

Our stock has not performed as well as the stock of many of our peers for some time, and we presently are aware of only a small number of securities analysts covering our stock, which means limited third-party information is available to investors. We believe that institutional and other investors value third-party information in making investment decisions regarding our stock. These factors, and many others, may affect our ability to access capital markets.

If additional financing is not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs.

We expect to announce results for our two most advanced product candidates by the middle of 2005, and our stock price could decline significantly based on those clinical results.

By the middle of 2005, we expect to announce results from separate clinical trials currently in progress for our two most advanced product candidates, APD356 and APD125. 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 in certain instances where clinical results were not favorable, were perceived negatively or otherwise did not meet expectations. Unfavorable results or negative perceptions regarding the results of our clinical trials of APD356, APD125, or any of our other product candidates could cause our stock price to decline significantly.

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

Clinical trials are very expensive and difficult to design and implement. The clinical trial process is also time consuming. We estimate that the clinical trials of our most advanced drug candidates will continue for several years, but may take significantly longer to complete. 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:

- 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;
- delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;
- slower than expected rates of patient recruitment and enrolment;
- uncertain dosing issues;
- inability or unwillingness of medical investigators to follow our clinical protocols;
- variability in the number and types of subjects available for each study and resulting difficulties in identifying and enrolling subjects who meet trial eligibility criteria;
- scheduling conflicts with participating clinicians and clinical institutions;
- difficulty in maintaining contact with subjects after treatment, resulting in incomplete data;
- unforeseen safety issues or side effects;
- lack of effectiveness during the clinical trials; or
- other regulatory delays.

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

Preclinical tests 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 animal studies and early clinical trials does not ensure that later large-scale trials will be successful nor does it predict final 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 repeated or terminated.

Initial clinical trials of APD356 have been conducted only in small numbers of subjects. Preclinical data and the limited clinical results we have obtained for APD356 may not predict results from studies in larger numbers of subjects drawn from more diverse populations, and also may not predict the ability of APD356 to achieve a sustained reduction in bodyweight, or to do so safely. We have designed 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, 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 our product candidates and may raise potential adverse publicity in the marketplace. In response to our IND submission for APD356, the FDA requested that we provide an assessment of the abuse potential of APD356 as well as 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 on-going. Preclinical data also may not predict the ability of APD125 to be effective at initiating sleep and/or improving sleep quality.

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. We expect to announce the results of clinical trials for both APD356 and APD125 by the middle of 2005. However, if we delay or abandon 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, and our stock price is likely to 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, preclinical or early clinical 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, financial and human resources. 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 establish or maintain a clinical development pipeline or generate revenue.

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

Our GPCR technologies 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 to the identification of drug leads that may possess therapeutic potential, and may not result in the regulatory approval and commercialization of any therapeutic products. We do not believe that there are any drugs on the market that have been discovered or developed using our proprietary technologies. If we are unable to identify additional 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 using GPCRs to discover and develop compounds into drugs more effectively or more 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 products involved. A new drug approval, or NDA, application 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 drug candidate. The FDA can delay, limit or deny approval of a product candidate for many reasons, including:

- not finding a product candidate safe and 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. 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 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 drug 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 19AJ 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 new financing or generate significant partnering revenues in the short term. If we do not receive new financing 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 financing 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, $12.8 million and $19.4 million for the years ended December 31, 2004, 2003 and 2002, respectively. Our revenues depend upon the success of our existing collaborations and on our ability to enter into new collaborations. We will receive little additional revenue under our existing collaboration agreements 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 into clinical testing, which may not occur for many years, if ever. We cannot guarantee that any of the 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 milestones.

For the year ended December 31, 2004, revenues recognized under our collaboration with Merck represented approximately 95% of our total revenues. On December 20, 2004, we entered into a collaboration and license agreement with Ortho-McNeil for which we received an upfront payment of $17.5 million in January 2005. In addition, we received milestone payments totaling $5.0 million upon Ortho-McNeil's selection of two Arena-discovered compounds for preclinical development in January 2005. We expect substantially all of our revenues for 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 a Phase 2 clinical trial, 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 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 collaborators, such collaborator may act in its self-interest, which may be 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 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 a new collaboration 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 payors. Government and third-party payors 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 DEA and corresponding state agencies to ensure strict compliance with cGMP and other applicable government regulations and corresponding foreign standards; however, 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 compounds developed by us or others. Additional potential transactions we may consider include a variety of different business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could harm our operations and financial results.

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

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

We may encounter significant delays or problems with our new 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.

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, 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 believe that 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 the 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 product liability insurance that covers our clinical trials up to an annual aggregate limit of $5.0 million. 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 be able to obtain 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.

We depend on our collaborators, contractors and vendors and on our laboratories and other facilities 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 reasonably adequate 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.

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 drug candidates, we will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we may also be subject to additional FDA post-marketing obligations, all of which may result in significant expense and limit our ability to commercialize our product.

If any of our product candidates receive United States regulatory approval, the FDA may still impose significant restrictions on the indicated uses for which the product 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 periodic 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 drug candidates or further restrict or regulate post-approval activities. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

In order to market any 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 ("FASB") issued Statement of Financial Accounting Standards ("SFAS") No. 123R "Share-Based Payment." This statement, which will be effective in our third quarter of 2005, 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 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. 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 become profitable, if ever.

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 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.

As of January 31, 2005, we owned, in part or in whole, or had exclusively licensed the following patents: 15 in the United States, 11 in European countries, six in Australia, five in New Zealand, one in Japan, one in Singapore and one in Israel. In addition, as of January 31, 2005, we had approximately 273 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 76 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. Eight of our patent families containing a total of seven patents and 23 patent applications were the subject of joint inventions by our employees and the employees of other entities. The remaining 67 patent families containing a total of 32 patents and 250 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. Our most advanced compounds, including APD356 and APD125, are the subject of patent applications and not patents.

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 with 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 third parties. 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 third parties 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 drug 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 third parties 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, third parties 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 third parties.

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 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.

Patent law outside the United States is also uncertain and many countries are currently reviewing and revising patent laws, particularly with respect to biotechnology and pharmaceutical inventions. The laws of some countries do not protect our intellectual property rights to the same extent as U.S. laws. It may be necessary or useful for us to participate in proceedings to determine the validity of our, or our competitors', foreign patents, which 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 December 31, 2004, the market price of our stock was as low as $3.48 per share and as high as $8.57 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, including, in the near term, the results from our clinical trials for either APD356 or APD125;
- 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, if any;
- changes in the research and development budgets of our existing or potential collaborators;
- others introducing new drug discovery techniques or new 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 Convertible Preferred Stock are entitled to require us to redeem their Series B Convertible Preferred Stock.

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 Convertible Preferred Stock, (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 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 Convertible Preferred Stock 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. The exercise price of our outstanding seven-year warrants are subject to weighted-average adjustment in certain circumstances. Any warrants issued upon exercise of our unit warrants will have similar anti-dilution protections for future issuances.

The holders of our Series B-1 Convertible Preferred Stock are entitled to require us to redeem all or some of their shares of Series B-1 Convertible Preferred Stock, 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 payment and any applicable penalties. The aggregate redemption price of our Series B-1 Convertible Preferred Stock at December 31, 2004, was approximately $36.5 million, and accrues interest at 4.0% annually.

Following the exercise of our unit warrants, the holders of our Series B-2 Convertible Preferred Stock will be entitled to require us to redeem their shares of Series B-2 Convertible Preferred Stock, at a price equal to the amount of the original holder's original investment, plus all accrued but unpaid dividends thereon to the date of payment and any applicable penalties, if, following the 21st month anniversary of the original issue date of the Series B-2 Convertible Preferred Stock, the closing price of our common stock for any 30 consecutive trading days is below the conversion price for the Series B-2 Convertible Preferred Stock.

Also, the holders of the Series B-2 Convertible Preferred Stock may require us to redeem their shares if we issue common stock or common stock equivalents (excluding, among other things, certain common stock and common stock equivalents issued or issuable (a) to our officers, directors, employees or consultants, (b) in connection with certain strategic partnerships or joint ventures, and (c) in connection with certain mergers and acquisitions) for an effective net price to us per share less than a price to be determined based on a formula. "Effective net price" is not defined in the Certificate of Designations governing our Series B-2 Convertible Preferred Stock. The holders of our Series B-2 Convertible Preferred Stock 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 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 115.0% of the stated value or the market value (as calculated under the Certificate of Designations for the Series B-1 Convertible Preferred Stock and the Series B-2 Convertible Preferred Stock) of such shares of Series B Convertible Preferred Stock plus all accrued but unpaid dividends thereon to the date of payment. "Triggering Events" include any of the following events: (a) immediately prior to a bankruptcy event; (b) 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; (c) any Event (as defined in the Registration Rights Agreement with the Series B Convertible Preferred Stock holders) occurs and remains uncured for 60 days; (d) we fail to make any cash payment required under the Series B Convertible Preferred Stock transaction documents and such failure is not timely cured; (e) the issuance of a going concern opinion by our independent registered public accounting firm that is not timely cured; (f) we breach a section of the Series B Convertible Preferred Stock purchase agreement relating to indebtedness and subordination; or (g) we default in the timely performance of any other obligation under the Series B Convertible Preferred Stock transaction documents and such default is not timely cured. We will also be required to redeem any shares of the Series B Convertible Preferred Stock 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 Convertible Preferred Stock and the Series B-2 Convertible Preferred Stock.

If we are required to redeem all or some of the currently outstanding shares of our Series B Convertible Preferred Stock, 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 Convertible Preferred Stock 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 Convertible Preferred Stock, 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 Convertible Preferred Stock, your ownership interest may be significantly diluted. If we are required or elect to redeem shares of the Series B Convertible Preferred Stock 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 35,205,869 shares of our common stock outstanding as of February 15, 2005. The outstanding shares of our Series B-1 Convertible Preferred Stock are convertible into up to 4,861,899 shares of common stock at $7.50 per share of common stock. Holders of the Series B-1 Convertible Preferred Stock 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-1 Convertible Preferred Stock. In addition, holders of our Series B-1 Convertible Preferred Stock own warrants to acquire common stock and unit warrants to acquire Series B-2 Convertible Preferred Stock and additional warrants to acquire common stock, which, if exercised and converted, would obligate us to issue up to 3,620,174 additional shares of common stock at a weighted average exercise price of $8.52 per share. In addition, as of February 15, 2005, there were 3,697,520 common stock options issued and outstanding under our equity compensation plans at a weighted average exercise price of $8.04, 625,712 additional shares of common stock issuable under our equity compensation plans, 690,268 shares of common stock reserved for issuance under our 2001 Employee Stock Purchase Plan and 141,669 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 fall 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 Convertible Preferred Stock 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 Convertible Preferred Stock 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.

We may face litigation or other adverse actions as a result of a result of our recent public stock sale.

On January 27, 2005, one of our stockholders informed us by letter that it was opposed to the public stock offering that we closed on February 4, 2005. On January 31, 2005, this same stockholder filed with the SEC a Schedule 13D which attached as an exhibit its January 27, 2005 letter. The Schedule 13D reiterated the stockholder's opposition to the offering, indicated that it believed the offering was not in the best interests of our stockholders, and stated that the stockholder is considering all potential legal remedies, including a potential suit against us and our Board of Directors for breach of fiduciary responsibility to our stockholders. The Schedule 13D also stated the stockholder may consider, among other options, solicitation of a proxy to replace certain of our Board members. Other of our stockholders verbally expressed opposition to the offering. Any litigation, proxy contest or other similar action could result in significant costs and divert management's attention and resources, which could adversely affect our business.

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

Provisions of our Series B Convertible Preferred Stock 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 Convertible Preferred Stock 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 Convertible Preferred Stock, 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.

Item 2. Properties.

The facilities that we occupy consist of approximately 206,000 square feet of research, development, warehouse and office space located at 6114, 6124-6126, 6138-6150, 6154 and 6166 Nancy Ridge Drive, San Diego, California. At our 6166 Nancy Ridge Drive facility, we lease approximately 37,000 square feet of space, of which 23,000 square feet is laboratory space and 14,000 square feet is office space. In 2001, we purchased the 6138-6150 Nancy Ridge Drive facility whose square footage is approximately 55,000 square feet and consists of 33,000 square feet of laboratory space and 22,000 square feet of office space. In December 2003, we completed a sale and leaseback of the 6138-6150 Nancy Ridge Drive facility for net proceeds of $12.6 million. In March 2002, we entered into a lease for our 6124-6126 Nancy Ridge Drive facility, which is approximately 31,000 square feet of space, and approximately 17,000 square feet is laboratory space and 14,000 square feet is office space. We sublease approximately 6,000 square feet, primarily office space, of the 6124-6126 facility to ChemNavigator. In November 2001, we acquired a 13,000 square foot warehouse facility at 6114 Nancy Ridge Drive. We have converted this facility into a 40,000 square foot chemical development facility of which approximately 5,000 square feet is office space. The remaining 35,000 square feet, which include engineering support areas, are dedicated to process research and scale up chemistry, the production of intermediates and other compounds for research and development purposes, and the manufacture of active pharmaceutical ingredients to support our clinical trials. We currently occupy this facility and it is in use for the production of scale-up lots for internal research programs, animal safety studies and human clinical trials. We commenced cGMP operations in this facility in the second quarter of 2004. Also in November 2001, we acquired a 49,000 square foot facility at 6154 Nancy Ridge Drive. We are using a portion of this facility as a warehouse and office space and are evaluating options for this facility, including, among others, expanding it for our own use or selling it. We believe these facilities will be adequate to meet our near-term space requirements.

Item 3. Legal Proceedings.

None.

Item 4. Submissions of Matters to a Vote of Security Holders.

No matters were submitted to a vote of security holders during the fourth quarter of the fiscal year covered by this Annual Report on Form 10-K.

PART II

Item 5. Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Our common stock has traded on the NASDAQ National Market under the symbol "ARNA" since our initial public offering on July 28, 2000. The following table sets forth, for the period indicated, the high and low sale prices for the common stock as reported by the NASDAQ National Market.

	High	Low
Year ended December 31, 2003		
First Quarter	$ 7.14	$ 6.11
Second Quarter	$ 8.36	$ 6.00
Third Quarter	$ 7.74	$ 6.50
Fourth Quarter	$ 8.57	$ 6.17

	High	Low
Year ended December 31, 2004		
First Quarter	$ 7.10	$ 5.68
Second Quarter	$ 6.70	$ 5.00
Third Quarter	$ 5.50	$ 3.48
Fourth Quarter	$ 6.80	$ 4.19

As of February 15, 2005, there were approximately 241 stockholders of record of our common stock, one of which is Cede & Co., a nominee for Depository Trust Company (or DTC). Shares of common stock that are held by financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC, and are considered to be held of record by Cede & Co. as one stockholder.

Dividends

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

Securities Authorized for Issuance Under Equity Compensation Plans

The following table summarizes our compensation plans under which our equity securities are authorized for issuance as of December 31, 2004:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	2,780,399	$ 8.66	2,237,651*
Equity compensation plans not approved by security holders	—	—	—
Total	2,780,399	$ 8.66	2,237,651*

* Includes 690,268 shares of common stock available for future issuance under our 2001 Employee Stock Purchase Plan.

In January 2005, we issued an aggregate of 931,335 stock options to our employees, executive officers and directors. The following table summarizes our compensation plans under which our equity securities are authorized for issuance as of January 31, 2005:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders ...	3,699,120	$ 8.04	1,314,480*
Equity compensation plans not approved by security holders ...	—	—	—
Total	3,699,120	$ 8.04	1,314,480*

* Includes 690,268 shares of common stock available for future issuance under our 2001 Employee Stock Purchase Plan.

Item 6. Selected Financial Data.

The following Selected Financial Data should be read in conjunction with "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Item 8. Financial Statements" included elsewhere in this Annual Report on Form 10-K.

	Years ended December 31,				
	2004	2003	2002	2001	2000
Revenues					
Collaborative agreements	$ 13,685,822	$ 12,734,279	$ 18,005,765	$ 16,643,999	$ 7,683,396
Collaborative agreements with affiliates	—	100,000	1,416,000	1,416,000	—
Total revenues	13,685,822	12,834,279	19,421,765	18,059,999	7,683,396
Expenses					
Research and development	57,729,138	50,885,417	44,399,136	22,864,250	12,080,204
General and administrative	10,449,281	8,553,910	7,499,011	5,390,446	2,678,980
Amortization of deferred compensation	1,466,245	3,236,087	2,264,934	4,239,740	4,342,896
Amortization of acquired technology and other purchased intangibles	1,824,761	1,621,220	1,586,127	1,280,830	—
Total operating expenses	71,469,425	64,296,634	55,749,208	33,775,266	19,102,080
Interest and other, net	(208,167)	4,402,916	5,284,302	8,832,543	5,056,714
Investment writedown	—	—	(1,786,797)	—	—
Net loss	(57,991,770)	(47,059,439)	(32,829,938)	(6,882,724)	(6,361,970)
Non-cash preferred stock charge ...	—	—	—	—	(22,391,068)
Dividends on redeemable convertible preferred stock	(1,437,384)	(26,858)	—	—	—
Accretion of discount and deemed dividend related to redeemable convertible preferred stock	(1,851,883)	(35,516)	—	—	—
Net loss allocable to common stockholders	$ (61,281,037)	$ (47,121,813)	$ (32,829,938)	$ (6,882,724)	$ (28,753,038)
Net loss per share, basic and diluted	$ (2.40)	$ (1.74)	$ (1.19)	$ (0.28)	$ (2.84)
Shares used in calculating net loss per share, basic and diluted	25,527,617	27,159,234	27,487,537	24,989,067	10,139,755

	As of December 31,				
	2004	2003	2002	2001	2000
Balance Sheet Data:					
Cash and cash equivalents	$ 58,686,129	$ 60,471,856	$ 61,871,305	$ 176,676,669	$ 144,413,176
Short-term investments	54,627,710	93,545,027	123,271,580	50,247,624	—
Accounts receivable	22,590,323	27,712	3,519,209	3,481,250	2,116,146
Total assets	206,364,995	229,898,109	254,890,047	276,973,710	152,711,929
Deferred revenues	30,070,188	3,972,848	6,592,938	2,776,856	705,000
Long-term obligations, net of current portion	13,259,326	13,000,000	45,737	402,092	960,517
Redeemable convertible preferred stock	29,092,228	25,776,104	—	—	—
Deferred compensation	(779,972)	(2,647,610)	(1,060,689)	(3,611,933)	(7,899,970)
Accumulated deficit	(168,806,515)	(107,525,478)	(60,403,665)	(27,573,727)	(20,691,003)
Total stockholders' equity	206,364,995	183,148,132	242,051,701	269,473,678	148,784,325

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis in conjunction with "Item 8. Financial Statements and Supplementary Data" included below in this Annual Report on Form 10-K (this "Annual Report"). Operating results are not necessarily indicative of results that may occur in future periods. This discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. The actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including, but not limited to, those set forth under "Risk Factors" in "Item 1. Business" included above in this Annual Report. All forward-looking statements included in this document are based on information available to us on the date of this document and, except as required by law, we undertake no obligation to publicly revise our forward-looking statements to reflect events or circumstances.

OVERVIEW

We have incurred net losses of approximately $168.8 million since our inception in April 1997 through December 31, 2004, and expect to incur substantial and increasing net losses for the next several years or more as we continue our research and development activities. To date, we have generated cash and funded our operations primarily through the sale of common and preferred equity securities, payments from collaborators and the sale and lease back of one of our facilities. From our inception through December 31, 2004, we have generated approximately $415.4 million in cash from these sources, of which approximately $326.9 million was through sales of equity and approximately $75.9 million was through payments from our collaborators. This does not include the proceeds from the public offering we completed in February 2005 or payments we received in January 2005 from Ortho-McNeil Pharmaceutical, Inc., a Johnson & Johnson Company ("Ortho-McNeil"), which are discussed below.

In October 2004, we extended and expanded our collaboration with Merck & Co., Inc., which is focused on developing therapeutics for atherosclerosis and related disorders, and Merck purchased $7.5 million of our stock at a price of $8.00 per share and selected one of our compounds for preclinical development. We believe one or more of the three GPCRs subject to this collaboration play a role in regulating plasma lipid profiles, including HDL cholesterol, the so-called "good cholesterol," and is responsible for the HDL-raising activity of niacin. In addition, under our agreement, Merck will pay us $5.7 million a year for collaboration research through October 19, 2007. During 2004, we achieved three milestones under the collaboration and received payments totaling $8.0 million.

In December 2004, we entered into a collaboration and license agreement with Ortho-McNeil to further develop compounds for the potential treatment of type 2 diabetes and other disorders. Our two lead compounds are currently in preclinical development with Ortho-McNeil. In January 2005, we received a $17.5 million upfront payment and two milestone payments of $2.5 million each. In addition, under our agreement, Ortho-McNeil will pay us $2.4 million a year for collaboration research through December 19, 2006.

In February 2005, we sold 8,625,000 shares of our common stock in a public offering at $6.00 per share and received net proceeds of approximately $48.3 million. As a result of the offering, the holders of our Series B-1 Convertible Preferred Stock are entitled to require us to redeem all or some of their outstanding preferred shares. The aggregate redemption price at December 31, 2004, was approximately $36.5 million. If required to redeem, we may be able to satisfy a portion of this amount with shares of our common stock.

Although we have recently been successful in our collaborative and financing efforts, certain industry trends may affect our ability to generate additional cash from collaborators and investors. First, companies in our industry with products on the market or in late-stage clinical development continue to be favored by investors and potential licensing partners over companies with technologies for discovering products. Our potential partners are now more interested in product candidates for a specific therapeutic area, and particularly drug candidates with clinical data, rather than just the technologies that could be used to find such candidates. We believe that this trend may delay our ability to partner our programs on favorable terms.

Other industry trends that may be significant to us are the consolidation that has occurred in our industry and setbacks to pharmaceutical companies caused by product litigation and competition by generics. In addition to reducing the number of potential partners, the consolidation and setbacks may make potential partners less willing to enter into new collaborations or cause existing partners to terminate or slow work on their existing collaborations for a variety of reasons, including their reluctance to enter new collaborations when they are integrating new operations, a change in research focus and direction following a merger or reduced budgets for research and development.

Our most significant short-term opportunities are with APD356 and APD125. If we are able to demonstrate in our Phase 2 clinical trial that APD356 is effective in humans, we believe that we will be able to successfully partner this program on favorable terms or issue additional equity securities, potentially at a valuation higher than our current market price. We expect to have the results of our Phase 2 clinical trial for APD356 in the second quarter of 2005. Our APD125 Phase 1 clinical trial will evaluate safety, tolerability and pharmacokinetics in healthy volunteers. We expect to have the results of our Phase 1 clinical trial in the middle of 2005. If either of these clinical trial programs is not successful, we expect to re-evaluate our currently planned expenditures for the remainder of this year. Even if the results of the clinical trials for APD125 and APD356 are favorable, we expect our losses will be substantial this year because it will take some period of time after learning such results to partner either product candidate.

In the long term, we will need to raise a substantial amount of cash to develop our product candidates and sustain our research efforts. We believe this will be possible through the issuance of additional equity securities or through partnering our more advanced programs which have entered into clinical development. We are optimistic about our pipeline of internally discovered compounds and our ability to find additional product candidates in attractive markets by using our technologies, and believe that over time many of these programs will enter into clinical trials. We believe our ability to successfully partner our most advanced programs on favorable terms will depend on the results of our pending and future clinical trials.

However, the risks we face are substantial. The drug discovery process is long and uncertain and our ability to achieve our goals depends on many factors, many of which are out of our control. We will seek to balance the need to invest heavily in research and development to find new drugs against the need to sustain our operations long enough for our collaborators or us to commercialize the results of our efforts.

SUMMARY OF REVENUES AND EXPENSES

We are providing the following summary of our revenues and expenses to supplement the more detailed discussion below.

Revenues (in millions)

	Years ended December 31,		
Collaborator	2004	2003	2002
Merck	$ 13.0	$ 7.9	$ 1.6
Ortho-McNeil	0.3	—	—
Eli Lilly	—	3.1	14.2
Others	0.4	1.8	3.6
Total revenues	$ 13.7	$ 12.8	$ 19.4

Research and development expenses (in millions)

	Years ended December 31,		
Type of expense	2004	2003	2002
Personnel costs	$ 23.8	$ 23.9	$ 20.2
Facility and equipment costs	11.7	9.9	6.9
Research supplies	10.4	12.6	14.2
External preclinical and clinical study fees and expenses	10.1	3.5	1.6
Other	1.7	1.0	1.5
Total research and development expenses	$ 57.7	$ 50.9	$ 44.4

General and administrative expenses (in millions)

Type of expense	Years ended December 31, 2004	2003	2002
Personnel costs	$ 5.1	$ 4.8	$ 4.2
Legal and other professional fees	2.2	1.5	1.2
Facility and equipment costs	1.9	1.5	1.3
Other	1.2	0.8	0.8
Total general and administrative expenses	$ 10.4	$ 8.6	$ 7.5

YEAR ENDED DECEMBER 31, 2004 COMPARED TO YEAR ENDED DECEMBER 31, 2003

Revenues. We recorded revenues of $13.7 million during the year ended December 31, 2004, compared to $12.8 million in revenues during the year ended December 31, 2003. Ninety-five percent of our revenues during the year ended December 31, 2004, were from our collaboration with Merck, which included research funding, milestone achievements, and technology access and development fees. Eighty-six percent of our revenues during the year ended December 31, 2003, were from our collaborations with Merck and Eli Lilly and Company, which included research funding, milestone achievements, and technology access and development fees. On April 14, 2003, we completed our research activities under our Eli Lilly collaboration, and, accordingly, we have not received research funding from Eli Lilly since such date. In October 2004, we extended and expanded our collaboration with Merck, and Merck purchased $7.5 million of our stock at a price of $8.00 per share, a 70% premium to the then current market price. In addition, under our agreement, Merck will pay us $5.7 million a year for collaboration research through October 19, 2007. We performed an evaluation on the Merck stock purchase and determined that $3.9 million of the $7.5 million purchase was an upfront payment related to the collaboration extension and expansion. Accordingly, we are recognizing the $3.9 million upfront payment as well as the remaining unamortized upfront payment balance of $1.3 million at October 2004 over the extended collaboration term of three years. In addition, in October 2004, we achieved a $1.0 million milestone under our Merck collaboration which we are recognizing over the extended collaboration term of three years as achievability was reasonably assured at the time we extended and expanded our collaboration with Merck. In December 2004, we entered into a collaboration and license agreement with Ortho-McNeil. This collaboration included a $17.5 million upfront payment, which we received in January 2005, as well as research funding of $2.4 million per year through December 19, 2006. Ortho-McNeil has the option to extend our collaboration one year until December 2007 and, therefore, we are amortizing the $17.5 million upfront payment over three years. In December 2004, we achieved two milestones under our Ortho-McNeil collaboration of $2.5 million each, which we are recognizing as revenues over three years as achievability was reasonably assured at the time we entered into the collaboration. We received the milestone payments in January 2005.

Our collaborators often pay us before we recognize such payments as current revenues and, accordingly, these payments are recorded as deferred revenues until earned. As of December 31, 2004, we had deferred revenues totaling approximately $30.0 million. Our revenues for 2005 are expected to be substantially dependent on our most significant collaborators, Merck and Ortho-McNeil. Future revenues for research or clinical milestones that have not yet been achieved are difficult to predict, and we expect our revenues from quarter to quarter and year to year to vary significantly. Our future revenues are dependent upon the clinical success of our partnered programs and whether we partner APD356, APD125 or other of our product candidates.

Research and development expenses. In 2004 and 2003, research and development expenses consisted primarily of costs associated with internal development of our product candidates, internal programs and our technologies. We generally do not track our research and development costs by project; rather, we track such costs by the type of cost incurred. Research and development expenses increased $6.8 million to $57.7 million for the year ended December 31, 2004, from $50.9 million for the year ended December 31, 2003. The difference was due primarily to (i) external preclinical and clinical study fees and expenses increasing by $6.6 million as we continued to develop APD356 and APD125, (ii) facility and equipment costs, including depreciation, increasing by $1.8 million due to the expansion of our facilities, and (iii) research supplies decreasing by $2.2 million due to cost saving efforts and a reduction in the number of our research employees. Included in the $10.1 million in external preclinical and clinical study fees and expenses for the year ended December 31, 2004, is $5.2 million in external fees and expenses related to our APD356 program and $2.4 million in external fees and expenses related to our APD125 program. We expect the number of our research and development employees totaling 239 at December 31, 2004, to be about the same at the end of 2005. We also expect research and development expenses to be greater in 2005 than in 2004 due to greater external preclinical and clinical study fees and expenses related to developing our product candidates, including APD356 and APD125.

General and administrative expenses. General and administrative expenses increased $1.8 million to $10.4 million for the year ended December 31, 2004, from $8.6 million for the year ended December 31, 2003. The increase is due primarily to (i) an increase in professional fees, including legal and accounting fees, of $700,000 related to the complexity and demands of the laws and regulations applicable to public companies, including the implementation of Section 404 of the Sarbanes-Oxley Act of 2002, and the cost of maintaining a growing and maturing portfolio of patent applications and patents, (ii) an increase of $400,000 from increases in utilities and other facility related costs, (iii) an increase in board and consulting services of $400,000, and (iv) an increase in personnel costs of $300,000 from increases in salaries and related benefits. We expect general and administrative expenses to be greater in 2005 than in 2004 due to increases in legal and accounting fees related to the complexity and demands of the laws and regulations applicable to public companies, and the cost of maintaining a growing and maturing portfolio of patent applications and patents.

Amortization of deferred compensation. For the year ended December 31, 2004, we recorded amortization of deferred compensation of $1.5 million, of which $850,000 relates to research and development employees and consultants and $617,000 relates to general and administrative employees. For the year ended December 31, 2003, we recorded amortization of deferred compensation of $3.2 million, of which $2.0 million relates to research and development employees and consultants and $1.2 million relates to general and administrative employees. In December 2004, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards ("SFAS") No. 123R "Share-Based Payment." We have begun, but have not completed, evaluating the impact of SFAS 123R on our results of operations. We expect amortization of deferred compensation as a result of our implementation of SFAS 123R to be significantly higher beginning in the third quarter of 2005 than in previous periods. Please see "Recently issued accounting standards" below for a more detailed discussion.

Interest income and other, net. Interest income and other, net, was a net expense of $208,000 for the year ended December 31, 2004, compared to a net income of $4.4 million for the year ended December 31, 2003. Interest income and other, net, for the year ended December 31, 2004, was primarily comprised of (i) $2.4 million in interest income and gains on sales of investments and assets of $75,000, (ii) interest expense and financing costs of $1.9 million, which includes lease payments accounted for in accordance with SFAS No. 66 "Accounting for Sales of Real Estate" on our 6138-6150 Nancy Ridge Drive facility that we sold in 2003 and are leasing back and (iii) $936,000 in expense attributable to our share of the net loss of TaiGen Biotechnology Co., Ltd. ("TaiGen"), which we have accounted for by the equity method of accounting. Interest income and other, net, for the year ended December 31, 2003, was primarily comprised of interest income of $3.6 million, gain on sale of investments and assets of $1.8 million and rental and other income of $164,000, partially offset by $1.1 million attributable to our share of the net loss of TaiGen.

Dividends on redeemable convertible preferred stock. We recorded a dividend expense of $1.4 million related to our redeemable convertible preferred stock in the year ended December 31, 2004, compared to $27,000 for the year ended December 31, 2003. This dividend expense, payable in additional shares of redeemable convertible preferred stock or in common stock, increases the net loss allocable to common stockholders. Assuming that the redeemable convertible preferred stock is held until the mandatory redemption date, we expect to record dividends on redeemable convertible preferred stock of $1.5 million for each of the years ending December 31, 2005, 2006 and 2007 and $1.4 million for the year ending December 31, 2008.

Accretion of discount and deemed dividend on redeemable convertible preferred stock. We recorded as an expense accretion of discount and deemed dividend on our redeemable convertible preferred stock in the amount of $1.9 million for the year ended December 31, 2004, compared to $36,000 for the year ended December 31, 2003. In accordance with Emerging Issues Task Force ("EITF") 00-27, "Application of Issue No. 98-5 to Certain Convertible Instruments," we allocated the total proceeds received in our preferred stock financing among the Series B-1 Convertible Preferred Stock, the warrants and the unit warrants. We estimated the value of the warrants and unit warrants at $6.5 million using the Black-Scholes method. The fair value of the common stock into which the redeemable convertible preferred stock was convertible into on the date of issuance exceeded the proceeds allocated to the redeemable convertible preferred stock by $2.8 million, resulting in a beneficial conversion feature that was recognized as an increase to paid-in capital and as a deemed discount to the redeemable convertible preferred stock. As a result of the public offering we completed in February 2005, the holders of our Series B-1 Convertible Preferred Stock are entitled to require us to redeem all or some of their outstanding preferred shares. At December 31, 2004, the aggregate redemption price was approximately $36.5 million. Due to this redemption right, we will record a charge of $7.4 million to accretion of discount and deemed dividend on redeemable convertible preferred stock in the first quarter of 2005.

YEAR ENDED DECEMBER 31, 2003 COMPARED TO YEAR ENDED DECEMBER 31, 2002

Revenues. We recorded revenues of $12.8 million during the year ended December 31, 2003, compared to $19.4 million in revenues during the year ended December 31, 2002. Eighty-six percent and 81% of our revenues during the years ended December 31, 2003, and 2002, respectively, were from our collaborations with Merck and Eli Lilly, which included research funding, milestone payments, and technology access and development fees. The decrease in revenues in 2003 was primarily the result of completing our research activities under our Eli Lilly collaboration on April 14, 2003. Accordingly, we have not received research funding from Eli Lilly since such date. TaiGen, a related party, accounted for $100,000 in royalty revenues and $1.4 million in revenues related to the transfer of activated receptors in the years ended December 31, 2003 and 2002, respectively. As of December 31, 2003, we had deferred revenues totaling approximately $4.0 million.

Research and development expenses. Research and development expenses increased $6.5 million to $50.9 million for the year ended December 31, 2003, from $44.4 million for the year ended December 31, 2002. The difference was due primarily to (i) personnel costs increasing by $3.7 million due to a higher average number of employees during all of 2003, (ii) research supplies decreasing by $1.6 million due to aggressive cost saving efforts, (iii) facility and equipment costs, including depreciation, increasing by $3.0 million due to expansion of our facilities, and (iv) preclinical study fees increasing by $1.9 million as we moved APD356 closer to clinical testing. As of December 31, 2003, all research and development costs have been expensed as incurred. Our research and development employees decreased from 276 at December 31, 2002, to 254 at December 31, 2003, primarily the result of our December 2003 reduction in our research and development staff of 28 employees. The cost of the reduction in force related to research and development personnel totaled approximately $310,000.

General and administrative expenses. General and administrative expenses increased $1.1 million to $8.6 million for the year ended December 31, 2003, from $7.5 million for the year ended December 31, 2002. The increase was due primarily to an increase in personnel costs of $600,000 due to a higher average number of employees during all of 2003 as well as professional fees, including legal and accounting fees, increasing by $300,000 due to increases in legal and accounting fees related to the complexity and demands of the laws and regulations applicable to public companies, and the cost of maintaining a growing and maturing portfolio of patent applications and patents.

Amortization of deferred compensation. For the year ended December 31, 2003, we recorded amortization of deferred compensation of $3.2 million, of which $2.0 million relates to research and development and $1.2 million relates to general and administrative. For the year ended December 31, 2002, we recorded amortization of deferred compensation of $2.3 million, of which $1.6 million relates to research and development and $700,000 relates to general and administrative.

Interest income and other, net. Interest income and other, net, was $4.4 million for the year ended December 31, 2003, compared to $5.3 million for the year ended December 31, 2002. Interest income and other, net, for the year ended December 31, 2003, was primarily comprised of interest income of $3.6 million and gains on sales of investments of $1.8 million, partially offset by $1.1 million attributable to our share of the net loss of TaiGen, which we have accounted for by the equity method of accounting. Interest income and other, net, for the year ended December 31, 2002, was primarily comprised of interest income of $5.4 million, gain on sale of investments of $417,000 and rental and other income of $560,000, partially offset by $1.0 million attributable to our share of the net loss of TaiGen.

Investment write-down. In the year ended December 31, 2002, we recorded a $1.8 million write-down of our investment in Axiom Biotechnologies, Inc. ("Axiom") which investment on September 3, 2002, was converted into 109,167 restricted shares of Sequenom, Inc. ("Sequenom") upon the closing of the acquisition of Axiom by Sequenom. In 2003, we sold all 109,167 shares of Sequenom stock for net proceeds of $405,000 and recognized a gain of $192,000.

Dividends on redeemable convertible preferred stock. We recorded a dividend expense of $27,000 related to our redeemable convertible preferred stock in the year ended December 31, 2003. We did not have any outstanding redeemable convertible preferred stock during the year ended December 31, 2002.

Accretion of discount and deemed dividend on redeemable convertible preferred stock. We recorded accretion of discount and deemed dividend on our convertible preferred stock in the amount of $36,000 in the year ended December 31, 2003. We did not have any outstanding redeemable convertible preferred stock during the year ended December 31, 2002.

LIQUIDITY AND CAPITAL RESOURCES

Short term

We anticipate increases in research and development expenditures as we continue to move our product candidates, APD356 and APD125, and our research programs forward. We believe we have sufficient cash to meet our objectives over the next year, including completing our current and planned clinical trials for APD356 and APD125, advancing our other lead internal development projects into clinical trials, discovering and developing additional small molecule product candidates, continuing to build our development capabilities and maintaining our research discovery capabilities. We will, however, continue to monitor and evaluate the proper level of research and development expenditures, and may adjust our expenditures based upon a variety of factors such as our clinical trial results and ability to generate cash through collaborative and financing activities.

In the short-term, our sources of liquidity include our cash balances and short-term investments. As of December 31, 2004, we had $113.3 million in cash and cash equivalents and short-term investments. In January 2005, we received approximately $23.2 million from Ortho-McNeil and, in February 2005, we received net proceeds of approximately $48.3 million from the public offering of 8,625,000 shares of our common stock at $6.00 per share. As a result of the offering, the holders of our Series B-1 Convertible Preferred Stock are entitled to require us to redeem all or some of their outstanding preferred shares. The aggregate redemption price at December 31, 2004, was approximately $36.5 million. If required to redeem, we may be able to satisfy a portion of this amount with shares of our common stock. Our ability and decision whether to use cash or equity to satisfy any redemption will depend on, among other factors, our stock price.

In addition to our cash balances and short-term investments, other potential sources of near-term liquidity are (i) the license of our product candidates, internal drug programs and technologies, (ii) the sale of two of the facilities that we own, neither of which is subject to any outstanding loans, and (iii) the sale of additional equity securities.

The industry trends discussed in the overview above will affect the terms of any near-term license agreement with a partner or issuance of equity. Our current licensing strategy, however, is generally to move our lead program compounds towards or into the clinic to potentially realize greater value from partners. If we partner a program, we expect that our partner will be responsible for a majority or all of the clinical trial expenses under the collaboration.

We also continue to regularly evaluate potential acquisitions and in-licensing opportunities. Any such transaction may impact our liquidity as well as affect our expenses if, for example, our operating expenses increase as a result of such license or acquisition or we use our cash to finance the license or acquisition.

Long term

Looking beyond 2005, we will need to raise or generate significant amounts of cash to execute our objectives of internally developing drugs, which take many years and potentially hundreds of millions of dollars to develop, and to continue our research programs. We do not currently have adequate internal liquidity to meet this long-term goal. In order to do so, we will need to continue our out-licensing activities and look to external sources of liquidity, including the public or private financial markets and strategic partners, if available.

The length of time that our current cash and cash equivalents, short-term investments and available borrowings will sustain our operations will be based on, among other things, the scientific progress in our research and development programs, our research and development costs (including personnel costs), our progress in preclinical and clinical testing, the time and costs related to current and planned clinical studies and regulatory approvals, if any, costs associated with securing in-licensing opportunities, if any, and costs associated with intellectual property. We do not know whether adequate funding will be available to us or, if available, that such funding will be available on acceptable terms. Any significant shortfall in funding could result in the partial or full curtailment of our development and/or research efforts, which, in turn, will affect our development pipeline and ability to generate cash in the future.

A source of potential liquidity in the long term is from milestone and royalty payments from existing collaborations. A more detailed discussion of our collaborations is set forth below. We believe it is important to find partners to share the costs, responsibilities and risks of developing drugs.

Sources and Uses of Our Cash

Net cash used in operating activities was approximately $39.2 million during the year ended December 31, 2004, and was used to fund our net loss in the period, adjusted for non-cash expenses, including $7.1 million in depreciation and amortization expense, $1.8 million in amortization of acquired technology and other purchased intangibles, $1.5 million in amortization of deferred compensation, $936,000 for our minority interest in TaiGen's operations, and changes in operating assets and liabilities. We expect net cash used in operating activities to be greater in 2005 than in 2004 as we continue to develop our product candidates, APD356 and APD125, as well as other programs and continue to experience increases in legal and accounting fees related to the complexity and demands of the laws and regulations applicable to public companies, and the cost of maintaining a growing and maturing portfolio of patent applications and patents. These increases in expenditures will be partially offset by funds received from our collaborators, including approximately $23.2 million we received from Ortho-McNeil in January 2005. Net cash used in operating activities was approximately $34.6 million during the year ended December 31, 2003, and was used to fund our net loss in the period, adjusted for non-cash expenses, including $5.6 million in depreciation and amortization expense, $3.2 million in amortization of deferred compensation, $1.6 million in amortization of acquired technology and other purchased intangibles, $1.1 million for our minority interest in TaiGen's operations, and changes in operating assets and liabilities. Net cash used in operating activities was approximately $17.2 million during the year ended December 31, 2002. The primary use of cash for the year ended December 31, 2002, was to fund our net loss in the period, adjusted for non-cash expenses, including $3.5 million in depreciation and amortization, $2.3 million in amortization of deferred compensation, $1.6 million in amortization of acquired technology and other purchased intangibles, $1.0 million for our minority interest in TaiGen's operations, and changes in operating assets and liabilities.

Net cash provided by investing activities was approximately $33.3 million during the year ended December 31, 2004, and was primarily the result of net proceeds received from the sale and maturities of short-term investments of $37.0 million partially offset by $4.4 million for the purchase of equipment, leasehold improvements to the facilities we lease and capital improvements to the facilities we own. We expect our capital expenditures in 2005 will be less than our capital expenditures in 2004. Net cash provided by investing activities was approximately $8.9 million during the year ended December 31, 2003, and was primarily the result of net proceeds received from the sale and maturities of short-term investments of $26.0 million partially offset by $17.3 million for the purchase of equipment, leasehold improvements to the facilities we lease and capital improvements to the facilities we own. In particular, we incurred $11.5 million in improvements to our chemical development facility. Net cash used in investing activities was approximately $97.6 million during the year ended December 31, 2002, and was primarily the result of net purchases of short-term investments of $71.8 million, as well as $24.3 million for the purchase of equipment, leasehold improvements to the facilities we lease and capital improvements to the facilities we own, including the capital improvements to our chemical development facility.

Net cash provided by financing activities was $4.0 million during the year ended December 31, 2004, and was primarily attributable to the equity component of the payment we received from Merck for the expansion and extension of our collaboration of $3.6 million and proceeds of $489,000 from the issuance of common stock upon exercise of options. Net cash provided by financing activities was $24.2 million during the year ended December 31, 2003, and was primarily attributable to net cash proceeds of $34.2 million from a private placement, net cash proceeds of $12.6 million from the sale and leaseback of one of our facilities, and proceeds of $892,000 from the issuance of common stock upon exercise of options. In February 2005, we sold 8,625,000 shares of our common stock in a public offering at $6.00 per share and received net proceeds of approximately $48.3 million. Net cash provided by financing activities was partially offset by the purchase of 3.0 million shares of our common stock from a group of related stockholders for an aggregate cash amount of $23.1 million. Net cash provided by financing activities was approximately $32,000 during the year ended December 31, 2002, and was attributable to the net proceeds of $524,000 from the issuance of common stock upon exercise of options partially offset by principal payments of $492,000 on our capital leases.

Contractual Obligations Table

The following summarizes our long-term contractual obligations as of December 31, 2004:

		Payment due by period			
Contractual Obligations	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Series B-1 Convertible Preferred Stock	$ 36,464,242	$ —	$ —	$ 36,464,242	$ —
Operating leases	8,483,940	976,887	2,027,147	2,129,152	3,350,754
Purchase obligations	98,195	98,195	—	—	—
Financing obligation	22,464,151	1,359,902	2,822,646	2,965,542	15,316,061
Total	$ 67,510,528	$ 2,434,984	$ 4,849,793	$ 41,558,936	$ 18,666,815

The aggregate redemption price of our Series B-1 Convertible Preferred Stock at December 31, 2004, was approximately $36.5 million and is mandatorily redeemable in December 2008. As a result of the public offering we completed in February 2005, the holders of our Series B-1 Convertible Preferred Stock are currently entitled to require us to redeem all or some of their outstanding preferred shares. If required to redeem, we may be able to satisfy a portion of this amount with shares of our common stock.

As of December 31, 2004, we have and we will continue to enter into agreements with clinical sites and contract research organizations to conduct clinical trials. We will make payments to these sites and organizations based upon the number of subjects enrolled and the length of their participation in the trials. In determining the amount of our purchasing obligations for these and other contracts, we have included only the minimum obligation we have under our contracts (which analysis often assumed that such contracts were terminated on December 31, 2004) and did not include any amount which was previously paid, accrued, expensed or associated with a contingent event, such as a change of control or termination of a key employee.

On December 30, 2003, we completed a sale and leaseback of our facility at 6138-6150 Nancy Ridge Drive for $13.0 million. We have accounted for this transaction in accordance with SFAS No. 98, "Accounting for Leases" and SFAS 66, "Accounting for Sales of Real Estate." Our ability to repurchase this facility at a future date is considered continued involvement under SFAS 98 and, therefore, we must use the financing method under SFAS 66. Under the financing method, the book value of the facility and related accumulated deprecation remain on our balance sheet and no sale is recognized. Instead, the sales price of the facility is recorded as a financing obligation and lease payments are being expensed to interest expense. We have included our lease obligations on this facility in "financing obligation" above.

The following is a summary of our significant collaborations as of December 31, 2004:

Ortho-McNeil Pharmaceutical, Inc.

In December 2004, we entered into a collaboration and license agreement with Ortho-McNeil to further develop compounds for the potential treatment of type 2 diabetes and other disorders. Our two lead compounds are currently in preclinical development with Ortho-McNeil. In January 2005, we received a non-refundable $17.5 million upfront payment, and two milestones payments of $2.5 million each. We are eligible to receive up to $295.0 million in milestone payments for each compound, as well as royalty payments associated with Ortho-McNeil's commercialization of any drugs discovered under the agreement. These milestone payments include development and approval milestone payments of up to $132.5 million for the first indication and $62.5 million for the second indication for each compound, and up to $100.0 million in sales milestone payments for each product resulting from the collaboration. In addition, under our agreement, Ortho-McNeil will pay us $2.4 million a year for collaboration research through December 19, 2006. Ortho-McNeil has the option to extend our two-year collaboration for one additional year. Under our agreement, we will have no further performance obligations beyond December 19, 2006, or, if the agreement is extended, December 19, 2007. As a result of the option to extend, we are recognizing the upfront payment ratably over three years. In addition, we are recognizing the two milestones we achieved over three years as achievability was reasonably assured at the time we entered into the collaboration.

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 our change of control (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.

For the year ended December 31, 2004, we recognized revenues under the Ortho-McNeil agreement of approximately $319,000, which included approximately $192,000 from the amortization of the upfront payment, research funding of approximately $77,000, and approximately $50,000 in amortization from the two milestones achieved. At December 31, 2004, deferred revenues under the agreement totaled approximately $22.3 million.

Merck & Co., Inc.

In October 2002, we entered into a research and licensing agreement with Merck to collaborate on three GPCRs to develop therapeutics for atherosclerosis and related disorders. We believe one or more of these GPCRs plays a role in regulating plasma lipid profiles, including HDL cholesterol, the so-called "good cholesterol," and is responsible for the HDL-raising activity of niacin. In October 2004, we extended and expanded our collaboration with Merck, and Merck selected one of our compounds for preclinical development. As of December 31, 2004, we had received $19.5 million from Merck in upfront and milestone payments and an equity investment. We may receive additional milestone payments of up to $34.0 million for Merck's clinical and marketing achievements, as well as royalty payments associated with Merck's commercialization of any drugs discovered under the agreement. There is no guarantee we will receive any further milestone payments or royalty payments under this agreement. In addition, we have received research funding from Merck since the inception of our collaboration, and, under our agreement, Merck will pay us $5.7 million a year for collaboration research through October 19, 2007.

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.

As part of the extension and expansion of our collaboration with Merck in October 2004, Merck purchased $7.5 million of our stock at a 70% premium to the then current market price. We performed an evaluation on the Merck stock purchase and determined that $3.9 million of this $7.5 million purchase was an upfront payment related to the collaboration extension and expansion. Accordingly, we are recognizing the $3.9 million upfront payment as well as the remaining unamortized upfront payment balance of $1.3 million at October 2004 over the extended collaboration term of three years. In addition, in October 2004, we achieved a $1.0 million milestone under the collaboration, which we are recognizing over the extended collaboration term of three years as achievability was reasonably assured at the time we extended and expanded our collaboration with Merck.

For the year ended December 31, 2004, we recognized revenues under the Merck agreement of approximately $13.0 million, which included $7.1 million in milestones, research funding of approximately $4.5 million and approximately $1.4 million from the amortization of the upfront payments. For the year ended December 31, 2003, we recognized revenues under the agreement of approximately $7.9 million, which included research funding of approximately $6.6 million and approximately $1.3 million from the amortization of the upfront payment. For the year ended December 31, 2002, we recognized revenues under the agreement of approximately $1.6 million, which included research funding of approximately $1.4 million and approximately $200,000 from the amortization of the upfront payment. At December 31, 2004, deferred revenues under the agreement totaled approximately $7.3 million.

Recently issued accounting standards

In December 2004, the FASB issued SFAS No. 123R "Share-Based Payment." This statement is a revision to SFAS 123 and supersedes Accounting Principles Board ("APB") Opinion No. 25, "Accounting for Stock Issued to Employees," and amends FASB Statement No. 95, "Statement of Cash Flows." The statement eliminates the ability to account for share-based compensation using the intrinsic value method allowed under APB 25 and 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. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements of these equity arrangements.

SFAS 123R permits public companies to choose between the following two adoption methods:

- A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS 123 for all awards granted to employees prior to the effective date of SFAS 123R that remain unvested on the effective date, or

- A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits companies to restate based on the amounts previously recognized under SFAS 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

We have begun, but have not completed, evaluating the impact of the adoption of SFAS 123R on our results of operations. 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 become profitable, if ever.

CRITICAL ACCOUNTING POLICIES AND MANAGEMENT ESTIMATES

The SEC defines critical accounting policies as those that are, in management's view, important to the portrayal of our financial condition and results of operations and demanding of management's judgment. Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP"). The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. We base our estimates on experience and on various assumptions that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from those estimates.

Our critical accounting policies include:

Revenue recognition. Our revenue recognition policies are in accordance with the SEC Staff Accounting Bulletin ("SAB") No. 101, "Revenue Recognition in Financial Statements," as amended by SAB No. 104, "Revenue Recognition," and EITF 00-21, "Revenue Arrangements with Multiple Deliverables," which provide guidance on revenue recognition in financial statements, and are based on the interpretations and practices developed by the SEC. Some of our agreements contain multiple elements, including technology access fees, research funding, milestones and royalty obligations.

Revenues from a milestone achievement is recognized when earned, as evidenced by acknowledgment from our collaborator, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, (ii) the milestone represents the culmination of an earnings process, (iii) the milestone payment is non-refundable and (iv) our performance obligations after the milestone achievement will continue to be funded by our collaborator at a level comparable to the level before the milestone achievement. If all of these criteria are not met, the milestone achievement is recognized over the remaining minimum period of our performance obligations under the agreement. We defer non-refundable upfront fees under our collaborations and recognize them over the period the related services are provided or over the estimated collaboration term using various factors specific to the collaboration. Amounts we receive for research funding for a specified number of full-time researchers are recognized as revenues as the services are performed. Advance payments we receive in excess of amounts earned are classified as deferred revenues until earned.

Clinical trial expenses. We review and accrue clinical trials expenses based on work performed. We rely on estimates of total costs incurred based on enrollment of subjects, completion of studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as clinical trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revisions become known.

Intangibles. Purchase accounting requires estimates and judgments to allocate the purchase price to the fair market value of the assets received and liabilities assumed. In February 2001, we acquired Bunsen Rush, Inc. for $15.0 million in cash and assumed $400,000 in liabilities. We allocated $15.4 million to the patented Melanophore technology acquired in such transaction. The Melanophore technology, our primary screening technology, is being amortized over its estimated useful life of 10 years, which was determined based on an analysis, as of the acquisition date, of the conditions in, and the economic outlook for, the pharmaceutical and biotechnology industries and the patent life of the technology. As with any intangible asset, we will continue to evaluate the value of the Melanophore technology, and we will record a future write-down of the carrying value of the technology if we determine that the technology has become impaired or we no longer use this technology internally as our primary screening technology or we will accelerate the amortization if we determine that the technology life has been shortened. In 2004, we wrote off the entire unamortized balance of $204,000 for acquired technology related to our agreement with the University of Glasgow.

Stock-based compensation. We account for stock options granted to employees and directors using the intrinsic value method in accordance with APB Opinion No. 25, "Accounting for Stock Issued to Employees," and its related interpretations. Pursuant to this method, we measure the intrinsic value of the option on its grant date as the difference between the exercise price of the option and the fair market value of our stock. We then expense the difference, if any, over the vesting period of the option, on an accelerated basis, in accordance with FASB Issued Interpretation No. 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans."

We have adopted the disclosure-only requirements of SFAS 123, "Accounting for Stock-Based Compensation." If we had adopted SFAS 123 to recognize an expense for options granted to employees and directors under our stock-based compensation plans, our earnings would have been materially impacted. The impact of this method is disclosed in the notes to the consolidated financial statements included elsewhere in this Annual Report.

Options issued to non-employees other than directors are accounted for under the fair value method in accordance with SFAS 123 and EITF Issue No. 96-18, "Accounting for Equity Instruments that are Issued to Other than Employees for Acquiring, or in Conjunction with Selling Goods or Services." Under the fair value method, compensation cost is measured at the grant date of the option based on the value of the award using the Black-Scholes method. Compensation cost is periodically remeasured as the underlying options vest in accordance with EITF Issue No. 96-18 and is recognized over the service period.

In December 2004, the FASB issued SFAS 123R. This statement is a revision to SFAS 123, supersedes APB 25, and amends SFAS 95, "Statement of Cash Flows." SFAS 123R eliminates the ability to account for share-based compensation using the intrinsic value method allowed under APB 25 and requires public companies to recognize such transactions 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 also provides guidance on valuing and expensing these awards, as well as disclosure requirements of these equity arrangements. This statement is effective for the first interim reporting period that begins after June 15, 2005, and the Company will adopt the statement on July 1, 2005. See "Recently Issued Accounting Pronouncements."

Valuation of our Series B Convertible Preferred Stock, and related warrants and unit warrants. In accordance with EITF 00-27, "Application of Issue No. 98-5 to Certain Convertible Instruments," we allocated the total proceeds received in our preferred stock financing among the Series B-1 Convertible Preferred Stock, the warrants and the unit warrants. We estimated the value of the warrants and unit warrants at $6.5 million using the Black-Scholes method. The fair value of the common shares into which the Series B-1 Convertible Preferred Stock was convertible into on the date of issuance exceeded the proceeds allocated to the Series B-1 Convertible Preferred Stock by $2.8 million, resulting in a beneficial conversion feature that was recognized as an increase to paid-in-capital and as a deemed dividend to the Series B-1 Convertible Preferred Stock. As a result of the public offering we completed in February 2005, the holders of our Series B-1 Convertible Preferred Stock are currently entitled to require us to redeem all or some of their outstanding preferred shares. At December 31, 2004, the aggregate redemption price was approximately $36.5 million. Due to this redemption right, we will record a charge of $7.4 million to accretion of discount and deemed dividend on redeemable convertible preferred stock in the first quarter of 2005.

The above listing is not intended to be a comprehensive list of all of our accounting policies. In many cases, the accounting treatment of a particular transaction is specifically dictated by GAAP. See our audited consolidated financial statements and notes thereto included elsewhere in this Annual Report which contains accounting policies and other disclosures required by GAAP.

INCOME TAXES

As of December 31, 2004, we had approximately $101.6 million of federal net operating loss carryforwards and $11.2 million of federal research and development tax credit carryforwards for income tax purposes. These carryforwards expire on various dates beginning in 2012. These amounts reflect different treatment of expenses for tax reporting than is used for financial reporting. United States tax law contains provisions that may limit our ability to use net operating loss and tax credit carryforwards in any year, including if there has been a significant ownership change.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our management establishes and oversees the implementation of board-approved policies covering our investments. We manage our market risk in accordance with our investment guidelines, which: (i) emphasize preservation of principal over other portfolio considerations, (ii) require investments to be placed with high credit quality institutions, (iii) establish guidelines for the diversification of our investment portfolio, and (iv) require investments to be placed with maturities that maintain safety and liquidity. We target our portfolio to have an average duration of no more than four years with no one instrument having a duration exceeding five years and one month. We do not invest in derivative instruments, or any financial instruments for trading purposes. Our primary market risk exposure as it affects our cash equivalents, short-term investments, and securities held for sale is interest rate risk. We monitor our interest rate risk on a periodic basis and we ensure that our cash equivalents, short-term investments, and securities held for sale are invested in accordance with our investments guidelines. Managing credit ratings and the duration of our financial investments enhances the preservation of our capital.

We model interest rate exposure by a sensitivity analysis that assumes a hypothetical parallel shift downwards in the U.S. Treasury yield curve of 100 basis points. Under these assumptions, if the yield curve were to shift lower by 100 basis points from the level existing at December 31, 2004, we would expect future interest income from our portfolio to decline by less than $1.1 million over the next 12 months.

As of December 31, 2003, our estimate for the effect of this same hypothetical reduction in interest rates was a decline in interest income of less than $1.5 million. The difference in these two estimates is due to the difference in the gross amount of our cash and cash equivalents, short-term investments, and securities held for sale between the two periods.

The model we use is not intended to forecast actual losses in interest income, but is used as a risk estimation and investment management tool. The hypothetical changes and assumptions are likely to be different from what actually occurs in the future. Furthermore, the computations do not incorporate actions our management could take if the hypothetical interest rate changes actually occur. As a result, actual earnings consequences will likely differ from those quantified herein.

Item 8. Financial Statements and Supplementary Data.

ARENA PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM ON FINANCIAL STATEMENTS

The Board of Directors and Stockholders of Arena Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Arena Pharmaceuticals, Inc. as of December 31, 2004 and 2003, and the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Arena Pharmaceuticals, Inc. as of December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004 in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Arena Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 25, 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California
February 25, 2005

ARENA PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	December 31, 2004	December 31, 2003
Assets		
Current assets:		
Cash and cash equivalents	$ 58,686,129	$ 60,471,856
Short-term investments, available-for-sale	54,627,710	93,545,027
Accounts receivable	22,590,323	27,712
Prepaid expenses and other current assets	5,331,799	4,730,961
Total current assets	141,235,961	158,775,556
Land, property and equipment, net	52,994,209	55,729,472
Acquired technology, net	9,486,216	11,023,212
Other non-current assets	2,648,609	4,369,869
Total assets	$ 206,364,995	$ 229,898,109
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 4,988,586	$ 1,741,981
Accrued compensation	1,300,371	1,281,486
Current portion of deferred revenues	11,497,209	2,861,736
Current portion of obligations under capital leases	—	43,874
Total current liabilities	17,786,166	5,929,077
Deferred rent	931,310	933,684
Deferred revenues, less current portion	18,572,979	1,111,112
Financing obligation	13,259,326	13,000,000
Commitments		
Series B-1 redeemable convertible preferred stock, $.0001 par value: 4,650 and no shares authorized at December 31, 2004 and 2003, respectively; 3,500 shares issued and outstanding at December 31, 2004 and 2003, respectively; Liquidation preference $35,000,000	29,092,228	25,776,104
Stockholders' equity:		
Series A preferred stock, $.0001 par value: 350,000 shares authorized at December 31, 2004 and 2003; no shares issued and outstanding at December 31, 2004 and 2003	—	—
Common stock, $.0001 par value: 67,500,000 shares authorized at December 31, 2004, and 2003; 26,566,419 and 25,548,372 shares issued and outstanding at December 31, 2004, and December 31, 2003, respectively	2,972	2,867
Additional paid-in capital	319,539,956	315,861,773
Treasury stock – 3,000,000 shares at December 31, 2004 and 2003	(23,070,000)	(23,070,000)
Accumulated other comprehensive income (loss)	(163,455)	526,580
Deferred compensation	(779,972)	(2,647,610)
Accumulated deficit	(168,806,515)	(107,525,478)
Total stockholders' equity	126,722,986	183,148,132
Total liabilities and stockholders' equity	$ 206,364,995	$ 229,898,109

See accompanying notes.

ARENA PHARMACEUTICALS, INC.

Consolidated Statements of Operations

	Years ended December 31,		
	2004	2003	2002
Revenues:			
Collaborative agreements	$ 13,685,822	$ 12,734,279	$ 18,005,765
Collaborative agreements with affiliates	—	100,000	1,416,000
Total revenues	13,685,822	12,834,279	19,421,765
Operating expenses:			
Research and development	57,729,138	50,885,417	44,399,136
General and administrative	10,449,281	8,553,910	7,499,011
Amortization of deferred compensation ($849,554, $1,981,648 and $1,576,661 related to, research and development expenses and $616,691, $1,254,439 and $688,273 related to general and administrative expenses for 2004, 2003 and 2002, respectively)	1,466,245	3,236,087	2,264,934
Amortization of acquired technology	1,824,761	1,621,220	1,586,127
Total operating expenses	71,469,425	64,296,634	55,749,208
Loss from operations	(57,783,603)	(51,462,355)	(36,327,443)
Other income (expense):			
Interest income	2,390,066	3,594,580	5,423,742
Investment write-down	—	—	(1,786,797)
Interest expense	(1,854,124)	(37,231)	(76,536)
Gain on sale of investments	74,926	1,820,246	416,910
Other income, net	116,496	163,929	552,849
Equity in losses of TaiGen	(935,531)	(1,138,608)	(1,032,663)
Net loss	(57,991,770)	(47,059,439)	(32,829,938)
Dividends on redeemable convertible preferred stock	(1,437,384)	(26,858)	—
Accretion of discount and deemed dividend related to redeemable convertible preferred stock	(1,851,883)	(35,516)	—
Net loss allocable to common stockholders	$ (61,281,037)	$ (47,121,813)	$ (32,829,938)
Net loss per share, basic and diluted	$ (2.40)	$ (1.74)	$ (1.19)
Shares used in calculating net loss per share, basic and diluted	25,527,617	27,159,234	27,487,537

See accompanying notes.

ARENA PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity

	Common Stock		Additional Paid-In	Treasury	Accumulated Other Comprehensive	Deferred	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Stock	Income	Compensation	Deficit	Equity
Balance at December 31, 2001	**27,585,048**	**$ 2,759**	**$ 300,649,789**	**$ —**	**$ 6,790**	**$ (3,611,933)**	**$ (27,573,727)**	**$ 269,473,678**
Issuance of common stock upon exercise of options, net of repurchases	83,975	8	50,391	—	—	—	—	50,399
Issuance of common stock under the employee stock purchase plan	77,513	8	474,047	—	—	—	—	474,055
Deferred compensation related to stock options	—	—	(286,310)	—	—	286,310	—	—
Amortization of deferred compensation	—	—	—	—	—	2,264,934	—	2,264,934
Net loss	—	—	—	—	—	—	(32,829,938)	(32,829,938)
Net unrealized gain on available-for-sale securities	—	—	—	—	2,618,573	—	—	2,618,573
Net comprehensive loss								(30,211,365)
Balance at December 31, 2002	**27,746,536**	**$ 2,775**	**$ 300,887,917**	**$ —**	**$ 2,625,363**	**$ (1,060,689)**	**$ (60,403,665)**	**$ 242,051,701**
Issuance of common stock upon exercise of options, net of repurchases	36,851	4	54,414	—	—	—	—	54,418
Issuance of common stock, warrants and units warrants related to preferred financing	45,000	4	9,561,808	—	—	—	—	9,561,812
Issuance of common stock under the employee stock purchase plan	103,486	10	534,700	—	—	—	—	534,710
Issuance of restricted stock, net of cancellations	744,000	74	4,811,611	—	—	(4,811,685)	—	—
Repurchase of common shares	(3,000,000)	—	—	(23,070,000)	—	—	—	(23,070,000)
Deferred compensation related to stock options	—	—	94,278	—	—	(49,371)	—	44,907
Amortization of deferred compensation	—	—	(82,955)	—	—	3,274,135	—	3,191,180
Dividends on redeemable convertible preferred stock	—	—	—	—	—	—	(26,858)	(26,858)
Accretion of discount and deemed dividend related to redeemable convertible preferred stock	—	—	—	—	—	—	(35,516)	(35,516)
Restricted shares deferred in company deferred compensation plan	(127,501)	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	(47,059,439)	(47,059,439)
Net unrealized loss on available-for-sale securities and investments	—	—	—	—	(2,098,783)	—	—	(2,098,783)
Net comprehensive loss								(49,158,222)
Balance at December 31, 2003	**25,548,372**	**$ 2,867**	**$ 315,861,773**	**$ (23,070,000)**	**$ 526,580**	**$ (2,647,610)**	**$ (107,525,478)**	**$ 183,148,132**
Issuance of common stock upon exercise of options, net of repurchases	63,700	6	37,564	—	—	—	—	37,570
Issuance of common stock under the employee stock purchase plan	105,098	11	451,475	—	—	—	—	451,486
Cancellations of restricted stock, net of issuances	(64,083)	(6)	(414,198)	—	—	414,204	—	—
Issuance of common stock to Merck	937,500	94	3,590,531	—	—	—	—	3,590,625
Deferred compensation related to stock options	—	—	12,811	—	—	(12,811)	—	—
Amortization of deferred compensation	—	—	—	—	—	1,466,245	—	1,466,245
Dividends on redeemable convertible preferred stock	—	—	—	—	—	—	(1,437,384)	(1,437,384)
Accretion of discount and deemed dividend related to redeemable convertible preferred stock	—	—	—	—	—	—	(1,851,883)	(1,851,883)
Restricted shares deferred in company deferred compensation plan, net of distributions and forfeitures	(24,168)	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	(57,991,770)	(57,991,770)
Net unrealized loss on available-for-sale securities and investments	—	—	—	—	(690,035)	—	—	(690,035)
Net comprehensive loss								(58,325,430)
Balance at December 31, 2004	**26,566,419**	**$ 2,972**	**$ 319,539,956**	**$ (23,070,000)**	**$ (163,455)**	**$ (779,972)**	**$ (168,806,515)**	**$ 126,722,986**

See accompanying notes.

ARENA PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Years ended December 31,		
	2004	2003	2002
OPERATING ACTIVITIES			
Net loss	$ (57,991,770)	$ (47,059,439)	$ (32,829,938)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	7,134,030	5,590,050	3,507,470
Equity in losses of TaiGen	935,531	1,138,608	1,032,663
Amortization of acquired technology	1,824,761	1,621,220	1,586,127
Amortization of deferred compensation	1,466,245	3,236,087	2,264,934
Amortization/accretion of short-term investment premium/discount	1,266,537	1,822,005	1,423,181
Deferred rent	(2,374)	20,743	41,074
Deferred interest expense	259,326	—	—
Loss on disposal of equipment	7,959	25,188	7,066
Investment write-down	—	—	1,786,797
Change in operating assets and liabilities:			
Accounts receivable	(22,562,611)	3,491,497	(37,959)
Prepaid expenses and other assets	(888,603)	84,338	(1,793,408)
Deferred revenues	26,097,340	(2,620,090)	3,816,082
Accounts payable and accrued expenses	3,292,347	(1,926,810)	1,973,589
Net cash used in operating activities	(39,161,282)	(34,576,603)	(17,222,322)
INVESTING ACTIVITIES			
Purchases of short-term investments, available-for-sale	(95,314,008)	(174,527,521)	(207,336,208)
Proceeds from sales/maturities of short-term investments	132,274,753	200,510,138	135,543,996
Purchases of land, property and equipment	(4,414,741)	(17,286,030)	(24,325,234)
Proceeds from sale of equipment	8,015	14,687	5,900
Deposits, restricted cash and other assets	785,729	225,872	(1,503,519)
Net cash provided by (used in) investing activities	33,339,748	8,937,146	(97,615,065)
FINANCING ACTIVITIES			
Principal payments on capital leases	(43,874)	(365,174)	(492,431)
Proceeds from issuance of redeemable convertible preferred stock and warrants	—	34,172,026	—
Proceeds from issuance of common stock	4,079,681	891,526	524,454
Proceeds from sale of facility	—	12,611,630	—
Purchase of common stock	—	(23,070,000)	—
Net cash provided by financing activities	4,035,807	24,240,008	32,023
Net decrease in cash and cash equivalents	(1,785,727)	(1,399,449)	(114,805,364)
Cash and cash equivalents at beginning of period	60,471,856	61,871,305	176,676,669
Cash and cash equivalents at end of period	$ 58,686,129	$ 60,471,856	$ 61,871,305
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:			
Interest paid	$ 1,418,591	$ 144,873	$ 70,120

See accompanying notes.

(1) THE COMPANY AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

The Company

Arena Pharmaceuticals, Inc. (the "Company") was incorporated on April 14, 1997, and commenced operations in July 1997. The Company operates in one business segment and is a biopharmaceutical company with a pipeline of internally discovered small molecule product candidates that target G protein-coupled receptors ("GPCRs").

Principles of Consolidation

The Company's financial statements include the activity of its wholly owned subsidiary, BRL Screening, Inc. since its formation in February 2001.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and highly liquid investments with original maturities of three months or less when purchased.

Short-term Investments, Available-for-sale

In accordance with Statement of Financial Accounting Standards ("SFAS") No. 115, "Accounting for Certain Debt and Equity Securities," short-term investments are classified as available-for-sale. The Company defines short-term investments as income-yielding securities that can be readily converted to cash. These securities are carried at fair value, with unrealized gains and losses reported as accumulated other comprehensive income. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in securities judged to be other than temporary, are included in other income or expense. The cost of securities sold is based on the specific identification method. Interest and dividends on available-for-sale securities are included in interest income. Investments held as of December 31, 2004, consist primarily of U.S. Federal agency notes and U.S. corporate debt securities.

Fair Value of Financial Instruments

Cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities, are carried at cost, which management believes approximates fair value due to the short-term maturity of these instruments. Short-term investments, available-for-sale are carried at fair value.

Concentration of Credit Risk and Major Customers

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist primarily of cash, cash equivalents and short-term investments. The Company limits its exposure to credit loss by placing its cash with high credit quality financial institutions and in accordance with the Company's investment policy, debt that is rated investment grade.

Merck & Co., Inc. ("Merck") accounted for 94.6% of total revenues during the year ended December 31, 2004, and Merck and Eli Lilly and Company ("Eli Lilly") together accounted for 86.3% of total revenues during the year ended December 31, 2003. Ortho-McNeil Pharmaceutical, Inc., a Johnson & Johnson company ("Ortho-McNeil"), accounted for 100% of accounts receivable as of December 31, 2004.

Property and Equipment

Property and equipment are stated at cost and depreciated over the estimated useful lives of the assets (three to seven years) using the straight-line method. Buildings and building improvements are stated at cost and depreciated over the estimated useful life of approximately 20 years using the straight-line method. Amortization of leasehold improvements and assets under capital leases are stated at cost and amortized over the shorter of the estimated useful lives of the assets or the lease term.

Intangible Assets

Purchase accounting requires estimates and judgments to allocate the purchase price to the fair market value of the assets received and liabilities assumed. In February 2001, the Company acquired Bunsen Rush Laboratories, Inc. ("Bunsen Rush") for $15.0 million in cash and assumed $400,000 in liabilities. Acquired technology from the Company's acquisition of Bunsen Rush is being amortized over its estimated useful life of 10 years, which was determined based on an analysis, as of the acquisition date, of the conditions in, and the economic outlook for, the pharmaceutical and biotechnology industries and the patent life of the technology. The Company allocated $15.4 million to the patented Melanophore technology, its primary screening technology, acquired in such transaction. As with any intangible asset, the Company will continue to evaluate the value of the Melanophore technology, and will record a future write-down of the carrying value of the technology if the Company determines that the technology has become impaired or no longer uses this technology internally as a primary screening technology or the Company will accelerate the amortization if it determines that the technology life has been shortened. Accumulated amortization from acquired technology totaled approximately $6.1 million and $4.5 million at December 31, 2004, and 2003, respectively. As of December 31, 2004, the Company anticipates that total charges to be recognized in future periods from the amortization of acquired technology will be approximately $1.5 million for each of the next five years.

In 2004, the Company wrote off the unamortized balance of $204,000 for acquired technology related to the Company's agreement with the University of Glasgow.

Long-lived Assets

The Company reviews the recoverability of long-lived and finite-lived intangible assets when circumstances indicate that the carrying amount of assets may not be recoverable. This evaluation is based on various analyses including undiscounted cash flow projections. In the event undiscounted cash flow projections indicate an impairment, the Company would record an impairment loss, if any, based on the fair value of the assets. Effective January 1, 2002, the Company accounts for impairments under SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." Other than the write-off of the unamortized balance of $204,000 for acquired technology related to the Company's agreement with the University of Glasgow, the Company did not record impairments or write-offs of long-lived assets in 2004, 2003 or 2002.

Deferred Rent

Rent expense is recorded on a straight-line basis over the term of the lease. The difference between rent expense and amounts paid under the lease agreements is recorded as deferred rent in the accompanying balance sheets.

Stock-based Compensation

The Company accounts for stock-based compensation in accordance with the provisions of Accounting Principles Board ("APB") Opinion No. 25, "Accounting for Stock Issued to Employees" and its related Interpretations, which state that no compensation expense is recorded for stock options or other stock-based awards to employees and directors that are granted with an exercise price equal to or above the fair value per share of the Company's common stock on the grant date. In the event that stock options are granted with an exercise price below the fair value of the Company's common stock on the grant date, the difference between the fair value of the Company's common stock and the exercise price of the stock option is recorded as deferred compensation. For stock options granted to its employees and directors, the Company has adopted the disclosure-only requirements of SFAS No. 123 "Accounting for Stock-Based Compensation," which allows compensation expense to be disclosed in the notes to the financial statements based on the fair value of the options granted at the date of the grant. Compensation expense for options granted to non-employees other than directors has been determined in accordance with SFAS 123 and Emerging Issues Task Force ("EITF") Issue No. 96-18, "Accounting for Equity Instruments that are Issued to Other than Employees for Acquiring, or in Conjunction with Selling Goods or Services." Such expense is based on the fair value of the options issued using the Black-Scholes method and is periodically remeasured as the underlying options vest in accordance with EITF Issue No. 96-18.

The Company issued an aggregate of 755,500 shares of restricted common stock to key employees in 2004 and 2003, which generally vest over a two or four-year period. In connection with the issuance of restricted stock to employees, the Company recorded deferred stock compensation totaling $30,000, $4.8 million and $0 during the years ended December 31, 2004, 2003 and 2002, respectively. This deferred compensation related to restricted stock awards was calculated by multiplying the quoted market value of the Company's stock by the number of shares issued and is amortized to expense over the vesting period.

The Company recorded amortization of deferred compensation expense of approximately $1.5 million, $3.2 million and $2.3 million during the years ended December 31, 2004, 2003 and 2002, respectively. The Company expects that charges to be recognized in future periods from amortization of deferred compensation related to equity grants will be $430,000, $323,000 and $27,000 for the years ending December 31, 2005, 2006 and 2007, respectively.

In 2003, the Company set up a deferred compensation plan for its executive officers, whereby executive officers may elect to defer their shares of restricted stock. At December 31, 2004 and 2003, a total of 151,669 and 127,501 shares of restricted stock were contributed to the plan, respectively.

The following pro forma information regarding net loss and net loss per share has been determined as if the Company had accounted for its employee and director stock options and stock issued under the employee stock purchase plan under the fair value method prescribed by SFAS 123. The fair value of options was estimated at the date of grant using a Black-Scholes option valuation model using the assumptions stated below.

	Years ended December 31,		
	2004	2003	2002
Net loss allocable to common stockholders, as reported	$ (61,281,037)	$ (47,121,813)	$ (32,829,938)
Add: Stock-based employee and non-employee compensation expense included in net loss allocable to common stockholders, as reported, net of related tax effects	1,466,245	3,236,087	2,264,934
Fair value of stock-based employee compensation	(6,009,292)	(7,272,597)	(8,825,934)
Pro forma net loss	$ (65,824,084)	$ (51,158,323)	$ (39,390,938)
Net loss per share:			
Basic and diluted — as reported	$ (2.40)	$ (1.74)	$ (1.19)
Basic and diluted — pro forma	$ (2.58)	$ (1.88)	$ (1.43)
Assumptions used for Employee Stock Options:			
Risk-free interest rate	3.0%	2.8%	2.8%
Dividend yield	0%	0%	0%
Stock price volatility	78%	81%	93%
Expected life (years)	5.0	5.0	5.0
Weighted-average fair value	$ 3.74	$ 4.38	$ 6.78
Assumptions used for Employee Stock Purchase Plan:			
Risk-free interest rate	2.1%	1.2%	1.8%
Dividend yield	0%	0%	0%
Stock price volatility	76%	86%	98%
Expected life (years)	0.25	0.25	0.25
Weighted-average fair value	$ 1.69	$ 2.22	$ 2.90

The effects of applying SFAS 123 for providing pro forma disclosures may not be representative of the effect on reported net income (loss) for future years.

Revenue Recognition

The Company's revenue recognition policies are in accordance with the SEC Staff Accounting Bulletin ("SAB") No. 101, "Revenue Recognition in Financial Statements," as amended by SAB No. 104, "Revenue Recognition," and EITF Issue 00-21, "Revenue Arrangements with Multiple Deliverables" which provides guidance on revenue recognition in financial statements, and are based on the interpretations and practices developed by the SEC. Some of the Company's agreements contain multiple elements, including technology access fees, research funding, milestones and royalty obligations.

Revenues from a milestone achievement is recognized when earned, as evidenced by acknowledgment from the Company's collaborator, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement, (ii) the milestone achievement represents the culmination of an earnings process, (iii) the milestone payment is non-refundable and (iv) the Company's performance obligations after the milestone achievement will continue to be funded by the Company's collaborator at a level comparable to the level before the milestone achievement. If all of these criteria are not met, the milestone is recognized over the remaining minimum period of the Company's performance obligations under the agreement. Non-refundable upfront fees under the Company's collaborations are deferred and recognized over the period the related services are provided or over the estimated collaboration term using various factors specific to the collaboration. Amounts received for research funding for a specified number of full-time researchers are recognized as revenues as the services are performed. Advance payments received in excess of amounts earned are classified as deferred revenues until earned.

Research and Development Costs

All research and development expenses are expensed in the year incurred and consist primarily of personnel related expenses and laboratory expenses.

Clinical Trial Expenses

The Company reviews and accrues clinical trials expenses based on work performed. The Company relies on estimates of total costs incurred based on enrollment of subjects, completion of studies and other events. The Company follows this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as clinical trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revisions become known.

Patent Costs

Costs related to filing and pursuing patent applications are expensed as incurred as recoverability of such expenditures is uncertain.

Income Taxes

In accordance with SFAS No. 109, "Accounting for Income Taxes," a deferred tax asset or liability is determined based on the difference between the financial statement and tax basis of assets and liabilities as measured by the enacted tax rates which will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized.

Comprehensive Loss

In accordance with SFAS No. 130, "Reporting Comprehensive Loss," all components of comprehensive loss, including net loss, are reported in the financial statements in the period in which they are recognized. Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company's accumulated other comprehensive income (loss) consisted of an unrealized loss on available-for-sale securities of $163,455 for the year ended December 31, 2004, and an unrealized gain on available for sale securities of $526,580 for the year ended December 31, 2003.

Net Loss Per Share

Basic and diluted net loss per common share are presented in conformity with SFAS No. 128, "Earnings per Share," for all periods presented. In accordance with SFAS 128, basic and diluted loss per share has been computed using the weighted-average number of shares of common stock outstanding during the period, less shares subject to repurchase.

The Company has excluded all outstanding stock options, preferred stock and warrants, and shares subject to repurchase from the calculation of diluted loss per common share because all such securities are antidilutive for all years presented. The total number of shares subject to repurchase excluded from the calculation of diluted net loss per share, prior to application of the treasury stock method for stock options, was 0, 54,249 and 184,123 for the years ended December 31, 2004, 2003 and 2002, respectively. Such securities, had they been dilutive, would have been included in the computation of diluted net loss per share.

Effect of New Accounting Standards

In December 2004, the FASB issued SFAS No. 123R "Share-Based Payment." This statement is a revision to SFAS 123, supersedes APB 25, and amends FASB Statement No. 95, "Statement of Cash Flows." SFAS 123R eliminates the ability to account for share-based compensation using the intrinsic value method allowed under APB 25 and 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. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements of these equity arrangements.

SFAS 123R permits public companies to choose between the following two adoption methods:

- A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS 123 for all awards granted to employees prior to the effective date of SFAS 123R that remain unvested on the effective date, or

- A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits companies to restate based on the amounts previously recognized under SFAS 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

The Company has begun, but has not completed, evaluating the impact of the adoption of SFAS 123R on its results of operations. In connection with evaluating the impact of SFAS 123R, the Company is considering the potential implementation of different valuation method to determine the fair value of share-based compensation. The Company believes the adoption of SFAS 123R will have a material impact on its 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 the Company's net operating cash flows and increase its net financing cash flows in periods after adoption. SFAS 123R may also delay when the Company may become profitable, if ever.

(2) INVESTMENT IN CHEMNAVIGATOR

In January 1999, the Company began development of an Internet-based search engine that allows scientists to search for compounds based primarily on the similarity of chemical structures. In May 1999, ChemNavigator was incorporated and in June 1999, the Company licensed to ChemNavigator a website, the trademark "ChemNavigator" and goodwill associated with the trademark, intellectual property related to the search engine, as well as technology needed to perform chemical similarity searches. In return, the Company received 2,625,000 shares of preferred stock in ChemNavigator valued at approximately $2.6 million based on independent investors' participation in ChemNavigator's Series A preferred round of financing. However, the Company's historical cost basis in the licensed technology was zero and the Company, therefore, recorded its investment in ChemNavigator at zero. As of both December 31, 2004, and 2003, the Company's equity ownership represented approximately 35% of the outstanding voting equity securities of ChemNavigator. Although ChemNavigator has an accumulated deficit, the Company is not under an obligation to reimburse other ChemNavigator stockholders for its share of ChemNavigator's losses, and, therefore, have not included any of ChemNavigator's losses in the Company's Consolidated Statements of Operations. In March 2002, the Company entered into an additional license agreement with ChemNavigator for the use of their cheminformatic software program and in September 2003, the Company amended this license agreement to include additional development work to be performed by ChemNavigator. In 2002, the Company paid ChemNavigator $165,000 under this agreement. In each of 2003 and 2004, the Company renewed its license under this agreement for $50,000. The Company paid ChemNavigator $86,000 and $68,000 for development work performed for the years ended December 31, 2004 and 2003, respectively. The Company has an option to renew its license in subsequent years for $50,000 per year.

The Company subleases office space to ChemNavigator. Lease payments were subject to a 2% increase in April 2003 and annually thereafter. In 2004 and 2003, the Company recognized approximately $100,000 and $98,000, respectively, in other income for this sublease.

Jack Lief, the Company's President and Chief Executive Officer, was the Chairman of the Board of ChemNavigator until he resigned in January 2004. As compensation for his services he has received 200,000 shares of common stock of ChemNavigator, which vested over a period of four years. Robert E. Hoffman, the Company's Vice President, Finance, was the Chief Financial Officer of ChemNavigator until he resigned in December 2004. Mr. Hoffman entered into a four-year service agreement with ChemNavigator in May of 1999, in which he agreed to provide up to 200 hours of service per year. As compensation for his services he has received 100,000 shares of common stock of ChemNavigator, which vested over a period of four years. Steven W. Spector, the Company's Senior Vice President and General Counsel, is a director of ChemNavigator. Mr. Spector does not receive any compensation from ChemNavigator for the services he provides to ChemNavigator.

(3) INVESTMENT IN AXIOM BIOTECHNOLOGIES, INC. AND SUBSEQUENT ACQUISITION BY SEQUENOM, INC.

In April 2001, the Company signed a binding letter of intent with Axiom Biotechnologies, Inc. ("Axiom") for a collaborative research program involving Axiom's proprietary RHACE™ Technology and Human Cell Bank, and purchased $2.0 million of Axiom's preferred stock. The Company accounted for this investment using the cost method of accounting. The Company determined that its investment in Axiom was impaired and accordingly recorded a $1.7 million write-down during the quarter ended June 30, 2002. In September 2002, Axiom was acquired by Sequenom, Inc. ("Sequenom"), and the Company further wrote down its investment by $87,000 to its fair value, less a discount for restrictions on the sale of Sequenom stock, on the date of acquisition of Axiom by Sequenom. At December 31, 2002, the Company valued its investment in Sequenom at its fair value as quoted on the NASDAQ national market, less a 10% discount for restrictions on the sale of Sequenom stock. In 2003, the Company sold all 109,167 shares of Sequenom stock for net proceeds of $405,000 and recognized a gain of $192,000.

(4) AVAILABLE-FOR-SALE SECURITITES

The following table summarizes the various investment categories for available-for-sale securities at December 31, 2004, and 2003:

December 31, 2004	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Federal agency notes	$ 40,741,844	$ —	$ (134,281)	$ 40,607,563
Corporate debt securities	14,050,203	2,635	(32,691)	14,020,147
Mortgage-backed securities	—	—	—	—
Total available-for-sale securities	$ 54,792,047	$ 2,635	$ (166,972)	$ 54,627,710

December 31, 2003	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Federal agency notes	$ 42,585,765	$ 112,383	$ (3,803)	$ 42,694,345
Corporate debt securities	35,251,013	239,594	(1,058)	35,489,549
Mortgage-backed securities	15,181,690	179,443	—	15,361,133
Total available-for-sale securities	$ 93,018,468	$ 531,420	$ (4,861)	$ 93,545,027

The amortized cost and estimated fair value of available-for-sale securities by contractual maturity at December 31, 2004, are shown below:

	Amortized Cost	Estimated Fair Value
Due in one year or less	$ 51,292,047	$ 51,125,075
Due after one year through four years	3,500,000	3,502,635
Total	$ 54,792,047	$ 54,627,710

In 2004, proceeds from the sale of available-for sale securities totaled $132.3 million; gross realized gains totaled $404,000 and gross realized losses totaled $321,000. In 2003, proceeds from the sales of available-for-sale securities totaled $200.5 million; gross realized gains totaled $2.1 million and gross realized losses totaled $437,000. In 2002, proceeds from the sales of available-for-sale securities totaled $135.5 million; gross realized gains totaled $592,000 and gross realized losses totaled $166,000.

(5) PROPERTY AND EQUIPMENT

Property and equipment consisted of the following:

	December 31, 2004	December 31, 2003
Laboratory and computer equipment	$ 23,297,791	$ 20,872,029
Furniture, fixtures and office equipment	1,357,518	1,241,384
Land, building and capital improvements	41,950,993	40,716,085
Leasehold improvements	5,217,791	4,631,013
	71,824,093	67,460,511
Less accumulated depreciation and amortization	(18,829,884)	(11,731,039)
Net property and equipment	$ 52,994,209	$ 55,729,472

Depreciation expense was approximately $7.1 million, $5.6 million and $3.5 million for the years ended December 31, 2004, 2003 and 2002, respectively.

(6) COMMITMENTS

Leases

In 1997, the Company leased its facility located at 6166 Nancy Ridge Drive in San Diego, California under an operating lease that had an expiration date in 2004. The Company had an option to buy the facility during the first 12 months of the lease term for approximately $2.1 million. In 1998, the Company assigned the option to a publicly traded Real Estate Investment Trust ("REIT") in exchange for approximately $733,000 in cash. The $733,000 is being recognized on a straight-line basis as a reduction in the rent expense on the underlying lease. In addition, the Company signed a new lease with the REIT, which expires in 2013. The lease provides the Company with an option to extend the lease term via two five-year options. Under the terms of the new lease, effective April 1998, monthly rental payments will be increased in April 2000 and annually thereafter by 2.75%. The Company recognizes rent expense on a straight line basis of the term of the lease. In accordance with the terms of the new lease, the Company is required to maintain restricted cash balances totaling approximately $80,000 on behalf of the landlord as rent deposits throughout the term of the lease.

In March 2002, the Company leased an additional facility located at 6124-6126 Nancy Ridge Drive in San Diego, California, consisting of approximately 31,000 square feet of office and laboratory space. Under the terms of the lease, effective April 2003, monthly rental payments increased by 2% and are subject to a 2% increase annually thereafter. At the end of the lease in March 2012, the lease provides the Company with an option to buy the entire building, comprised of approximately 58,000 square feet, for $7.9 million. The Company subleases approximately 6,000 square feet, primarily office space, of the 6126 facility to ChemNavigator on a month-to-month basis. Sublease payments from ChemNavigator were subject to a 2% increase in April 2003 and annually thereafter. In 2004, the Company received approximately $100,000 for the sublease.

On December 30, 2003, the Company completed a sale and leaseback of its facility at 6138-6150 Nancy Ridge Drive. The sales price for this facility was $13.0 million and net proceeds to the Company were $12.6 million. The Company has accounted for this transaction in accordance with SFAS 98 "Accounting for Leases" and SFAS 66 "Accounting for Sales of Real Estate." The Company's ability to repurchase this facility at a future date is considered continued involvement under SFAS 98 and therefore the Company has applied the financing method under SFAS 66. Under the financing method, the book value of the facility and related accumulated deprecation remain on the Company's balance sheet and no sale is recognized. Instead, the sales price of the facility is recorded as a financing obligation and all lease payments are being expensed to interest expense. The term of the lease, which became effective December 2003, is 15 years. Under the terms of the lease, monthly rental payments will be increased in January 2005 and annually thereafter by 2.5%. For the years ended December 31, 2004 and 2003, the Company recorded interest expense of $1.6 million and $4,000, respectively, related to this lease. In accordance with the terms of the lease, the Company is required to maintain restricted cash balances totaling approximately $663,000, included in other non-current assets, on behalf of the landlord as rent deposits throughout the term of the lease. The Company has the right to repurchase the facility through year 14 of the lease.

The Company recognizes rent expense on a straight line basis over the term of a lease. Rent expense was $953,000, $953,000 and $869,000 for the years ended December 31, 2004, 2003 and 2002, respectively.

Annual future obligations as of December 31, 2004, are as follows:

Year ending December 31,	Financing Obligation	Operating Leases
2005	1,359,902	976,887
2006	1,393,899	1,001,142
2007	1,428,747	1,026,005
2008	1,464,465	1,051,503
2009	1,501,077	1,077,649
Thereafter	15,316,061	3,350,754
Total minimum lease payments	$ 22,464,151	$ 8,483,940

(7) COLLABORATIONS

Ortho-McNeil Pharmaceutical, Inc.

In December 2004, the Company entered into a collaboration and license agreement with Ortho-McNeil to further develop compounds for the potential treatment of type 2 diabetes and other disorders which included a non-refundable upfront fee of $17.5 million. The Company's two lead compounds are in preclinical development with Ortho-McNeil. In addition, under the agreement, Ortho-McNeil will pay the Company $2.4 million a year for collaboration research through December 19, 2006. Ortho-McNeil has the option to extend the two-year collaboration for one additional year and, therefore, the Company is amortizing the $17.5 million upfront fee over three years. In December 2004, the Company achieved two milestones under the collaboration of $2.5 million each, which the Company is recognizing as revenues over three years as achievability was reasonably assured at the time the Company entered into the collaboration. Under the agreement, the Company will have no further performance obligations beyond December 19, 2006, or, if the collaboration is extended, December 19, 2007. At December 31, 2004, the Company had an accounts receivable balance of $22.6 million for the upfront fee, the milestone achievements and for research funding and received payment in January 2005. The Company is eligible to receive up to $295.0 million in milestone payments for each compound, as well as royalty payments associated with Ortho-McNeil's commercialization of any drugs discovered under the agreement. The milestone payments include development and approval milestone payments of up to $132.5 million for the first indication and $62.5 million for the second indication for each compound, and up to $100.0 million in sales milestone payments for each product resulting from the collaboration.

The 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. The Company 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 the Company the balance of its research funding obligation in a lump sum, unless the termination is due to the Company's change of control (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 the Company. 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 the Company.

For the year ended December 31, 2004, the Company recognized revenues under the Ortho-McNeil agreement of approximately $319,000, which included approximately $192,000 from the amortization of the upfront payment, research funding of approximately $77,000, and approximately $50,000 in amortization from the two milestones achieved. At December 31, 2004, deferred revenues under the Ortho-McNeil collaboration totaled approximately $22.3 million.

Merck & Co., Inc.

In October 2002, the Company entered into a research and licensing agreement with Merck to collaborate on three GPCRs to develop therapeutics for atherosclerosis and related disorders. The Company believes one or more of these GPCRs plays a role in regulating plasma lipid profiles, including HDL cholesterol, the so-called "good cholesterol," and is responsible for the HDL-raising activity of niacin. In October 2004, Merck extended and expanded the collaboration and selected one compound for preclinical development. From the inception of the collaboration through December 31, 2004, the Company has received $19.5 million from Merck, which was comprised of a nonrefundable upfront fee of $4.0 million, milestone payments of $8.0 million, and an equity investment of $7.5 million. The Company may receive additional milestone payments of up to $34.0 million for Merck's clinical and marketing achievements, as well as royalty payments associated with Merck's commercialization of any drugs discovered under the agreement. There is no guarantee the Company will receive any further milestone payments or royalty payments under the agreement. In addition, the Company has received research funding from Merck since the inception of the collaboration, and, under the Company's agreement with Merck, Merck will pay the Company $5.7 million a year for collaboration research through October 19, 2007.

The term of the 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 the Company agree that Technical Grounds have occurred; or (ii) in the event of a change in control of Arena (as defined in the agreement), by giving 30 days prior notice. Technical Grounds include circumstances where: (1) the joint research committee (a committee of an equal number of Merck and Company 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 the Company's 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 the Company materially breaches its 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 the Company does not commence and diligently continue good faith efforts to cure such default during such period.

As part of the extension and expansion of the collaboration with Merck in October 2004, Merck purchased $7.5 million of the Company's stock at a 70% premium to the then current market price. The Company performed an evaluation on the Merck stock purchase and determined that $3.9 million of the $7.5 million purchase was an upfront payment related to the collaboration extension and expansion. Accordingly, the Company will recognize the $3.9 million upfront payment as well as the remaining unamortized upfront payment balance of $1.3 million at October 2004 over the extended collaboration term of three years. In addition, in October 2004, the Company achieved a $1.0 million milestone under the collaboration which the Company is recognizing over the extended collaboration term of three years as achievability was reasonably assured at the time the Company extended and expanded its collaboration with Merck.

For the year ended December 31, 2004, the Company recognized revenues under the Merck agreement of approximately $13.0 million, which included $7.1 million in milestones, research funding of approximately $4.5 million and approximately $1.4 million from the amortization of the original and extension and expansion upfront payments. For the year ended December 31, 2003, the Company recognized revenues under the Merck agreement of approximately $7.9 million, which included research funding of approximately $6.6 million and approximately $1.3 million from the amortization of the upfront payment. For the year ended December 31, 2002, the Company recognized revenues under the Merck agreement of approximately $1.6 million, which included research funding of approximately $1.4 million and approximately $200,000 from the amortization of the upfront payment. At December 31, 2004, deferred revenues under the Merck agreement totaled approximately $7.3 million.

Eli Lilly and Company

In April 2000, the Company entered into a research and licensing agreement with Eli Lilly focused on GPCRs in the central nervous system, or CNS. The Company received an upfront payment of $500,000, which the Company was amortizing ratably over five years. The Company received research funding from Eli Lilly for its internal resources committed to the collaboration, which had been augmented by substantial resources at Eli Lilly.

The Company's research activities under this collaboration were completed on April 14, 2003. Accordingly the Company has not received research funding from Eli Lilly under this collaboration since such date. Upon receiving notice from Eli Lilly that the Company's research activities were scheduled to be completed under the collaboration, the Company amortized the remaining upfront payment over the remaining period the Company performed services. The Company will, however, be eligible to receive additional preclinical milestones of $750,000 per receptor based upon Eli Lilly's sanction of drug discoveries based on internal milestones which Eli Lilly has an obligation to apply reasonable commercial efforts to obtain, clinical milestones totaling $6.0 million based upon clinical development for each drug candidate discovered, and marketing milestone payments of up to $6.0 million for each drug that is marketed for a disease not already covered by another drug marketed under the collaboration, and royalties on sales of products discovered by Eli Lilly as a result of this collaboration, if any. There is no guarantee the Company will receive any royalty payments or further milestone payments under this agreement.

For the year ended December 31, 2004, the Company did not recognize any revenues under the Eli Lilly collaboration. For the year ended December 31, 2003, the Company recognized revenues under the Eli Lilly collaboration of approximately $3.1 million, consisting of research funding of $1.7 million, milestone achievements of $1.3 million, and approximately $100,000 from amortization of the upfront payment. For the year ended December 31, 2002, the Company recognized revenues under the Eli Lilly collaboration of approximately $14.2 million, consisting of research funding of $6.0 million, milestone achievements of $8.0 million, and approximately $200,000 from amortization of the upfront payment.

TaiGen Biotechnology Co., Ltd.

In July 2001, the Company entered into a license agreement with TaiGen Biotechnology Co., Ltd., a biopharmaceutical organization ("TaiGen") focused on the discovery and development of innovative therapeutics, particularly in the fields of oncology and immunology. Under the agreement, as amended, in exchange for a license to the Company's technologies, including TaiGen's right to select and obtain four GPCRs from the Company, the Company received $3.3 million in equity in TaiGen's Series A Preferred financing. The Company recorded the $3.3 million in equity as deferred revenues to be recognized as revenues upon the transfer of activated receptors. The $3.3 million valuation was based on independent investors purchasing for cash, shares of TaiGen's Series A preferred stock. For each GPCR that TaiGen selects, the Company will have an obligation to work diligently to transfer a screening assay to TaiGen for the selected receptor. TaiGen, in turn, will develop or license to third parties compounds for each receptor the Company transfers. The Company may also receive royalty payments based on TaiGen's licensing revenues and drug sales for products, if any, they develop using the receptors the Company provides them. The Company may receive additional equity of approximately $3.3 million in 2005 in exchange for TaiGen receiving the right to obtain five additional GPCRs. If TaiGen or its licensees are not successful in developing drugs at a particular receptor, the Company will have the right to such receptor and any compounds identified using the Company's assays. In such event, the Company may have an obligation to pay royalties to TaiGen. There is no guarantee that the Company will achieve any further milestones or receive further royalty payments under this agreement.

The Company accounts for its ownership interest in TaiGen using the equity method of accounting because of the level of the Company's ownership and the Company's President and CEO, Jack Lief, is a member of TaiGen's board of directors. This is a method of accounting for an investment that requires increasing or decreasing the value of the Company's investment on its balance sheet based on its proportionate share of TaiGen's earnings or losses. The Company shared in TaiGen's losses and thereby increased its net loss for the year ended December 31, 2004, 2003, and 2002 by approximately $936,000, $1.1 million and $1.0 million, respectively. The Company's investment in TaiGen was valued at $936,000 at December 31, 2003. At December 31, 2004, the Company's investment in TaiGen was valued at zero and, therefore, will not share in any additional losses TaiGen incurs until the Company receives additional equity from TaiGen. The Company is not under an obligation to reimburse other TaiGen stockholders for its share of TaiGen's losses.

This agreement is effective until the expiration of TaiGen's obligation to make royalty payments under the agreement, if any. Additionally, either party may terminate this agreement if the other party fails to cure a material breach of the agreement within two months of receiving notice of such breach, becomes insolvent or commences bankruptcy proceedings, or dissolves or liquidates.

For the year ended December 31, 2004, the Company did not recognize any revenues under the TaiGen agreement. For the year ended December 31, 2003, the Company recognized related party royalty revenues under the TaiGen agreement of $100,000. For the year ended December 31, 2002, the Company recognized non-cash related party revenues under the TaiGen agreement of $1.4 million for the transfer of GPCR assays to TaiGen. At December 31, 2004, deferred revenues under the TaiGen agreement totaled $478,000.

(8) STOCKHOLDERS' EQUITY

Preferred Stock

In October 2002, and in conjunction with the stockholders rights plan (see "Stockholders' Rights Plan" below in this note), the Company's board of directors created a series of preferred stock, consisting of 350,000 shares, par value $.0001 per share, designated as Series A Junior Participating Preferred Stock (the "Series A Preferred Stock"). Such number of shares may be increased or decreased by the board of directors, provided that no decrease shall reduce the number of shares of Series A Preferred Stock to a number less than the number of shares then outstanding, plus the number of shares reserved for issuance upon the exercise of outstanding options, rights or warrants or upon the conversion of any outstanding securities issued by the Company convertible into Series A Preferred Stock. As of December 31, 2004, no shares of Series A Preferred Stock were issued or outstanding.

Treasury Stock

In October 2003, Biotechnology Value Fund, L.P. and certain of its affiliates accepted the Company's offer to purchase from them 3.0 million shares of the Company's common stock at a cash price per share of $7.69. The Company made the offer on October 7, 2003, pursuant to the Stockholders Agreement dated as of January 17, 2003, with the Company and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., BVF Investments, L.L.C., BVF Partners L.P., BVF Inc. and Investment 10, L.L.C. The Company paid $23.1 million for this purchase.

Equity Compensation Plans

Since inception through December 31, 2004, the Company has authorized an aggregate of 6.25 million shares of common stock for issuance under the Amended and Restated 1998 Equity Compensation Plan, the Amended and Restated 2000 Equity Compensation Plan and the 2002 Equity Compensation Plan (collectively the "Option Plans"). The Option Plans provide designated employees of the Company, certain consultants and advisors who perform services for the Company, and non-employee members of the Company's board of directors with the opportunity to receive grants of incentive stock options, nonqualified stock options and restricted stock. The options generally vest 25% a year for four years and are immediately exercisable up to 10 years from the date of grant. The restricted stock generally vest over a two or four-year period and the recipient, at the date of grant, has all rights of a stockholder, subject to certain restrictions on transferability and a risk of forfeiture.

Unvested shares issued to the Company's employees, consultants, advisors and non-employee members of the Company's board of directors pursuant to the exercise of options are subject to repurchase, at the original purchase price, in the event of termination of employment or engagement. In the event the Company elects not to buy back any such unvested shares, the unvested options will be expensed at their fair value at that point in time. In accordance with SFAS 128, the Company has excluded unvested common stock arising from exercised options in its net basic loss per share calculations.

The following tables summarize the Company's stock option activity and related information for the years ended December 31:

	2004		2003		2002	
	Options	Weighted- Average Exercise Price	Options	Weighted- Average Exercise Price	Options	Weighted- Average Exercise Price
Outstanding at January 1,	1,945,468	$ 11.20	2,505,775	$ 13.95	1,730,200	$ 16.21
Granted	1,400,100	5.80	311,875	9.24	1,136,075	10.91
Exercised	(63,700)	0.59	(37,226)	1.47	(89,375)	0.60
Cancelled	(501,469)	11.52	(834,956)	19.16	(271,125)	20.07
Outstanding at December 31,	2,780,399	$ 8.66	1,945,468	$ 11.20	2,505,775	$ 13.95

Pursuant to stock option agreements between the Company and its employees, its employees are all entitled to exercise their options prior to vesting. The following table summarizes information concerning outstanding and exercisable options as of December 31, 2004.

	Options Outstanding			Options Exercisable	
Range of Exercise Price	Number Outstanding at December 31, 2004	Weighted- Average Remaining Contractual Life	Weighted- Average Exercise Price	Number Exercisable at December 31, 2004	Weighted - Average Exercise Price
$0.20 — $5.86	451,758	7.5 Years	$ 2.93	451,758	$ 2.93
$5.87 — $6.00	869,888	9.1 Years	6.00	869,888	6.00
$6.30 — $10.46	568,100	8.1 Years	8.52	568,100	8.52
$10.47 — $12.25	580,202	7.3 Years	11.62	580,202	11.62
$13.60 — $31.34	310,451	6.2 Years	19.18	310,451	19.18
$0.20 — $31.34	2,780,399	7.9 Years	$ 8.66	2,780,399	$ 8.66

At December 31, 2003 and 2002, 54,249 and 184,123 shares of common stock issued upon the exercise of options were subject to repurchase at the original purchase price at a weighted-average price of $.61 and $.60 per share, respectively. No shares of common stock issued upon the exercise of options were subject to repurchase at December 31, 2004. At December 31, 2004, 2003 and 2002, 1,547,383, 2,374,431 and 2,594,975 shares, respectively, were available for future grant. The 2,780,399 options not exercised at December 31, 2004, can be exercised at any time; however, unvested shares are subject to repurchase at the original purchase price if a grantee terminates employment prior to vesting.

Employee Stock Purchase Plan

The 2001 Arena Employee Stock Purchase Plan (the "Purchase Plan") was adopted by the Company's board of directors in March 2001. The Purchase Plan qualifies under Section 423 of the Internal Revenue Service and permits substantially all employees to purchase shares of common stock of the Company. Under the Purchase Plan, employees can choose to have up to 15 percent of their annual compensation withheld to purchase shares of common stock. The purchase price of the common stock is at 85 percent of the lower of the fair market value of the common stock at the enrollment date or the purchase date. The aggregate number of shares of the Company's common stock that may be issued pursuant to the Purchase Plan is 1,000,000. As of December 31, 2004, 309,732 shares have been issued pursuant to the Purchase Plan.

Common Shares Reserved for Future Issuance

The following shares of Common Stock are reserved for future issuance at December 31, 2004:

Stock option plans	4,327,782
Deferred compensation plan	151,699
Warrants	1,936,200
Series B-1 redeemable convertible preferred stock	4,861,899
Series B-2 redeemable convertible preferred stock	1,642,857
Payment of dividends	2,671,883
Employee stock purchase plan	690,268
Total	16,282,588

Stockholders' Rights Plan

In October 2002, the Company's board of directors adopted a stockholders' rights plan (the "Rights Agreement") under which all stockholders of record as of November 13, 2002, received rights to purchase shares of the Series A Preferred Stock (the "Rights"). Each Right entitles the registered holder to purchase from the Company one one-hundredth of a share of the Series A Preferred Stock at an initial exercise price of $36, subject to adjustment. The Rights are not exercisable until the tenth day after such time as a person or group acquires beneficial ownership of 10% or more, or announces a tender offer for 10% or more, of the Company's common stock. At such time, all holders of the Rights, other than the acquiror, will be entitled to purchase shares of the Company's common stock at a 50% discount from the then current market price.

The Rights will trade with the Company's common stock, unless and until they are separated due to a person or group acquiring beneficial ownership of 10% or more, or announcing a tender offer for 10% or more, of the Company's common stock. The Company's board of directors may terminate the Rights Agreement at any time or redeem the Rights prior to the time a person acquires 10% or more of the common stock.

(9) REDEEMABLE CONVERTIBLE PREFERRED STOCK AND WARRANTS

In December 2003, the Company sold 3,500 shares of Series B-1 redeemable convertible preferred stock ("Series B-1 Preferred") together with (i) seven-year warrants to purchase up to 1,486,200 shares of common stock at an exercise price of $10.00 per share; and (ii) unit warrants giving such investors the right to purchase from the Company for a period of approximately 16 months from December 24, 2003, at their option, up to $11.5 million of Series B-2 redeemable convertible preferred stock ("Series B-2 Preferred") and additional seven-year warrants to purchase up to 450,000 shares of common stock at an exercise price of $10.00 per share, to two institutional investors for an aggregate purchase price of $35.0 million. The Company received approximately $34.2 million in net cash proceeds after closing costs.

At December 31, 2004, the Series B-1 Preferred is convertible into 4,861,899 shares common stock of the Company at a fixed conversion price of $7.50 per share. If not previously converted, the Company must redeem the Series B-1 Preferred in five years or earlier under certain circumstances at the original amount invested, plus all accrued but unpaid dividends. Any such redemption may be made by the Company in cash or, if certain conditions have been met, in shares of common stock. Dividends on the Series B-1 Preferred are payable at a rate of 4% per annum, payable quarterly, commencing on March 31, 2004, by issuing common stock or by increasing the amount of common stock that is issuable upon conversion of the Series B-1 Preferred.

If issued, the Series B-2 Preferred would be convertible into common stock at a fixed conversion price, calculated as 110% of the market price of the common stock at the time of issuance of the Series B-2 Preferred, but not less than $7.00 per share or greater than $10.00 per share.

Each investor agrees that for so long as it holds Series B-1 Preferred and Series B-2 Preferred, it shall vote its shares of Series B-1 Preferred and Series B-2 Preferred and 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 the Company's board of directors to all of its stockholders unless the Company's board of directors elects to permit the investors to vote such shares in their own discretion.

f the Company issues common stock or common stock equivalents (excluding, among other things, certain common stock and ·ommon stock equivalents issued or issuable (a) to the Company's officers, directors, employees, or consultants, (b) in connection vith certain strategic partnerships or joint ventures, and in connection with certain mergers and acquisitions) for an effective net price ıer share of less than $6.72, in the case of the Series B-1 Preferred, or a price to be determined based on a formula, in the case of the ;eries B-2 Preferred, the holders of the Series B Preferred may require the Company to redeem their shares and the exercise price and ıumber of outstanding seven-year warrants are subject to weighted-average adjustment in certain circumstances. Any warrants issued ıpon exercise of our unit warrants will have similar anti-dilution protections for future issuances.

f a change of control occurs before the two-year anniversary of the original issue date of the Series B Preferred, the Company can epurchase the Series B Preferred at a price equal to the greater of 125% of the stated value or the market value of such shares of ;eries B Preferred plus all accrued but unpaid dividends thereon to the date of payment. If such change of control occurs following the wo-year anniversary of the original issue date of the Series B Preferred, the Company can repurchase the Series B Preferred at a price ·qual to the greater of 115% of the stated value or the market value of such shares of Series B Preferred plus all accrued but unpaid lividends thereon to the date of payment. The Company can elect to pay such redemption price in shares of common stock.

The Company received net cash proceeds from the Series B-1 Preferred of $34.2 million. In addition, the Company issued 45,000 :hares of common stock as a finder's fee valued at $302,000 based on the fair value of the common stock at the date of the closing of he Series B-1 Redeemable Convertible Preferred Stock.

The Company valued the components of the Series B-1 Preferred Stock as follows:

Series B-1 redeemable convertible preferred stock.....	$	25,740,588
Warrants.....		4,534,693
Deemed dividend		2,800,000
Unit warrants.....		1,924,719
Total.....	$	35,000,000

n accordance with EITF 00-27, "Application of Issue No. 98-5 for Certain Convertible Instruments," the Company allocated the ·omponents of the sale of the Series B-1 Preferred between the Series B-1 Preferred, the warrants and the unit warrants on the basis of he relative fair values at the date of issuance using the Black-Scholes model. The aggregate amount allocated to the warrants and unit varrants was $6.5 million. The fair value of the common shares into which the Series B-1 Preferred was convertible into on the date ›f issuance exceeded the proceeds allocated to the Series B-1 Preferred by $2.8 million, resulting in a beneficial conversion feature hat was recognized as an increase to paid-in capital and as a deemed dividend to the Series B-1 Preferred. The Company will record ımortization of the value of the discount, warrants, unit warrants and deemed dividend of $1.9 million for each of the years ending)ecember 31, 2005, 2006 and 2007 and $1.8 million for the year ending December 31, 2008. The Company recorded accretion of the liscount and deemed dividend of $1.9 million and $36,000 in 2004 and 2003, respectively.

(10) EMPLOYEE BENEFIT PLAN

The Company has a defined contribution retirement plan that complies with Section 401(k) of the Internal Revenue Code. All :mployees of the Company are eligible to participate in the plan. The Company matches 100% of each participant's voluntary :ontributions, subject to a maximum Company contribution of 6% of the participant's compensation. The Company's matching ›ortion, which totaled $876,000, $815,000 and $796,000 for the years ended December 31, 2004, 2003, and 2002 respectively, vests ›ver a five-year period.

(11) INCOME TAXES

Significant components of the Company's deferred tax assets at December 31, 2004, and 2003 are shown below. A valuation allowance of $70.3 million and $43.3 million has been recognized to offset the deferred tax assets as of December 31, 2004, and 2003, respectively, as realization of such assets is uncertain.

	December 31,	
	2004	2003
Deferred tax assets:		
Net operating loss carryforwards	$ 37,422,000	$ 25,824,000
Research and development credits	16,488,000	11,553,000
Capitalized R&D (state)	3,150,000	3,417,000
Deferred revenues	11,978,000	1,582,000
Other, net	1,743,000	1,540,000
Net deferred tax assets	70,781,000	43,916,000
Valuation allowance for deferred tax assets	(70,265,000)	(43,324,000)
Total deferred tax assets	516,000	592,000
Deferred tax liabilities:		
Depreciation	(516,000)	(592,000)
Net deferred tax assets	$ —	$ —

The Company's effective tax rate differed from the federal statutory rate due to the Company establishing a reserve against deferred tax assets, primarily net operating losses and tax credits, in the current year.

At December 31, 2004, the Company had federal and state tax net operating loss carryforwards of approximately $101.6 million and $49.3 million, respectively. The federal and California tax net operating loss carryforwards will begin to expire in 2012 and 2005, respectively, unless previously utilized. The Company also has federal and California research tax credit carryforwards of approximately $11.2 million and $8.1 million respectively, which will begin to expire in 2012 unless previously utilized.

Pursuant to Sections 382 and 383 of the Internal Revenue Code, annual use of the Company's net operating loss and credit carryforwards could be limited in the event of cumulative changes in ownership of more than 50%. Such a change occurred in prior years. However, the Company does not believe such limitation will have a material effect upon the Company's ability to utilize the carryforwards.

(12) SUBSEQUENT EVENT

In February 2005, the Company completed a public offering by selling 8,625,000 shares of its common stock at $6.00 per share and received net proceeds of approximately $48.3 million.

As a result of the Company's public offering in February 2005, the holders of the Series B-1 Preferred are entitled to require the Company to redeem all or some of their shares of the Series B-1 Preferred, 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 payment and any applicable penalties. The aggregate redemption price of the Company's Series B-1 Preferred at December 31, 2004, was approximately $36.5 million, and accrues interest at 4.0% annually. The Company may be able to satisfy a portion of any redemption with shares of its common stock. Due to the Series B-1 Preferred being currently redeemable, the Company will record a charge of $7.4 million to accretion of discount and deemed dividend on redeemable convertible preferred stock in the first quarter of 2005. Any redemption amount settled in equity would be computed as the lesser of the applicable conversion price of $7.50 and 95% of the arithmetic average of the volume weighted average prices of common stock for the ten consecutive trading days prior to the date of delivery of such applicable Series B-1 Preferred redemption notice.

The Company's public offering completed in February 2005 triggered an anti-dilution clause requiring the Company to issue an additional 41,117 warrants with an exercise price of $9.73 per share to the warrant holders and reduced the exercise price of the existing 1,486,200 outstanding warrants from $10.00 per share to $9.73 per share.

13) QUARTERLY FINANCIAL DATA (UNAUDITED)

2004 for quarter ended	Dec. 31	Sept. 30	June 30	March 31	Year
Revenues	$ 2,120,822	$ 4,383,332	$ 1,398,334	$ 5,783,334	$ 13,685,822
Net loss	(17,364,434)	(12,799,380)	(16,138,364)	(11,689,592)	(57,991,770)
Net loss allocable to common stockholders	(18,193,177)	(13,624,454)	(16,955,929)	(12,507,477)	(61,281,037)
Basic and diluted loss per share	$ (0.70)	$ (0.54)	$ (0.67)	$ (0.49)	$ (2.40)

2003 for quarter ended	Dec. 31	Sept. 30	June 30	March 31	Year
Revenues	$ 1,616,394	$ 2,868,675	$ 2,973,770	$ 5,375,440	$ 12,834,279
Net loss	(14,610,054)	(11,875,635)	(11,762,315)	(8,811,435)	(47,059,439)
Net loss allocable to common stockholders	(14,672,428)	(11,875,635)	(11,762,315)	(8,811,435)	(47,121,813)
Basic and diluted loss per share	$ (0.58)	$ (0.43)	$ (0.42)	$ (0.32)	$ (1.74)

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended (the Exchange Act). Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this annual report.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of our management, including our CEO and VP, Finance and Chief Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in *Internal Control — Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2004.

Our management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004, has been audited by Ernst &Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Changes in Internal Control Over Financial Reporting

There was no change in our internal controls over financial reporting during the fourth quarter of the period covered by this Annual report that has materially affected, or is reasonably likely to materially affect, our internal controls over financial reporting.

Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting

The Board of Directors and Stockholders of Arena Pharmaceuticals, Inc.

We have audited management's assessment included in the accompanying Management's Report of Internal Control Over Financial Reporting, that Arena Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Arena Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that Arena Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Arena Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Arena Pharmaceuticals, Inc. as of December 31, 2004 and 2003, and the related consolidated statements of income, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2004 of Arena Pharmaceuticals, Inc. and our report dated February 25, 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California
February 25, 2005

'ART III

tem 10. Directors and Executive Officers of the Registrant.

:ode of Ethics

Ve have adopted a Code of Business Conduct and Ethics that applies to our directors and employees (including our principal :xecutive officer, principal financial officer, principal accounting officer and controller), and have posted the text of the policy on our vebsite (www.arenapharm.com) in connection with "Investor" materials. In addition, we intend to promptly disclose (i) the nature of :ny amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or :ontroller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of he policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the vaiver on our website in the future.

The other information required by this item is incorporated herein by reference from the information under the caption "Election of Directors" and the caption "Compensation And Other Information Concerning Officers, Directors And Certain Stockholders" and the :aption "Section 16(a) Beneficial Ownership Reporting Compliance" contained in our proxy statement for our fiscal year ended December 31, 2004 (the "Proxy Statement").

tem 11. Executive Compensation.

The information required by this item is incorporated herein by reference from the information under the caption "Compensation And Other Information Concerning Officers, Directors And Certain Stockholders" under the caption "Compensation Committee Interlocks :nd Insider Participation" contained in the Proxy Statement.

tem 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder matters.

Information relating to securities authorized for issuance under our equity compensation plans is set forth in "Item 5. Market for the Registrant's Common Equity and Related Stockholder Matters" above in this Annual Report. The other information required by this item is incorporated herein by reference from the information under the caption "Security Ownership Of Certain Beneficial Owners And Management" contained in the Proxy Statement.

Item 13. Certain Relationships and Related Transactions.

The information required by this item is incorporated herein by reference from the information under the caption "Certain Relationships and Related Transactions" contained in the Proxy Statement.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated herein by reference from the information under the caption "Audit Committee Report" contained in the Proxy Statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) 1. **FINANCIAL STATEMENTS.**

Reference is made to the Index to Financial Statements under Item 8, Part II hereof.

2. **FINANCIAL STATEMENT SCHEDULES.**

The Financial Statement Schedules have been omitted either because they are not required or because the information has been included in the financial statements or the notes thereto included in this Annual Report on Form 10-K.

3. **EXHIBITS**

EXHIBIT NO.	DESCRIPTION
3.1	Fifth Amended and Restated Certificate of Incorporation of Arena Pharmaceuticals, Inc. (incorporated by reference to Exhibit 3.1 to Arena'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 Arena (incorporated by reference to Exhibit 3.2 to Arena's 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 Series A Junior Participating Preferred Stock of Arena, dated November 4, 2002 (incorporated by reference to Exhibit 3.3 to Arena's quarterly report on Form 10-Q for the period ended September 30, 2002, filed with the Securities and Exchange Commission on September 30, 2002, Commission File No. 000-31161)
3.4	Certificate of Designations of the Series B Convertible Preferred Stock of Arena, dated December 24, 2003 (incorporated by reference to Exhibit 3.1 to Arena's 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 Arena and Computershare Trust Company, Inc. (incorporated by reference to Exhibit 4.1 to Arena's 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 Arena and Computershare Trust Company, Inc. (incorporated by reference to Exhibit 4.1 to Arena's 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161)
4.3	Form of common stock certificates (incorporated by reference to Exhibit 4.2 to Arena'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)
10.1	1998 Equity Compensation Plan (incorporated by reference to Exhibit 10.1 to Arena's registration statement on Form S-1, as amended, filed with the Securities and Exchange Commission on June 22, 2000, Commission File No. 333-3594)
10.2	Amended and Restated 2000 Equity Compensation Plan (incorporated by reference to Exhibit 10.2 to Arena's report on Form 10-K for the year ended December 31, 2001, filed with the Securities and Exchange Commission on March 15, 2002, Commission File No. 000-31161)
10.3	Lease, dated March 1998, by and between ARE 6166 Nancy Ridge, LLC and Arena, as amended by First Amendment to Lease dated as of June 30, 1998 (incorporated by reference to Exhibit 10.6 to Arena's registration statement on Form S-1, as amended, filed with the Securities and Exchange Commission on June 22, 2000, Commission File No. 333-3594)
10.4+	Research Collaboration and License Agreement, effective as of April 14, 2000, by and between Arena and Eli Lilly and Company (incorporated by reference to Exhibit 10.9 to Arena'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)
10.5	2001 Arena Employee Stock Purchase Plan (incorporated by reference to Exhibit B of Arena's Proxy Statement regarding Arena's May 8, 2001, Annual Stockholders Meeting, filed with the Securities and Exchange Commission on March 21, 2001, Commission File No. 000-31161)
10.6	Arena Pharmaceuticals, Inc. 2002 Equity Compensation Plan (incorporated by reference to Exhibit A to Arena's Proxy Statement regarding Arena's June 11, 2002, Annual Stockholders Meeting, filed with the Securities and Exchange Commission on April 23, 2002, Commission File No. 000-31161)
10.7	Stockholders Agreement dated as of January 17, 2003, by and among Arena, Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., BVF Investments, L.L.C., BVF Partners L.P., BVF Inc. and Investment 10, L.L.C. (incorporated by reference to Exhibit 10 to Arena's report on Form 8-K filed with the Securities and Exchange Commission on January 21, 2003, Commission File No. 000-31161)
10.8+	Research Collaboration and License Agreement, dated effective as of October 21, 2002, by and between Arena and Merck & Co., Inc., a New Jersey corporation (incorporated by reference to Exhibit 10.20 to Arena's annual report on Form 10-K for the period ended December 30, 2003, filed with the Securities and Exchange Commission on March 28, 2003)
10.9*	Form of Termination Protection Agreement, dated December 20, 2002, by and among Arena and the employees listed on Schedule 1 thereto (incorporated by reference to Exhibit 10.1 to Arena's quarterly report on Form 10-Q for period ended June 30, 2003, filed with the Securities and Exchange Commission on August 13, 2003)
10.10*	Form of Termination Protection Agreement, dated December 20, 2002, by and among Arena and the employees listed on Schedule 1 thereto (incorporated by reference to Exhibit 10.1 to Arena's quarterly report on Form 10-Q for the June 30, 2003, filed with the Securities and Exchange Commission on August 13, 2003)

10.11	Securities Purchase Agreement for Arena's Series B Convertible Preferred Stock and warrants dated December 24, 2003, among Arena and the investor signatories thereto (incorporated by reference to Exhibit 10.1 to Arena's 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161)
10.12	Registration Rights Agreement dated December 24, 2003, among Arena and the investor signatories thereto (incorporated by reference to Exhibit 10.2 to Arena's 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161)
10.13	Form of Warrant dated December 24, 2003 (incorporated by reference to Exhibit 10.3 to Arena's 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161)
10.14	Form of Unit Warrant dated December 24, 2003 (incorporated by reference to Exhibit 10.4 to Arena's 8-K filed with the Securities and Exchange Commission on December 30, 2003, Commission File No. 000-31161)
10.15	Purchase and Sale Agreement and Joint Escrow Instructions, dated December 22, 2003, between Arena and ARE — Nancy Ridge No. 3, LLC (incorporated by reference to Exhibit 10.1 to Arena's 8-K filed with the Securities and Exchange Commission on January 6, 2004, Commission File No. 000-31161)
10.16	Lease Agreement, dated December 30, 2003, between Arena and ARE — Nancy Ridge No. 3, LLC (incorporated by reference to Exhibit 10.2 to Arena's 8-K filed with the Securities and Exchange Commission on January 6, 2004, Commission File No. 000-31161)
10.17*	Arena's Deferred Compensation Plan, effective November 11, 2003, between Arena and participating executive officers (incorporated by reference to Exhibit 10.29 to Arena's 10-K filed with the Securities and Exchange Commission on March 1, 2004, Commission File No. 000-31161)
10.18	Letter Agreement, dated February 5, 2004, by and between Arena and William R. Shanahan, Jr., M.D., J.D. (incorporated by reference to Exhibit 10.1 to Arena's 10-Q filed with the Securities and Exchange Commission on May 7, 2004, Commission File No. 000-31161)
10.19++	First Amendment to Research Collaboration and License Agreement, dated as of October 20, 2004, by and between Arena and Merck
10.20++	Collaboration and License Agreement, dated as of December 20, 2004, by and between Arena and Ortho-McNeil Pharmaceutical, Inc., a New Jersey corporation
10.21*	Summary of 2005 compensation for non-employee directors (incorporated by reference to the description of such compensation in Arena's 8-K filed with the Securities and Exchange Commission on January 21, 2005, Commission File No. 000-31161)
10.22*	Form of stock option grant for non-employee directors (incorporated by reference to Exhibit 10.1 to Arena's 8-K filed with the Securities and Exchange Commission on January 21, 2005, Commission File No. 000-31161)
21.1	Subsidiaries of the registrant-None
23.1	Consent of Independent Registered Public Accounting Firm
31.1	Section 302 Certification by Arena's chief executive officer
31.2	Section 302 Certification by Arena's principal financial officer
32.1	Section 906 Certification by Arena's chief executive officer and principal financial officer

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+ Confidential treatment has been granted for portions of this document.
++ Confidential treatment has been requested for portions of this document.
* This is an agreement with management.

(c) **EXHIBITS**

See Item 15(a)(3) above.

(d) **FINANCIAL STATEMENT SCHEDULES**

See Item 15(a)(2) above.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on March 1, 2005.

Arena Pharmaceuticals, Inc.,
a Delaware Corporation

By: /s/ Jack Lief
Jack Lief
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated on March 1, 2005.

Signatures		Title
By:	/s/ Jack Lief Jack Lief	President, Chief Executive Officer and Director
By:	/s/ Robert E. Hoffman Robert E. Hoffman, CPA	Vice President, Finance and Chief Accounting Officer (principal financial and accounting officer)
By:	/s/ Dominic P. Behan Dominic P. Behan, Ph.D.	Director
By:	/s/ Donald D. Belcher Donald D. Belcher	Director
By:	/s/ Scott H. Bice Scott H. Bice	Director
By:	/s/ Duke K. Bristow Duke K. Bristow, Ph.D.	Director
By:	/s/ Harry F. Hixson Harry F. Hixson, Ph.D.	Director
By:	/s/ J. Clayburn La Force, Jr. J. Clayburn La Force, Jr., Ph.D.	Director
By:	/s/ Louis J. Lavigne, Jr. Louis J. Lavigne, Jr.	Director
By:	/s/ Tina S. Nova Tina S. Nova, Ph.D.	Director
By:	/s/ Robert L. Toms Robert L. Toms	Director

directory

BOARD OF DIRECTORS

Jack Lief
President and Chief Executive Officer
Arena Pharmaceuticals, Inc.

Dominic P. Behan, Ph.D.
Senior Vice President and
Chief Scientific Officer
Arena Pharmaceuticals, Inc.

Donald D. Belcher
Former Chairman and
Chief Executive Officer
Banta Corporation

Scott H. Bice
Robert C. Packard Professor
University of Southern California
Law School

Duke K. Bristow, Ph.D.
Economist
Anderson Graduate School
of Management at UCLA

Harry F. Hixson, Jr., Ph.D.
Chairman and
Chief Executive Officer
BrainCells, Inc.

J. Clayburn La Force, Jr., Ph.D.
Dean Emeritus
Anderson Graduate School of
Management at UCLA

Louis J. Lavigne, Jr.
Former Executive Vice President
and Chief Financial Officer
Genentech, Inc.

Tina S. Nova, Ph.D.
President and
Chief Executive Officer
Genoptix, Inc.

Robert L. Toms, Sr.
Attorney at Law
Former California State
Commissioner of Corporations

ADVISORY DIRECTOR

Frederick Frank
Vice Chairman and a Director of
Lehman Brothers, Inc.

EXECUTIVE OFFICERS

Jack Lief
President and Chief Executive Officer

K.A. Ajit-Simh
Vice President, Quality Systems

Dominic P. Behan, Ph.D.
Senior Vice President and
Chief Scientific Officer

Robert E. Hoffman, CPA
Vice President, Finance
and Chief Accounting Officer

Louis J. Scotti
Vice President, Marketing
and Business Development

William R. Shanahan, Jr., M.D., J.D.
Vice President and Chief Medical Officer

Steven W. Spector
Senior Vice President,
General Counsel and Secretary

CORPORATE HEADQUARTERS

Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, California 92121
Telephone: 858.453.7200
Facsimile: 858.453.7210

ANNUAL MEETING

The Annual Meeting of Stockholders will be held on Monday, June 13, 2005, at 9:00 a.m. local time, at 6150 Nancy Ridge Drive, San Diego, California 92121. For further information, call 858.453.7200, ext. 1315.

INVESTOR RELATIONS

Stockholders' inquiries should be directed to:
Investor Relations
Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, California 92121
Telephone: 858.453.7200, ext. 1315
Facsimile: 858.677.0065

INFORMATION AVAILABLE

A copy of Arena's annual report to the Securities and Exchange Commission on Form 10-K is available without charge by writing Investor Relations at Arena's corporate headquarters or calling 858.453.7200, ext. 1315.

In addition, Arena's annual report on Form 10-K, other filings with the Securities and Exchange Commission, and press releases, along with general information on Arena's business and technology, are available through Arena's home page on the Internet at the following address: www.arenapharm.com

TRANSFER AGENT AND REGISTRAR

Computershare Investor Services
350 Indiana Street, Suite 800
Golden, Colorado 80401
Telephone: 303.262.0600
Facsimile: 303.262.0604

STOCK LISTING

Arena's common stock trades on The NASDAQ Stock Market® under the symbol ARNA.

INDEPENDENT AUDITORS

Ernst & Young LLP
501 West Broadway, Suite 1100
San Diego, California 92101
Telephone: 619.235.5000
Facsimile: 619.235.5151

TRADEMARKS AND SERVICE MARKS

WHOLLY OWNED SUBSIDIARY

BRL Screening, Inc.

Arena Pharmaceuticals, Inc.
6166 Nancy Ridge Drive
San Diego, CA 92121