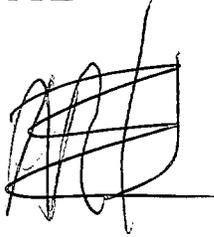


ARIAD



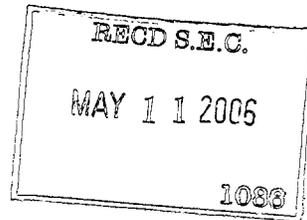
ARIAD  
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## 2005 Annual Report



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[www.ariad.com](http://www.ariad.com)

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

FORM 10-K

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2005  
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 0-21696

**ARIAD Pharmaceuticals, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**22-3106987**  
(I.R.S. Employer Identification No.)

**26 Landsdowne Street, Cambridge, Massachusetts 02139-4234**  
(Address of principal executive offices) (Zip Code)

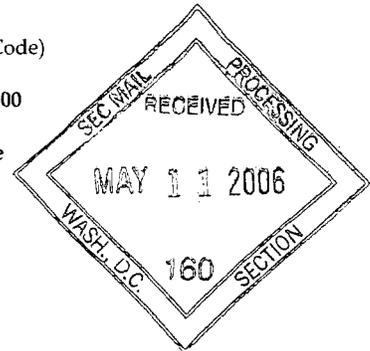
Registrant's telephone number, including area code: (617) 494-0400

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

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

Common Stock, \$.001 Par Value

Rights to Purchase Series A Preferred Stock



Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act.

Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of "accelerated filer" and "large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer  Accelerated filer  Non-accelerated filer

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes  No

The aggregate market value of the registrant's common stock held by nonaffiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate), computed by reference to the price at which the common stock was last sold, as of the last business day of the registrant's most recently completed second fiscal quarter was \$338 million.

As of February 28, 2006, the registrant had 61,840,329 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on June 14, 2006.

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## PART I

### ITEM 1: BUSINESS

The following Business Section contains forward-looking statements, which involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors (see Part I, Item 1A: Risk Factors). Unless the content requires otherwise, references to "ARIAD," "we," "our," and "us," in this Annual Report on Form 10-K refers to ARIAD Pharmaceuticals, Inc. and our subsidiaries.

#### Overview

We are engaged in the discovery and development of breakthrough medicines to treat cancers by regulating cell signaling with small molecules. We are developing a comprehensive approach to patients with cancer that addresses the greatest medical need - aggressive and advanced-stage cancers for which current treatments are inadequate. Our goal is to build a fully integrated oncology company focused on novel, molecularly targeted therapies to treat solid tumors and hematologic cancers, as well as the spread of primary tumors to distant sites.

Human cells - both healthy and malignant - share an elaborate system of molecular pathways that carry signals back and forth from the cell surface to the nucleus and within the cell. Such signaling is essential to cell functioning and viability. When disrupted or over-stimulated, such pathways may trigger diseases such as cancer. For example, growth and proliferation of cancer cells are dependent on signals from external growth factors, as well as signals indicating the availability of sufficient nutrients and blood supply. These signals are conveyed along well-defined pathways, several of which are regulated by a protein called the mammalian target of rapamycin, or mTOR.

Our lead cancer product candidate, AP23573, is an internally discovered, potent mTOR inhibitor. The protein, mTOR, serves as a "master switch" and appears to have a central function in cancer cells. Blocking mTOR creates a starvation-like effect in cancer cells by interfering with cell growth, division, metabolism and angiogenesis.

As part of our global clinical development plan and registration strategy, AP23573 has been studied in multiple Phase 2 and 1b clinical trials in the U.S. and Europe as a single agent in patients with solid tumors, including sarcomas, hormone refractory prostate cancer and endometrial cancer. In addition, three multi-center Phase 1b trials of AP23573 in combination with other anti-cancer therapies are underway, which are focused primarily on patients with various types of solid tumors, especially breast, ovarian, non-small-cell lung, and prostate cancers, as well as sarcomas. Further combination studies are planned. In addition, we have concluded enrollment in Phase 1b and Phase 2 clinical trials in patients with brain cancer and leukemias and lymphomas, respectively. Eleven clinical trials of AP23573 are ongoing or completed. Intravenous and oral formulations of AP23573 have been studied in these trials.

In November 2005, at the AACR-NCI-EORTC International Conference on "Molecular Targets and Cancer Therapeutics," investigators presented preliminary Phase 2 clinical data on AP23573 in advanced sarcoma patients, which showed that 27% (51/188) of patients treated with AP23573 and evaluable for at least four months demonstrated sustained anti-tumor responses. Enrollment in this trial has been completed and, based on these positive data, we expect to start our initial registration trial for AP23573 in patients with sarcomas. The U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMEA, have designated AP23573 as an orphan drug for treatment of soft-tissue and bone sarcomas. The FDA has also designated AP23573 as a fast-track product for the same indications.

In clinical trials to date, AP23573 has been well tolerated at the fixed doses administered, and adverse events were generally mild to moderate in severity and readily reversible. The most common treatment-related adverse events were oral mucositis, rash, fatigue, nausea and lipid abnormalities.

Two clinical trials of AP23573 that have concluded enrollment provide important insights that may be useful in planning follow-up studies. In patients with brain cancer, AP23573 was shown to cross the blood-brain barrier and inhibit brain tumor mTOR activity, while being well tolerated in severely ill patients. In heavily pretreated patients with leukemias and lymphomas, 40% of evaluable patients had AP23573 anti-cancer activity, providing a basis for further studies in selected hematologic malignancies.

The oral dosage form of AP23573 is being studied in a multi-center Phase 1b clinical trial of patients with various solid tumors. Initial results from this trial indicate that the oral dosage form can be administered safely using several daily and intermittent dosing schedules and achieves blood levels over time and mTOR inhibition generally consistent with those observed with intravenous administration.

As an mTOR inhibitor, AP23573 has also been shown to potently block the growth, proliferation and migration of vascular smooth muscle cells, the primary cause of narrowing and blockage of injured vessels. In 2005, we entered into a partnership with Medinol Ltd., one of the leading cardiovascular medical device companies, to develop and commercialize stents and other medical devices to deliver AP23573 to prevent reblockage of injured vessels following stent-assisted angioplasty, a common non-surgical procedure for dilating or opening narrowed arteries.

Inhibition of the mTOR pathway may be useful for additional indications beyond oncology and drug-delivery stents, and we are evaluating such indications as part of the broader clinical development plan for AP23573.

In addition to our lead clinical development program, we have a focused drug discovery program centered on small-molecule, molecularly targeted therapies and cell-signaling pathways implicated in cancer. Currently, our preclinical pipeline includes: inhibitors of mutant oncogenic or cancer-causing proteins (kinases) that regulate cell signaling (*e.g.*, Bcr-Abl – the target of imatinib, which becomes resistant to further treatment through various mutations, including one called T315I); single compounds that target multiple cancer pathways (*e.g.*, cell survival, metastases and angiogenesis); and new mTOR inhibitors (*i.e.*, bone-targeted compounds to treat primary bone cancers and cancers that have spread to bone).

We have an exclusive license to pioneering technology and patents related to methods of treating human disease through regulation of the cell-signaling activity of a protein called NF- $\kappa$ B, and the discovery, development and use of drugs to regulate NF- $\kappa$ B cell-signaling activity. NF- $\kappa$ B can be generally thought of as a “biological switch” that can be turned off using these treatment methods to treat disorders such as inflammation, cancer, sepsis and osteoporosis. We permit broad use of our NF- $\kappa$ B intellectual property, at no cost, by investigators at academic and not-for-profit institutions to conduct non-commercial research. Our goal is to license our NF- $\kappa$ B technology to pharmaceutical and biotechnology companies that are conducting research to discover and develop drugs that modulate NF- $\kappa$ B cell signaling and/or that are marketing such drugs.

We have also developed a proprietary portfolio of cell-signaling regulation technologies, our ARGENT technology, to control intracellular processes with small molecules, which may be useful in the development of therapeutic vaccines and gene and cell therapy products, and which provide versatile tools for applications in cell biology, functional genomics and drug discovery research. We distribute our ARGENT technologies at no cost to academic investigators in the form of our Regulation Kits to use in various research applications in an academic setting. Over 1,000 academic investigators worldwide are

using or have used this technology in diverse areas of research, and over 250 scientific papers describing their use have been published. In addition, we are seeking opportunities to license our ARGENT technology to pharmaceutical and biotechnology companies to accelerate their drug discovery. To date, we have entered into several research and development licenses for use of our ARGENT technology.

Our current business strategy is to:

- build a fully integrated oncology company – a leader in the discovery, development and commercialization of molecularly targeted oncology therapies;
- establish a U.S. commercial platform;
- enter into partnerships with major pharmaceutical or biotechnology companies, after obtaining definitive clinical data, to assist in developing our cancer product candidates and commercializing them outside the U.S.;
- broadly develop our lead oncology product, AP23573, and build a pipeline of innovative follow-on product candidates;
- license our NF- $\kappa$ B and ARGENT cell-signaling regulation technologies to pharmaceutical and biotechnology companies; and
- develop and commercialize through medical device companies AP23573 drug-delivery stents and other medical devices to decrease reblockage of injured vessels following stent-assisted angioplasty.

We conduct research and development programs on behalf of our 80%-owned subsidiary, ARIAD Gene Therapeutics, Inc., hereinafter referred to as AGTI, relating to our product candidates which are small-molecule mTOR inhibitors. These product candidates include our lead product candidate, AP23573, and compounds in our bone-targeted mTOR inhibitor program. AGTI owns the intellectual property relating to these product candidates and related ARGENT technology. We also seek opportunities on behalf of AGTI to license the ARGENT cell-signaling regulation technology to develop and commercialize products and for research applications.

ARIAD was organized as a Delaware corporation in April 1991. Our principal executive offices are located at 26 Landsdowne Street, Cambridge, Massachusetts 02139-4234, and our telephone number is (617) 494-0400. We maintain an internet website at <http://www.ariad.com>, the contents of which are not incorporated herein. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and all amendments to such reports are made available free of charge through the Investor Relations section of our website as soon as reasonably practicable after they have been electronically filed with or furnished to the United States Securities and Exchange Commission, or SEC.

ARIAD and the ARIAD logo are our registered trademarks. ARGENT is our trademark. Other service marks, trademarks and trade names appearing in this report are the property of their respective owners.

## Our Lead Development Programs

### *Oncology Indications of our mTOR Inhibitor, AP23573*

Human cells – both healthy and malignant – share an elaborate system of molecular pathways that carry signals back and forth from the cell surface to the nucleus and within the cell. Such signaling is essential to cell functioning and viability. When disrupted or over-stimulated, such pathways may trigger diseases such as cancer. For example, growth and proliferation of cancer cells are dependent on signals from external growth factors, as well as signals indicating the availability of sufficient nutrients and blood supply. These signals are conveyed along well-defined pathways, several of which are regulated by the protein mTOR.

Our lead cancer product candidate, AP23573, is an internally discovered, potent mTOR inhibitor. The protein, mTOR, serves as a “master switch” and has a central function in cancer cells. Blocking mTOR creates a starvation-like effect in cancer cells by interfering with cell growth, division, metabolism and angiogenesis.

As part of our global clinical development plan and registration strategy, AP23573 has been studied in multiple Phase 2 and 1b clinical trials in the U.S. and/or Europe as a single agent in patients with solid tumors, including sarcomas, hormone refractory prostate cancer and endometrial cancer. In addition, three multi-center Phase 1b trials of AP23573 in combination with other anti-cancer therapies are underway, which are focused primarily on patients with various types of solid tumors, especially breast, ovarian, non-small-cell lung, and prostate cancers, as well as sarcomas. Further combination studies are planned. In addition, we concluded enrollment in Phase 1b and Phase 2 clinical trials in patients with brain cancer and leukemias and lymphomas, respectively. Eleven clinical trials of AP23573 are ongoing or completed. Intravenous and oral formulations of AP23573 have been studied in these trials.

Our most advanced Phase 2 trial of AP23573 is in sarcoma patients. In November 2005, at the AACR-NCI-EORTC International Conference on “Molecular Targets and Cancer Therapeutics,” investigators presented preliminary Phase 2 clinical data on AP23573 in advanced sarcoma patients, who had generally failed alternative anti-cancer treatments and had progressive disease upon entering the trial. This trial includes four subgroups of bone and soft-tissue sarcoma patients. Based on these preliminary data, 27% (51/188) of patients treated with AP23573 and evaluable for at least four months demonstrated sustained anti-tumor responses as defined by RECIST (Response Evaluation Criteria in Solid Tumors), including four patients with partial responses (confirmed tumor regression >30%) and 47 patients with stable disease for at least four months. In addition, the preliminary six-month progression free survival (PFS) rate in the patients in the first stage of the trial was 22%. Enrollment in this trial has been completed. Based on these positive data from our Phase 2 trial, we expect to start our initial registration trial for AP23573 in patients with sarcomas.

In clinical trials to date, AP23573 has been well tolerated at the fixed doses administered, and adverse events were generally mild to moderate in severity and readily reversible. The most common treatment-related adverse events were oral mucositis, rash, fatigue, nausea and lipid abnormalities.

Two clinical trials of AP23573 that have concluded enrollment provide important insights that may be useful in planning follow-up studies. In patients with brain cancer, AP23573 was shown to cross the blood-brain barrier and inhibit brain tumor mTOR activity, while being well tolerated in severely ill patients. In heavily pretreated patients with leukemias and lymphomas, 40% of evaluable patients had AP23573 anti-cancer activity, providing a basis for further combination studies in selected hematologic malignancies.

The oral dosage form of AP23573 is being studied in a multi-center Phase 1b clinical trial of patients with various solid tumors. Initial results from this trial indicate that the oral dosage form can be administered safely using several daily and intermittent dosing schedules and achieves blood levels over time and mTOR inhibition generally consistent with those observed with intravenous administration.

The FDA and the EMEA have designated AP23573 as an orphan drug for treatment of soft-tissue and bone sarcomas. The FDA has also designated AP23573 as a fast-track product for the same indications. Our goal is to initiate the first global registration trial of AP23573 in patients with advanced sarcomas. Beforehand, we expect to finalize selection of the dosing regimen to be used in the Phase 3 clinical trial and finalize the design of the protocol for the pivotal trial with the FDA and EMEA.

In the malignant cells of many of the cancers that we are studying in the AP23573 clinical trials, signaling in the mTOR pathway may be abnormal due to genetic mutations and/or alterations in the activity of key proteins upstream or downstream of mTOR itself. We believe that some of these patients may be particularly responsive to mTOR inhibition. Our scientists and other investigators are leading the identification and development of biomarker assays to identify patients with tumors that harbor such alterations in the mTOR pathway. In addition, our clinical development strategy includes extensive use of biomarkers and functional imaging technologies, such as positron emission tomography, to augment the assessment of the efficacy and safety of AP23573 in patients enrolled in our trials.

#### *Cardiovascular Indications of our mTOR Inhibitor, AP23573*

As an mTOR inhibitor, AP23573 has also been shown to potently block the growth, proliferation and migration of vascular smooth muscle cells, the primary cause of narrowing and blockage of injured vessels. In 2005, we entered into a partnership with Medinol Ltd., hereinafter referred to as Medinol, one of the leading cardiovascular medical device companies, to develop and commercialize stents and other medical devices to deliver AP23573 to prevent reblockage of injured vessels following stent-assisted angioplasty, a common non-surgical procedure for dilating or opening narrowed arteries.

Cardiovascular disease afflicts more than a quarter of the U.S. population and causes more than five million hospitalizations, over \$300 billion in healthcare expenditures, and one million deaths annually. Products expected to have the most profound impact on coronary artery and myocardial disorders - including drug-eluting stents - have only recently been introduced into clinical practice. By 2008, the growing drug-eluting stent market is expected to exceed \$6 billion.

Numerous drugs, including many antiplatelet agents, anticoagulants, ACE inhibitors, and cytotoxic agents, administered to patients following coronary angioplasty have failed to significantly reduce the overall incidence of vascular reblockage, which runs as high as 30% in the first few months, depending on the configuration and location of the vascular lesion and other clinical factors, such as diabetes. Recent clinical studies have found lower reblockage rates in patients treated with stents that deliver small-molecule drugs, such as sirolimus, an mTOR inhibitor, or paclitaxel, a cytotoxic agent, locally to the site of vascular injury. Such stents have become the standard-of-care for patients undergoing interventional procedures to open narrowed coronary arteries.

We may grant up to two additional licenses, under our rights to AP23573, to medical device companies for their use in developing and commercializing drug-delivery stents and other medical devices to reduce reblockage of injured vessels following stent-assisted angioplasty.

## *Additional Non-Oncology Indications of our mTOR Inhibitor, AP23573*

Inhibition of the mTOR pathway may be useful for additional indications beyond oncology and drug-delivery stents, and we are evaluating such indications as part of the broader clinical development plan for AP23573.

### **Our Preclinical Programs**

Our research and development programs are focused on discovering and developing small-molecule drugs that regulate cell signaling. Many of the critical functions of cells, such as cell growth, differentiation, gene transcription, metabolism, motility and survival, are dependent on signals carried back and forth from the cell surface to the nucleus and within the cell through a system of molecular pathways. When disrupted or over-stimulated, such pathways may trigger diseases such as cancer. From our inception, our research has focused on exploring cell-signaling pathways, identifying their role in specific diseases, and discovering drug candidates to treat those diseases by interfering with the aberrant signaling pathways of cells. The specific cellular proteins blocked by our product candidates have been well characterized and validated as targets. All of our product candidates are developed in-house through the integrated use of structure-based drug design and computational chemistry, and their targets have been validated with techniques such as functional genomics, proteomics, and chemical genetics.

We have a focused drug discovery program centered on small-molecule, molecularly targeted therapies and cell-signaling pathways implicated in cancer. Currently, our preclinical pipeline includes: inhibitors of mutant oncogenic, or cancer-causing, proteins (kinases) that regulate cell signaling (e.g., Bcr-Abl - the target of imatinib, which becomes resistant to further treatment through various mutations, including one called T315I); single compounds that target multiple cancer pathways (e.g., cell survival, metastases and angiogenesis); and new mTOR inhibitors (i.e., bone-targeted compounds to treat primary bone cancers and cancers that have spread to bone).

### **Our Proprietary Technologies**

#### *NF- $\kappa$ B Cell-signaling Technology*

Dr. David Baltimore, formerly director of the Whitehead Institute for Biomedical Research, Dr. Phillip Sharp of the Massachusetts Institute of Technology, and Dr. Thomas Maniatis of Harvard University, together with a team of scientists in their respective laboratories, discovered a family of genes that encode proteins they called NF- $\kappa$ B and I- $\kappa$ B, its inhibitor; the critical role played by NF- $\kappa$ B cell-signaling in regulating cellular processes involved in various difficult-to-treat diseases; methods to identify compounds to regulate NF- $\kappa$ B cell-signaling activity; and methods of treating disease by inhibiting NF- $\kappa$ B. NF- $\kappa$ B can be generally thought of as a "biological switch" that can be turned off using these methods to treat disorders, such as inflammation, cancer, sepsis and osteoporosis.

We have an exclusive license from these academic institutions to pioneering technology and patents related to methods of treating human disease through modulation of NF- $\kappa$ B cell-signaling activity, and the discovery and development of drugs to regulate NF- $\kappa$ B cell-signaling activity. We have a program to license this technology and these treatment methods to pharmaceutical and biotechnology companies that are conducting research to discover and develop drugs that modulate NF- $\kappa$ B cell-signaling and/or that are marketing such drugs. One of the NF- $\kappa$ B patents is the subject of reexamination proceedings in the U.S. Patent and Trademark Office, or PTO, and a patent infringement lawsuit filed in 2002 by us and the academic institutions against Eli Lilly and Company, hereinafter referred to as Lilly, alleging infringement based on sales of Lilly's osteoporosis drug, Evista®, and Lilly's septic shock drug, Xigris®, and seeking monetary damages. This trial is scheduled to commence in the United States District Court for the District of Massachusetts on April 10, 2006. See Part I, Item 3: Legal Proceedings.

## ***ARGENT Cell-signaling Regulation Technology***

Our proprietary portfolio of cell-signaling regulation technologies includes the ARGENT signaling and transcription technologies. Our ARGENT technologies allow intracellular processes to be controlled with small molecules, which may be useful in the development of therapeutic vaccines and gene and cell therapy products, and which provide versatile tools for applications in cell biology, functional genomics and drug-discovery research, including three-hybrid screening approaches to discover and characterize targets and lead molecules. To maximize their use by the scientific community, we distribute our technologies at no cost to academic investigators in the form of our Regulation Kits. Over 1,000 investigators worldwide are using or have used our Regulation Kits in diverse areas of research, and over 250 scientific papers describing their use have been published. For researchers in pharmaceutical and biotechnology companies, we have established a licensing program to provide them with access to our ARGENT cell-signaling regulation technologies on commercial terms.

### **Our Business Strategy**

Our business strategy is to:

- build a fully integrated oncology company - a leader in the discovery, development and commercialization of molecularly targeted oncology therapies;
- establish a U.S. commercial platform;
- enter into partnerships with major pharmaceutical or biotechnology companies, after obtaining definitive clinical data, to assist in developing our cancer product candidates and commercializing them outside the United States;
- broadly develop our lead oncology product, AP23573, and build a pipeline of innovative follow-on product candidates;
- license our NF- $\kappa$ B and ARGENT cell-signaling regulation technologies to pharmaceutical and biotechnology companies; and
- develop and commercialize through medical device companies AP23573 in drug-delivery stents and other medical devices to decrease reblockage of injured vessels following stent-assisted angioplasty.

### **Our Intellectual Property**

Patents and other intellectual property rights are essential to our business. We file patent applications to protect our technology, inventions and improvements to our inventions that are considered important to the development of our business.

As of February 28, 2006 we have 93 patents and pending patent applications in the United States, which are owned, co-owned or exclusively licensed by us or by our subsidiary, AGTI. In addition, we have filed foreign counterparts, as appropriate. We also have several nonexclusive technology licenses from certain institutions in support of our research programs. We anticipate that we will continue to seek licenses from universities and others where applicable technology complements our research and development efforts.

Approximately one third of the patents and patent applications in our portfolio relate generally to our mTOR inhibitor, AP23573, or to our preclinical drug discovery programs. The former cover AP23573, various analogs and uses thereof, as well as the related use of biomarkers, related therapies and

inventions involving the mTOR gene. The latter include various families of kinase inhibitor compounds, as well as our bone-targeted mTOR inhibitors. The remainder of the portfolio is primarily focused on ARGENT cell-signaling regulation technologies. These patents and pending applications cover regulatory technologies, specialized variants of the technologies, critical nucleic acid components, small-molecule drugs, the identification and use of dimerizer hormone mimetics, and various uses of the technologies in health care and drug discovery. Patents issued to date include 30 patents covering our cell-signaling regulation technologies.

We also rely on unpatented trade secrets and proprietary know-how. However, trade secrets are difficult to protect. We enter into confidentiality agreements with our employees, consultants, investigators, contractors, collaborators and other third parties to whom we disclose confidential information. In addition, we believe that certain technologies utilized in our research and development programs are in the public domain. Accordingly, we do not believe that patent or other protection is available for these technologies.

### **Our Licenses to Third Parties**

We have a program to license our NF- $\kappa$ B cell-signaling technology and treatment methods to pharmaceutical and biotechnology companies conducting research to discover and develop drugs that modulate NF- $\kappa$ B cell-signaling and/or marketing such drugs. To date, we have entered into several licenses for this technology with pharmaceutical companies and companies manufacturing and commercializing kits, technologies and tools for research applications.

We also have a program to license our ARGENT cell-signaling regulation technologies to pharmaceutical and biotechnology companies to develop and commercialize innovative therapeutic products and to conduct drug discovery research. To date, we have entered into several licenses for use of our ARGENT cell-signaling regulation technologies for a variety of applications. In addition, several biotechnology companies are conducting collaborative studies of these technologies for use in gene and cell therapy applications.

In January 2005, we and our subsidiary, AGTI, entered into non-exclusive license and supply agreements with Medinol Ltd. for the development and commercialization of stents and other medical devices to deliver our mTOR inhibitor, AP23573, to prevent reblockage of injured vessels following stent-assisted angioplasty. The license agreement provides for the payment by Medinol to us of an upfront license fee, payments based on achievement of development, regulatory, and commercial milestones, and royalties based on commercial sales of products, if any, developed by Medinol. We are required to provide Medinol, and Medinol is required to purchase from us, agreed upon quantities of AP23573.

### **Our Licenses from Third Parties**

In 1991, we entered into an exclusive license agreement with Massachusetts Institute of Technology and the Whitehead Institute (on behalf of themselves and Harvard University) to the rights to our NF- $\kappa$ B cell-signaling technologies and treatment methods. This license agreement was amended in 1995 and provides for the payment by us to these academic institutions of an upfront fee, license maintenance fees, a milestone payment, sublicense fees, and royalties based on commercial sales of products and processes developed using the NF- $\kappa$ B cell-signaling technologies and treatment methods. The license agreement also grants us the right to undertake the enforcement and/or defense of these patent rights at our sole expense, subject to our right to withhold a percentage of the royalties otherwise due the academic institutions to be applied toward reimbursement of our fees and expenses in connection with any such litigation, including our litigation against Lilly. The license agreement also provides that we will share a percentage of any damages, net of fees and expenses, awarded in such litigation with the academic institutions.

We and, in some instances AGTI, our 80% owned subsidiary, have entered into license agreements with various academic institutions pursuant to which we and/or AGTI are the licensees of certain technologies relating to our research and development programs for our product candidates which are small-molecule mTOR inhibitors and our ARGENT cell-signaling regulation technologies. In particular, in 1997, AGTI entered into an amended and restated exclusive license agreement with Stanford University (on behalf of itself and Harvard University) to rights to certain of our ARGENT cell-signaling regulation technologies. This license agreement was amended in 2003 and provides for the payment by AGTI of an upfront fee, license maintenance fees, milestone payments based on achievement of development and commercial milestones, royalties on commercial sales of products, including therapies and research reagents, by AGTI, its co-venturers and partners, and the issuance of 180,000 shares of common stock, or 3% of the initial capitalization, of AGTI.

In some instances, our third party licenses also impose insurance, development, sublicensing and other obligations. Failure by us to comply with these requirements could result in the termination of the applicable agreement, which, depending upon the technologies which are the subject of the applicable agreement, could have a material adverse effect on our business, financial condition, and results of operations.

### **Research and Development Spending**

During each of the three years ended December 31, 2005, 2004, and 2003, we spent approximately \$45.9 million, \$27.7 million, and \$14.9 million respectively, on our research and development activities.

### **Manufacturing**

Our drug candidates and preclinical compounds are small molecules that can be readily synthesized by processes that we have developed. We are able to manufacture in-house the quantities of our product candidates necessary for certain preclinical studies. We contract with third party manufacturers to assist in the development and optimization of our manufacturing processes and methods and to supply sufficient quantities of our lead product candidate in bulk quantities and in suitable dosage forms for use in our clinical trials. We also expect to depend on third-party manufacturers for the supply of our products upon commercialization.

Our lead product candidate, AP23573, is produced by an established manufacturing process using conventional synthetic and natural-product fermentation techniques. The production of AP23573 is based in part on technology that we believe is proprietary to us. We may license this technology to contract manufacturers to enable them to manufacture AP23573 for us. In addition, a contract manufacturer may develop process technology related to the manufacture of our drug candidate that the manufacturer owns either independently or jointly with us. This would increase our reliance on that manufacturer or require us to obtain a license from that manufacturer in order to have our product manufactured. We are currently discussing with our existing suppliers and other third-party manufacturers the long-term supply and manufacture of AP23573 to ensure we have provided for sufficient supply of our product at commercially reasonable costs with appropriate redundancy upon commercialization.

Contract manufacturers are subject to extensive governmental regulation and we depend on them to manufacture our product candidates in accordance with the FDA's current good manufacturing practices, or cGMP. We have established a quality assurance program intended to ensure that third-party manufacturers under contract produce our compounds in accordance with cGMP, and other applicable domestic and foreign regulations. We believe that our current contractors comply with such regulations.

## Competition

The pharmaceutical and biotechnology industries are intensely competitive. We compete directly and indirectly with other pharmaceutical companies, biotechnology companies and academic and research organizations, many of whom have greater resources than us. We compete with companies who have products on the market or in development for the same indications as our product candidates. We may also compete with organizations that are developing similar technology platforms.

In the area of oncology, pharmaceutical and biotechnology companies such as Amgen Inc., AstraZeneca PLC, Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech, Inc., GlaxoSmithKline plc, Hoffmann LaRoche & Co., Johnson & Johnson, Merck KGaA, Novartis AG, Pfizer, Inc., and Wyeth Corp. are developing and marketing drugs to treat cancer, including mTOR inhibitors. Biotechnology companies such as Amgen Inc., Biogen-Idec, Inc., ImClone Systems, Inc., Millennium Pharmaceuticals, Inc., Onyx Pharmaceuticals, Inc., OSI Pharmaceuticals, Inc., Telik, Inc., and Vertex Pharmaceuticals, Inc. are developing drugs to treat various diseases, including cancer, by inhibiting cell-signaling pathways. Other companies have products on the market or in development against which our drug candidates, if approved, may have to compete. We may also experience competition from companies that have acquired or may acquire technology from companies, universities, and other research institutions. As these companies develop their technologies, they may develop proprietary positions that may materially and adversely affect us.

## Government Regulation

Our ongoing research and development activities, our clinical trials, the manufacturing and testing procedures and the marketing of our product candidates, if they are approved, all are subject to extensive regulation by numerous governmental authorities in the United States and other countries. Any drug or device developed by us and/or a partner must undergo rigorous preclinical studies and clinical testing and extensive regulatory review administered by the FDA under the federal Food, Drug and Cosmetic Act prior to marketing in the United States. Satisfaction of such regulatory requirements, which includes demonstrating that a product is both safe and effective for its intended indications for use, typically takes several years or more depending upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Preclinical studies must be conducted in conformance with FDA regulations, including its current Good Laboratory Practices, or cGMP, regulations. Before commencing clinical trials in the United States, we must submit extensive information about the results of preclinical studies, toxicity, manufacturing and control procedures and our proposed clinical research protocol to the FDA in an Investigational New Drug, or IND, application, or an Investigational Device Exemption, or IDE, as the case may be. If the FDA does not respond with any questions on the IND, we can commence clinical trials thirty days after the submission. In addition, an independent institutional review board, or IRB, at each institution at which any clinical trial is being performed, must review and approve the clinical protocol before clinical testing may begin, and it will have ongoing overview of the clinical trial at that institution. With respect to an IDE for certain medical devices, such as drug-delivery stents, clinical trials may not begin until both the FDA and an IRB approve. There can be no assurance that submission of an IND or IDE will result in the commencement of such clinical trials.

We have a limited history of conducting preclinical studies and the clinical trials necessary to obtain regulatory approval. Furthermore, we, the FDA or an IRB may suspend clinical trials at any time if we or they believe that the subjects participating in such trials are being exposed to unacceptable risks or if the FDA finds deficiencies in the conduct of the trials or other problems with our product under development.

Before receiving FDA approval to market a product, we will have to demonstrate that the product is safe and effective in the patients for whom the product is indicated. Data obtained from preclinical studies

and clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory clearances. In addition, delays or rejections may be encountered based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. Similar or even more extensive delays also may be encountered in foreign countries. There can be no assurance that even after such time and expenditures, regulatory approval will be obtained for any product candidates developed by us, or, even if approval is obtained, that the approved indication and related labeling for such products will not limit the product's condition of use, which could materially impact the marketability and profitability of the product. If regulatory approval of a product is granted, such approval will be limited to those disease states and conditions for which the product has been shown useful, as demonstrated by clinical trials. Furthermore, approval may entail ongoing requirements for post-market studies. Even if such regulatory approval is obtained, a marketed product, its manufacturer and its manufacturing facilities and procedures are subject to continual review and periodic inspections by the FDA. Discovery of previously unknown problems with a product, manufacturer, manufacturing procedures or facility may result in restrictions on such product or manufacturer, including costly recalls, an injunction against continued marketing and manufacturing until the problems have been adequately addressed to the FDA's satisfaction or even withdrawal of the product from the market.

There can be no assurance that any compound developed by us alone or in conjunction with others will prove to be safe and efficacious in clinical trials and will meet all of the applicable regulatory requirements needed to receive and maintain marketing approval. Additionally, the marketing, labeling and advertising for an approved product is subject to ongoing FDA scrutiny and the failure to adhere to applicable requirements can result in regulatory action that could have a material adverse impact on the profitability of the product.

Outside the United States, our ability to market a product will be contingent upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, obtaining marketing authorization, and pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union, or EU, certain centralized and mutual recognition registration procedures are available to companies wishing to market a product in more than one Member State. These procedures alleviate the need to file a separate application in each EU country. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization will be granted. This foreign regulatory approval process includes all of the risks associated with FDA clearance set forth above.

### **Our Employees**

As of February 28, 2006, we had 108 employees, 50 of whom hold post-graduate degrees, including 35 with a Ph.D., M.D. or J.D. Most of our employees are engaged directly in research and development. We have entered into confidentiality, assignment of inventions and non-competition agreements with all of our employees. None of our employees are covered by a collective bargaining agreement, and we consider relations with our employees to be good.

## ITEM 1A: RISK FACTORS

**THE RISKS AND UNCERTAINTIES DESCRIBED BELOW ARE THOSE THAT WE CURRENTLY BELIEVE MAY MATERIALLY AFFECT OUR COMPANY. ADDITIONAL RISKS AND UNCERTAINTIES THAT WE ARE UNAWARE OF ALSO MAY BECOME IMPORTANT FACTORS THAT AFFECT OUR COMPANY. IF ANY OF THE FOLLOWING RISKS ACTUALLY OCCUR, THEY MAY MATERIALLY HARM OUR BUSINESS, OUR FINANCIAL CONDITION AND OUR RESULTS OF OPERATIONS.**

### **Risks Relating to Our Business**

*We and our partners may never succeed in developing marketable products or generating product revenues.*

We are a biopharmaceutical company focused on the discovery and development of drugs to provide therapeutic intervention in treating human diseases at the cellular level. As with all science, we face much trial and error, and we may fail at numerous stages along the way, which would inhibit us from successfully developing, manufacturing and marketing our drug candidates. Our lead product candidate, AP23573, is currently in Phase 2 clinical trials for certain cancers, and we do not currently have any products on the market and have no product revenues. Factors which would affect our ability to obtain regulatory approval and to achieve market acceptance and gain market share for our product candidates include, among other factors, product formulation, dose, dosage regimen, our ability to obtain timely and sufficient patient enrollment in our clinical trials, our ability to manufacture, directly or indirectly, sufficient and cost-effective quantities of our product candidates, and our ability to sell, market and distribute, directly or indirectly, such product candidates. We and our medical device partner have limited experience in designing, conducting and managing the clinical testing necessary to obtain such regulatory approval. Additionally, we do not currently have any partners to assist in developing and commercializing our cancer product candidates and expect to be dependent upon such partners to successfully develop and commercialize such cancer products outside the United States. In particular, failure to secure one or more partners to assist in development and commercialization of AP23573 would have a material adverse effect on our ability to generate significant product revenues for AP23573 for cancer indications outside the United States.

We are also dependent upon the success of Medinol and any future medical device partners (collectively, our partners) to develop, manufacture and market stents or other medical devices to deliver AP23573 to reduce reblockage of injured arteries following stent-assisted angioplasty. To date, we have entered into only one such agreement, with Medinol. If Medinol is not successful and/or if we are not able to enter into agreements with additional medical device companies experienced in the development, manufacture, and marketing of medical devices to deliver AP23573, we will not be able to generate revenues from the marketing of stents or other medical devices that deliver AP23573.

Other than AP23573, we do not have any product candidates in clinical development, and we have not designated any clinical candidates from our existing preclinical programs. We do not expect to have any products on the market before 2008, at the earliest, and, ultimately, we and our partners may not have any products on the market for several years, if at all. We and our partners may not succeed in developing or commercializing any products which will generate product revenues for our company. If we and our partners are not successful in developing or marketing AP23573 or other product candidates, we will not be profitable.

*We have incurred significant losses to date and may never be profitable.*

We have incurred significant operating losses in each year since our formation in 1991 and have an accumulated deficit of \$247.1 million from our operations through December 31, 2005. Losses have resulted principally from costs incurred in research and development of our product candidates, including clinical development of AP23573, our lead product candidate, and from general and administrative costs associated with our operations. It is likely that we will incur significant operating losses for the foreseeable future. We currently have no product revenues, limited license revenues and limited commitments for future licensing revenues, and may not be able to generate such revenues in the future. If our losses continue and we and our partners are unable to successfully develop, commercialize, manufacture and market our product candidates and/or we are unable to enter into agreements and licenses of our intellectual property, we may never generate sufficient revenues to achieve profitability. Even if we and our partners are able to commercialize products and we are able to enter into agreements or licenses in the future, we may never generate sufficient revenues to have profitable operations.

*Insufficient funding may jeopardize our research and development programs and may prevent commercialization of our products and technologies.*

We have funded our operations to date through sales of equity securities, debt and operating revenue. Most of our operating revenue to date has been generated through previous collaborative research and development agreements and existing licenses. We currently do not have any committed funding from any pharmaceutical or biotechnology company to advance any of our product development programs. Although we believe that our current available funds will be adequate to satisfy our capital and operating requirements into mid 2007, we will require substantial additional funding for our research and development programs (including pre-clinical development and clinical trials), for operating expenses (including intellectual property protection and enforcement), for the pursuit of regulatory approvals and for establishing manufacturing, marketing and sales capabilities. We received net proceeds of \$57.9 million from the sale of 8,625,000 shares of our common stock in August 2005. We have effective shelf registration statements on file with the SEC under which we can sell up to 2,815,000 shares of our common stock. We may sell part or all of these shares at our discretion, and may be able to increase the number of shares to be sold in connection with an offering of these shares, subject to certain limitations under federal securities laws and the rules of the Nasdaq National Market. While we intend to seek additional funding from product-based collaborations, technology licensing, and public or private financings, such additional funding may not be available on terms acceptable to us, or at all. Accordingly, we may not be able to secure the significant funding which is required to maintain and continue each of our research and development programs at their current levels or at levels that may be required in the future. If we cannot secure adequate financing, we may be required to delay, scale back, eliminate or terminate clinical trials and/or seeking marketing approval for AP23573 for one or more indications, to delay, scale back or eliminate one or more of our research and development programs, or to enter into license or other arrangements with third parties to purchase, commercialize or otherwise obtain rights in products or technologies that we would otherwise seek to develop ourselves.

*We have limited manufacturing experience and are dependent upon the ability of third parties to manufacture our product candidates, which raises uncertainty as to our ability to develop and commercialize our product candidates.*

We have no experience in manufacturing any of our product candidates on a large scale and have contracted with third party manufacturers to provide material for clinical trials and to assist in the development and optimization of our manufacturing processes and methods. Our ability to conduct clinical trials and commercialize our product candidates will depend on the ability of such third parties to manufacture our products on a large scale at a competitive cost and in accordance with cGMP and other regulatory requirements. If we are not able to obtain contract manufacturing on commercially reasonable

terms, obtain or develop the necessary materials and technologies for manufacturing, or obtain intellectual property rights necessary for manufacturing, we may not be able to conduct or complete clinical trials or commercialize our product candidates. There can be no assurance that we will be able to obtain such requisite terms, materials, technologies and intellectual property necessary to successfully manufacture our product candidates for clinical trials or commercialization.

*The loss of key members of our scientific and management staff could delay and may prevent the achievement of our research, development and business objectives.*

Our performance as a specialized scientific business is substantially dependent on our key officers and members of our scientific staff responsible for areas such as drug development, clinical trials, regulatory affairs, drug discovery, manufacturing, marketing, business development and intellectual property protection and licensing. We also are dependent upon a few of our scientific advisors to assist in formulating our research and development strategy. While we have entered into employment agreements with all of our executive officers, these officers may terminate their employment with us at any time. The loss of, and failure to promptly replace, any member of our management team could significantly delay and may prevent the achievement of our research, development and business objectives.

*We are dependent upon the ability of our medical device partner and potential additional partners to develop, manufacture, test and market stents or other medical devices to deliver AP23573.*

We have no experience in the development of medical devices and will not ourselves develop stents or other medical devices to deliver AP23573. Instead, we have granted one license, and may grant up to two additional licenses, under our rights to AP23573 to medical device companies for their use in developing and commercializing such medical devices to reduce blockage of injured vessels following stent-assisted angioplasty.

While we expect to supply AP23573 to our medical device partner and any additional partners (collectively, our partners), we will be otherwise dependent upon them to develop and commercialize stents or other medical devices to deliver AP23573. Such medical device partners will have various degrees of scientific, technical, medical and regulatory experience and resources to, directly or through third parties, develop, manufacture, test or market stents or other medical devices to deliver AP23573. Their ability to conduct clinical trials and commercialize such medical devices will be dependent on the safety profile of AP23573 and our ability to manufacture and supply AP23573, either directly or through third parties, at a competitive cost and in accordance with cGMP and other regulatory requirements. We depend upon third-party manufacturers or collaborative partners for the production of AP23573 for clinical trials and intend to use third-party manufacturers to produce AP23573 on commercial scale. Our reliance on third-party manufacturers and their potential inability to meet our supply commitments to one or more of our partners could adversely impact the ability of our partners to commercialize stents or other medical devices to deliver AP23573.

We anticipate that our partners will seek to develop and commercialize stents or other medical devices to deliver AP23573 that do not infringe third-party patents. However, there can be no assurance that the devices delivering AP23573 marketed by our partners will not be subject to third-party claims. Furthermore, the patents issued to us or our partners covering AP23573 and/or medical devices, including stents, may be subject to challenge and may be subsequently narrowed, invalidated or circumvented. Either such event would adversely impact the ability of one or more of our partners to market their stents or other medical devices to deliver AP23573.

Our existing license agreement with Medinol allows either party to terminate under certain circumstances, including Medinol's reasonable business judgment that development of a medical device

to deliver AP23573 is not feasible. Accordingly, Medinol may be unable to develop a medical device to deliver AP23573 and we may also not be able to enter into any additional licensing agreements with any other medical device companies to develop such devices on terms which are acceptable to us, or at all. Our inability to enter into such transactions, or the inability of one or more of our partners to develop or commercialize stents or other medical devices to deliver AP23573 for any reason, will adversely impact our ability to generate revenues from any licenses of AP23573.

*We will continue to expend significant resources on the enforcement and licensing of our NF- $\kappa$ B patent portfolio and may be unable to generate material revenues from these efforts, if we are unable to enforce against, or license our NF- $\kappa$ B patents to, pharmaceutical and biotechnology companies.*

We are the exclusive licensee of a family of patents, three in the U.S. and one in Europe, including a pioneering U.S. patent covering methods of treating human disease by regulating NF- $\kappa$ B cell-signaling activity, hereinafter referred to as the '516 Patent, awarded to a team of inventors from The Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology and Harvard University. We have initiated a licensing program to generate revenues from the discovery, development, manufacture and sale of products covered by our NF- $\kappa$ B patent portfolio. These patents have been, and in the future may be, challenged and may be subsequently narrowed, invalidated, declared unenforceable or circumvented, any of which could materially impact our ability to generate licensing revenues from them.

On June 25, 2002, we, together with these academic institutions, filed a lawsuit in the United States District Court for the District of Massachusetts, or the U.S. District Court, against Eli Lilly and Company, hereinafter referred to as Lilly, alleging infringement upon of certain claims of the '516 Patent through sales of Lilly's osteoporosis drug, Evista®, and its septic shock drug, Xigris®. Several cases have been decided by the U.S. Court of Appeals and the Supreme Court addressing issues pertinent to this litigation since its inception. The trial in this case is scheduled to commence on April 10, 2006 in the U.S. District Court.

On April 4, 2005, Lilly filed an *ex parte* request in the United States Patent and Trademark Office, or PTO, to reexamine the patentability of certain claims of the '516 Patent. In addition, a third party filed an *ex parte* request in the PTO on December 2, 2005 to reexamine the patentability of certain claims of the '516 Patent.

As exclusive licensee of this patent, we are obligated for the costs expended for its prosecution in the PTO, for its enforcement in this litigation and otherwise. Therefore, we will continue to expend significant capital and management resources pursuing this litigation through trial and subsequent appeals and in the reexamination process in the PTO, and the outcome is uncertain.

If the claims of the '516 Patent which are at issue in this litigation are invalidated by the PTO or in the courts or found not to be infringed in this litigation, we will not realize any revenues on sales of Evista or Xigris, and could be liable under certain limited circumstances for Lilly's litigation costs and potentially attorneys' fees. If we prevail at trial in our litigation against Lilly, any damages we may be awarded by the jury could be subsequently eliminated or limited by an adverse finding upon appeal or in the event that the claims of the '516 patent are invalidated by the PTO. Invalidation of these or other claims of the '516 Patent in the litigation or by the PTO would have a significant adverse impact on our ability to generate revenues from our NF- $\kappa$ B licensing program. Moreover, significant expenditures to enforce these patent rights without generating revenues or accessing additional capital could adversely impact our ability to further our clinical programs and our research and development programs at the current levels or at levels that may be required in the future.

*Because we do not own all of the outstanding stock of our subsidiary, AGTI, we may not realize all of the potential future economic benefit from products developed based on technology licensed to or owned by our subsidiary.*

Our majority-owned subsidiary, AGTI, holds licenses from Harvard University, Stanford University and other universities relating to our ARGENT cell-signaling regulation technology, and owns the intellectual property on our mTOR inhibitors derived from our ARGENT programs, including AP23573. The two directors of AGTI are also members of the Board of Directors of ARIAD. Minority stockholders of AGTI, including Harvard University, Stanford University, several of our scientific advisors, and several current and former members of our management and Board of Directors, own 20% of the issued and outstanding common stock of AGTI. We own the remaining 80% of the issued and outstanding common stock of AGTI.

We do not currently have a license agreement with AGTI that provides us with rights to commercialize product candidates, based on our ARGENT cell-signaling regulation technology or mTOR inhibitors derived from our ARGENT programs, solely for our own benefit, as opposed to for the benefit of AGTI. If we determine it to be in the best interests of our stockholders to commercialize these product candidates solely for our own benefit, we may negotiate with AGTI to obtain a license, on terms to be determined, granting us the sole rights to commercialize such product candidates. If we enter into such a license, the future economic benefit to our stockholders from our commercialization of such products, if any, will be diminished by any royalties or other payments paid under a future agreement with AGTI. If we do not enter into such a license, then the future economic benefit to our stockholders from our commercialization of such products on behalf of AGTI would be in the form of a dividend or other payments received in respect of our 80% interest in AGTI.

Alternatively, if we determine it to be in the best interests of our stockholders, we may seek to acquire some or all of the interests of the minority stockholders in AGTI for cash, shares of our common stock or other securities in a merger, exchange offer or other transaction. If we acquire all of the interests of the minority stockholders in AGTI, then our stockholders will receive all of the future economic benefit from our commercialization of such products on our own behalf. If we acquire these minority interests, we anticipate that this transaction will result in dilution to our stockholders and will require our incurrence of significant transaction costs, which are currently unknown. On January 13, 2004, we acquired an additional 351,909 shares of AGTI common stock, representing approximately 6% of AGTI's outstanding common stock, for a total purchase price of approximately \$8.8 million, effected through the reduction of inter-company debt, subject to adjustment in certain circumstances, in order to maintain our 80% interest in AGTI. While such valuation was based on a good-faith determination made by the independent and disinterested members of our Board of Directors as of that date, the economic value of the minority stockholders' interests is difficult to quantify in the absence of a public market. If we acquire all of the interests of the minority stockholders in AGTI, a variety of valuation methodologies may be employed to determine the value per share of AGTI common stock. Factors impacting this valuation would include the progress, likelihood and cost of development and commercialization of product candidates, potential future income streams there from, availability of funding and other factors. If we acquire the minority interests for consideration valued in excess of the value implicitly attributed to such AGTI shares by the market, this could result in a decline in our stock price. If we choose to acquire some or all of these minority interests through a merger in which we do not solicit the consent of the minority stockholders of AGTI, we could become subject to litigation or an appraisal procedure, which would result in additional expense and diversion of management resources.

There can be no assurance that we will, at any time, enter into a license with AGTI or acquire some or all of the interests of the minority stockholders in AGTI. If we pursue either of these alternatives, there can be no assurance as to the timing of any such transaction, the form of such transaction, the particular

transaction terms such as the form or amount of consideration offered or provided by us, or the consequences of any such proposed or completed transaction to us or the AGTI minority stockholders.

***Because members of our management team and/or Board of Directors beneficially own a material percentage of the capital stock of our subsidiary, AGTI, and we have agreements with AGTI, there are conflicts of interest present in dealings between ARIAD and AGTI.***

Four members of our management team and/or Board of Directors own approximately 5.6% of the outstanding capital stock of AGTI. Harvey J. Berger, M.D., our Chairman, and Chief Executive Officer, owns 3.2%, David L. Berstein, Esq., our Senior Vice President and Chief Patent Counsel, owns 0.2%, John D. Iuliucci, Ph.D., our Senior Vice President and Chief Development Officer, owns 0.6% and Jay R. LaMarche, one of our directors, owns 1.6%. These same individuals beneficially own an aggregate of approximately 3.1% of our outstanding common stock. Dr. Stuart L. Schreiber, a Harvard professor who is one of our scientific founders, owns approximately 3.2% of the outstanding capital stock of AGTI. Additionally, Dr. Berger and Mr. LaMarche are the two members comprising the Board of Directors of AGTI. As part of the formation of AGTI, we entered into certain agreements with AGTI to provide for the operations of AGTI. As a result, conflicts of interest exist in dealings between AGTI and us. AGTI is the exclusive licensee of the ARGENT cell-signaling intellectual property from Harvard University and Stanford University and of related technologies from other universities, and owns the intellectual property on our mTOR inhibitors derived from our ARGENT programs, including AP23573, which is in Phase 2 clinical trials for use in cancer and in development for use in drug delivery stents and other medical devices, and our bone-targeted mTOR inhibitors. Because of the apparent conflicts of interest, the market may be more inclined to perceive the terms of any transaction between us and AGTI as being unfair to us.

***We may not be able to protect our intellectual property relating to our research programs, technologies and products.***

We and our licensors have issued patents and pending patent applications covering research methods useful in drug discovery, new chemical compounds discovered in our drug discovery programs including, among others, AP23573, certain components, configurations and uses of our cell-signaling regulation technologies and products-in-development, methods and materials for manufacturing our products-in-development and other pharmaceutical products and methods and materials for conducting pharmaceutical research. We have a licensing program to generate revenues from the use of our ARGENT cell-signaling regulation technologies and our NF- $\kappa$ B intellectual property. Pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or sell our products or in countries where others develop, manufacture and sell products using our technologies. In addition, patents issued to us or our licensors may be challenged, as is the case with the Lilly litigation and related PTO proceedings regarding the NF- $\kappa$ B '516 Patent, and they may be subsequently narrowed, invalidated or circumvented. In that event, such patents may not afford meaningful protection for our technologies or product candidates, which would materially impact our ability to develop and market our product candidates and to generate licensing revenues from our patent portfolio. Certain technologies utilized in our research and development programs are already in the public domain. Moreover, a number of our competitors have developed technologies, filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and may cover or conflict with our patent applications, technologies or product candidates. Such conflicts could limit the scope of the patents that we may be able to obtain or may result in the denial of our patent applications. If a third party were to obtain intellectual proprietary protection for any of the foregoing, we may be required to challenge such protection, terminate or modify our programs impacted by such protection or obtain licenses from such third parties, which might not be available or acceptable terms or at all.

*We may be unable to develop or commercialize our product candidates, if we are unable to obtain or maintain certain licenses on commercial terms or at all.*

We have entered, and will continue to enter, into agreements, either directly or through AGTI, with third parties to test compounds, blood and tissue samples, to perform gene expression analysis and to develop biological tests for use with our product candidates, which testing may yield new inventions and discoveries requiring us to obtain licenses in order to exclusively develop or market new products, alone or in combination with our product candidates, or to develop or market our product candidates for new indications. We have also entered into license agreements for some of our technologies, either directly or through AGTI. We use third parties to test blood and tissue samples and other biological materials in our clinical programs and to develop biological tests, with respect to which we may be required to obtain licenses or pay royalties or other fees in order to commercialize such tests for use with our product candidates. We also use gene sequences or proteins encoded by those sequences and other biological materials in each of our research programs which are, or may become, patented by others and to which we would be required to obtain licenses in order to develop or market our product candidates. Manufacturing of our products may also require licensing biological materials, technologies and intellectual property from third parties. Our inability to obtain any one or more of these licenses, on commercially reasonable terms, or at all, or to circumvent the need for any such license, could cause significant delays and cost increases and materially affect our ability to develop and commercialize our product candidates. Obtaining licenses for these discoveries, materials and technologies may require us to make cumulative royalty payments or other payments to several third parties, potentially reducing amounts paid to us or making the cost of our products commercially prohibitive.

Some of our licenses obligate us to exercise diligence in pursuing the development of product candidates, to make specified milestone payments and to pay royalties. In some instances, we are responsible for the costs of filing and prosecuting patent applications. These licenses generally expire upon the earlier of a fixed term of years after the date of the license or the expiration of the applicable patents, but each license is also terminable by the other party upon default by us of our obligations. Our inability or failure to meet our diligence requirements or make any payments required under these licenses would result in a reversion to the licensor of the rights granted which, with respect to the licenses pursuant to which we have obtained exclusive rights, would materially and adversely affect our ability to develop and market products based on our licensed technologies.

*Competing technologies may render some or all of our programs or future products noncompetitive or obsolete.*

Many well-known pharmaceutical, healthcare and biotechnology companies, academic and research institutions and government agencies, which have substantially greater capital, research and development capabilities and experience than us or our potential partners, are presently engaged in one or more of the following activities:

- developing products based on cell signaling, genomics, proteomics, and computational chemistry;
- conducting research and development programs for the treatment of the various disease indications in which we are focused; and
- manufacturing, promoting, marketing and selling pharmaceutical or medical device products for treatment of diseases in all of the various disease indications in which we or our current or possible future partners are focused.

Some of these entities already have competitive products on the market or product candidates in clinical trials or in more advanced preclinical studies than we do. By virtue of having or introducing competitive

products on the market before us, these entities may gain a competitive advantage. Competing technologies may render some or all of our programs or future products noncompetitive or obsolete, and we may not be able to make the enhancements to our technology necessary to compete successfully with newly emerging technologies. If we are unable to successfully compete in our chosen markets, we will not become profitable.

*If our product candidates are not accepted by patients, physicians and insurers, we will not be successful.*

Our success is dependent on the acceptance of any approved products. Our product candidates may not achieve market acceptance among patients, physicians or third-party payors, even if we obtain necessary regulatory and reimbursement approvals. Physicians and health care payors may conclude that any of our product candidates are not as safe and/or effective as competing therapies or are not as attractive based on a cost/benefit analysis as alternative treatments. Failure to achieve significant market acceptance of our product candidates will harm our business. We believe that recommendations by physicians and health care payors will be essential for market acceptance of any product candidates.

*If we are unable to establish sales, marketing and distribution capabilities or to enter into agreements with third parties to do so, we may be unable to successfully market and sell any products.*

We are currently establishing a commercial oncology organization, but we have no experience in marketing or selling any products. While we intend to commercialize our product candidates in the United States and to enter into agreements with partner(s) to commercialize our product candidates elsewhere, we may be unable to successfully, directly or indirectly, sell any products that we obtain marketing approval to sell. If we are unable to effectively sell our products, our ability to generate revenues will be materially adversely affected. We may not be able to hire, in a timely manner, the qualified sales and marketing personnel we need, if at all. In addition, we may not be able to enter into any marketing or distribution agreements on acceptable terms, if at all. If we cannot establish sales, marketing and distribution capabilities as we intend, either by developing our own capabilities or entering into agreements with third parties, sales of future products, if any, may be harmed.

*If we develop a product for commercial use, a subsequent product liability-related claim or recall could have an adverse effect on our business.*

Our business exposes us to potential product liability risks inherent in the testing, manufacturing and marketing of pharmaceutical products. Prior to obtaining regulatory approval to market our products, we are required to test such products in human clinical trials at health care institutions pursuant to agreements which indemnify such institutions in case of harm caused to patients by our products. We may not be able to avoid significant product liability exposure resulting from use of our products. A product liability-related claim or recall could be detrimental to our business. In addition, except for insurance covering product use in our clinical trials, we do not currently have any product liability insurance, and we may not be able to obtain or maintain such insurance on acceptable terms, or we may not be able to obtain any insurance to provide adequate coverage against potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or limit the commercialization of any products that we develop.

*Significant additional losses or insufficient funding may cause us to default on certain covenants of our loan documents.*

At December 31, 2005, we had \$7.7 million outstanding under a term loan agreement with a bank, pursuant to which we are required to maintain certain financial and non-financial covenants, including minimum cash, cash equivalents and investments of \$13 million, a default of any of which would allow

the bank to demand payment of its loan. We currently maintain sufficient liquidity to fund payment of this loan if demand for payment were made. However, if we are unable to raise adequate financing to fund continuing operations or otherwise to refinance our loan, we may not be able to maintain compliance with loan covenants, may be required to pay off the loan and may be required to reduce our spending on operations.

### **Risks Relating to Governmental Approvals**

*We have limited experience in conducting clinical trials, which may cause delays in commencing and completing clinical trials of our product candidates.*

Clinical trials must meet FDA and foreign regulatory requirements. We have limited experience in designing, conducting and managing the preclinical studies and clinical trials necessary to obtain regulatory approval for our product candidates in any country. We or our collaborative partners may encounter problems in clinical trials that may cause us or the FDA or foreign regulatory agencies to delay, suspend or terminate our clinical trials at any phase. These problems could include the possibility that we may not be able to manufacture sufficient quantities of cGMP materials for use in our clinical trials, conduct clinical trials at our preferred sites, enroll a sufficient number of patients for our clinical trials at one or more sites, or begin or successfully complete clinical trials in a timely fashion, if at all. Furthermore, we, the FDA or foreign regulatory agencies may suspend clinical trials of our product candidates at any time if we or they believe the subjects participating in the trials are being exposed to unacceptable health risks as a result of adverse events occurring in our trials or if we or they find deficiencies in the clinical trial process or conduct of the investigation. With respect to AP23573, the FDA or foreign regulatory agencies may also suspend our clinical trials if we or they believe the subjects participating in the trials are being exposed to unacceptable health risks as a result of adverse events occurring in the trials of medical devices delivering AP23573 sponsored by our medical device partner or future partners. If clinical trials of any of our product candidates fail, we will not be able to market the product candidate which is the subject of the failed clinical trials. The FDA and foreign regulatory agencies could also require additional clinical trials before or after granting of marketing approval for any of our products, which would result in increased costs and significant delays in the development and commercialization of our products and could result in the withdrawal of our products from the market after obtaining marketing approval. Our failure to adequately demonstrate the safety and efficacy of a product candidate in clinical development could delay or prevent obtaining marketing approval of the product candidate and, after obtaining marketing approval, data from post-approval studies could result in the product being withdrawn from the market, either of which would likely have a material adverse effect on our business.

*We may not be able to obtain government regulatory approval to market our product candidates.*

To date, we have not submitted a marketing application for any product candidate to the FDA or any foreign regulatory agency, and none of our product candidates has been approved for commercialization in any country. Prior to commercialization, each product candidate would be subject to an extensive and lengthy governmental regulatory approval process in the United States and in other countries. We or any prospective partners or our medical device partners may not be able to obtain regulatory approval for any product candidates, or even if approval is obtained, the labeling for such products may place restrictions on their use that could materially impact the marketability and profitability of the product subject to such restrictions. Satisfaction of these regulatory requirements, which includes satisfying the FDA and foreign regulatory authorities that the product is both safe and effective for its intended uses, typically takes several years or more depending upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Uncertainty with respect to meeting the regulatory requirements governing our product candidates may result in excessive costs or extensive delays in the regulatory approval process, adding to the already lengthy review process. If regulatory approval of a

product is granted, such approval will be limited to those disease states and conditions for which the product is proven safe and effective, as demonstrated by clinical trials, and may not include all of the indications necessary to successfully market the product. Even though we have obtained orphan drug designation by the FDA and EMEA for AP23573 in bone and soft-tissue sarcomas, this designation may be challenged by others or may prove to be of no practical benefit.

*We will not be able to sell our product candidates if we or our third-party manufacturers fail to comply with FDA manufacturing regulations.*

Before we can begin to commercially manufacture our product candidates, we must either secure manufacturing in an FDA approved manufacturing facility or obtain regulatory approval of our own manufacturing facility and processes. In addition, the manufacturing of our product candidates must comply with cGMP requirements of the FDA and similar requirements of regulatory agencies in other countries. These requirements govern, among other things, quality control and documentation procedures. We, or any third-party manufacturer of our product candidates, may not be able to comply with these requirements, which would prevent us from selling such products. Material changes to the manufacturing processes of our products after approvals have been granted are also subject to review and approval by the FDA or other regulatory agencies. Post approval, such facilities are subject to continuing FDA and foreign regulatory inspections and failure to comply with cGMPs or similar regulations can result in regulatory action up to and including cessation of shipment of product.

*Even if we bring products to market, we may be unable to effectively price our products or obtain adequate reimbursement for sales of our products, which would prevent our products from becoming profitable.*

If we succeed in bringing any product candidates to the market, they may not be considered cost-effective, and coverage and adequate payments may not be available or may not be sufficient to allow us to sell our products on a competitive basis. In both the United States and elsewhere, sales of medical products and treatments are dependent, in part, on the availability of reimbursement from third-party payors, such as health maintenance organizations and other private insurance plans and governmental programs such as Medicare. Third-party payors are increasingly challenging the prices charged for pharmaceutical products and services. Our business is affected by the efforts of government and third-party payors to contain or reduce the cost of health care through various means. In the United States, there have been and will continue to be a number of federal and state proposals to implement government controls on pricing. Similar government pricing controls exist in varying degrees in other countries. In addition, the emphasis on managed care in the United States has increased and will continue to increase the pressure on the pricing of pharmaceutical products. We cannot predict whether any legislative or regulatory proposals will be adopted or the effect these proposals or managed care efforts may have on our business.

#### **Risks Relating to Our Common Stock**

*Results of our operations, general market conditions for biotechnology stocks and other factors could result in the sudden change in the value of our stock.*

As a biopharmaceutical company, we have experienced significant volatility in our common stock. In 2005, our stock price ranged from a high of \$8.75 to a low of \$5.23. Factors that can contribute to such volatility may include: results and timing of preclinical studies and clinical trials; evidence of the safety or efficacy of pharmaceutical products; decisions by regulatory agencies that impact or may impact our product candidates; the results and timing of efforts by our partner or future partners to develop stents or other medical devices to deliver AP23573; announcements of new collaborations; announcements of new equity or debt financings; failure to enter into collaborations; our funding requirements; announcements

of technological innovations or new therapeutic products; developments relating to intellectual property rights, including licensing, litigation and governmental regulation and, in particular, our litigation with Lilly in the U.S. District Court and reexamination proceedings in the PTO with respect to the '516 Patent; healthcare or cost-containment legislation; general market trends for the biotechnology industry and related high-technology industries; the impact of exchange rates for the U.S. dollar; the impact of changing interest rates and policies of the Federal Reserve; and public policy pronouncements. These and other factors could have a significant impact on the value and volatility of our common stock in future periods.

*Raising additional capital by issuing securities or through collaboration and licensing arrangements may cause dilution to existing stockholders, restrict our operations or require us to relinquish proprietary rights.*

We may seek the additional capital necessary to fund our operations through public or private equity offerings, debt financings, and collaboration and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect our stockholders' rights. Under an existing loan agreement with a bank, we are required to maintain certain financial and non-financial covenants, including covenants limiting or restricting our ability to incur additional debt or declare dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

#### **ITEM 1B: UNRESOLVED STAFF COMMENTS**

We have received no written comments from the SEC staff regarding our periodic or current reports under the Securities Exchange Act of 1934, as amended, which comments remain unresolved.

#### **ITEM 2: PROPERTIES**

We have leased approximately 100,000 square feet (approximately 34,000 square feet currently under sublease to a third party) of laboratory and office space at 26 Landsdowne Street, Cambridge, Massachusetts. The lease originally had a ten-year term, which ended in July of 2002, with two consecutive five-year renewal options. We have extended the lease for the first five-year option period through July 2007. We believe that our currently leased facility will, in large part, be adequate for our research and development activities at least through the year 2007. We believe that any additional space we may require will be available on commercially reasonable terms.

#### **ITEM 3: LEGAL PROCEEDINGS**

##### **NF-κB Patent Infringement Litigation and Reexamination**

In 2002, we, together with Massachusetts Institute of Technology, The Whitehead Institute for Biomedical Research and Harvard University (collectively, the Plaintiffs) filed a lawsuit in the United States District Court for the District of Massachusetts, or the U.S. District Court, against Eli Lilly and Company, hereinafter referred to as Lilly, alleging infringement of certain claims, or the NF-κB '516 Claims, of the Plaintiffs' U.S. Patent No. 6,410,516, or the '516 Patent, covering methods of treating human disease by regulating NF-κB cell-signaling activity through sales of Lilly's osteoporosis drug, Evista®, and Lilly's septic shock drug, Xigris®, and seeking monetary damages from Lilly.

### *Re-examination Proceedings in PTO*

On April 4, 2005, Lilly filed an *ex parte* request in the United States Patent and Trademark Office, or PTO, to reexamine the patentability of certain claims of the '516 Patent. On June 8, 2005, the PTO mailed to counsel for the patentees of the '516 Patent its Order granting a reexamination of all of the claims of the '516 Patent. On August 4, 2005, counsel for the patentees of the '516 Patent filed a Petition requesting the PTO to vacate its Order granting reexamination of the '516 Patent and a Petition requesting the PTO to stay its reexamination, or Patentees' Petitions. On October 6, 2005, the PTO mailed to counsel for the patentees of the '516 Patent its Decision denying Patentees' Petitions, or PTO's October 6 Decision, whereupon, on November 25, 2005, counsel for the patentees filed a Request for Reconsideration of the PTO's October 6 Decision. On February 8, 2006, the PTO mailed to counsel for the patentees of the '516 Patent its Decision granting patentees' Request for Reconsideration and denying the relief sought by patentees thereunder.

In addition, an unrelated third party filed an *ex parte* request in the PTO on December 2, 2005 to reexamine the patentability of certain claims of the '516 Patent, or the Second Request. On December 12, 2005, the PTO mailed to counsel for the patentees of the '516 Patent its Order granting a reexamination based on this Second Request. On February 13, 2006, counsel for the patentees of the '516 Patent filed Petitions requesting the PTO to vacate its Order granting reexamination of the '516 Patent based on this Second Request and requesting the PTO to stay this reexamination.

### *Motions to Stay Litigation*

In connection with its request for reexamination of the '516 Patent, Lilly filed a motion in the U.S. District Court on April 4, 2005 requesting a stay of the NF- $\kappa$ B patent infringement litigation by the Court pending reexamination of the '516 Patent by the PTO. On June 6, 2005, the U.S. District Court denied Lilly's motion. On January 17, 2006, Lilly filed a renewed motion to stay pending reexamination of the '516 Patent by the PTO, which was denied by the U.S. District Court on February 13, 2006.

### *Trial and Pre-Trial Motions*

On December 23, 2005, Lilly filed two motions for summary judgment of invalidity. At a status conference held on March 9, 2006, the U.S. District Court confirmed that the trial would begin on April 10, 2006 and gave no indication as to when it would rule on the pending summary judgment motions. A pre-trial conference in this case is scheduled for April 5, 2006, with trial scheduled to commence on April 10, 2006.

The ultimate outcome of the request for reexamination and the litigation cannot be determined at this time, and, as a result, no determination can be made with respect to whether the PTO will allow the claims of the '516 Patent in the reexamination proceeding, nor can any determination be made with respect to the validity or infringement of the claims of the '516 Patent in the Lilly litigation, nor can an estimate of a damage award or range of awards in the Lilly litigation, if any, be made. If we prevail at trial in the Lilly litigation, any damages we may be awarded by the jury could be subsequently eliminated or limited by an adverse finding upon appeal or in the event that the claims of the '516 Patent are invalidated by the PTO.

### **ITEM 4: SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

No matters were submitted to a vote of security holders during the quarter ended December 31, 2005.

## PART II

### ITEM 5: MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

#### Market Information

Our common stock is traded on the Nasdaq National Market under the symbol "ARIA". The following table sets forth the high and low sales prices of our common stock as quoted on the Nasdaq National Market for the periods indicated.

	<u>High</u>	<u>Low</u>
<b>2005:</b>		
First Quarter	\$ 8.05	\$ 5.42
Second Quarter	7.40	5.23
Third Quarter	8.75	6.45
Fourth Quarter	7.73	5.52
<b>2004:</b>		
First Quarter	\$ 11.32	\$ 6.96
Second Quarter	13.74	6.75
Third Quarter	7.50	3.70
Fourth Quarter	7.63	5.25

On February 28, 2006, the last reported sale price of our common stock was \$6.71.

#### Stockholders

The approximate number of holders of record of our common stock as of February 28, 2006 was 480, and the approximate total number of beneficial holders of our common stock as of February 28, 2006 was 39,000.

#### Dividends

We have not declared or paid dividends on our common stock in the past and do not intend to declare or pay such dividends in the foreseeable future. Our long-term debt agreement prohibits the payment of cash dividends.

#### Unregistered Sales of Securities

Not applicable.

#### Issuer Purchases of Equity Securities

Not applicable.

## ITEM 6: SELECTED FINANCIAL DATA

The selected financial data set forth below as of December 31, 2005, 2004, 2003, 2002 and 2001 and for each of the years then ended have been derived from the audited consolidated financial statements of the Company, of which the financial statements as of December 31, 2005 and 2004 and for the years ended December 31, 2005, 2004 and 2003 are included elsewhere in this Annual Report on Form 10-K, and are qualified by reference to such financial statements. The information set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the audited consolidated financial statements, and the notes thereto, and other financial information included herein.

<i>In thousands, except share and per share data</i>	Years Ended December 31,				
	2005	2004	2003	2002	2001
<b>Consolidated Statements of Operations Data:</b>					
Revenue	\$ 1,217	\$ 742	\$ 660	\$ 67	\$ 4
Operating expenses:					
Research and development	45,916	27,711	14,889	23,018	16,587
General and administrative	12,261	9,442	5,547	5,718	4,469
Operating expenses	58,177	37,153	20,436	28,736	21,056
Loss from operations	(56,960)	(36,411)	(19,776)	(28,669)	(21,052)
Other income (expense):					
Interest income	1,900	1,110	353	615	1,578
Interest expense	(422)	(272)	(303)	(323)	(285)
Other income - tax refund				534	
Other income (expense), net	1,478	838	50	826	1,293
Net loss	\$ (55,482)	\$ (35,573)	\$ (19,726)	\$ (27,843)	\$ (19,759)
Net loss per share	\$ (0.99)	\$ (0.69)	\$ (0.51)	\$ (0.86)	\$ (0.68)
Weighted average number of shares of common stock outstanding	56,283,948	51,294,160	39,036,073	32,475,083	29,256,767

<i>In thousands</i>	As of December 31,				
	2005	2004	2003	2002	2001
<b>Consolidated Balance Sheet Data:</b>					
Cash, cash equivalents and marketable securities	\$ 81,516	\$ 75,506	\$ 66,740	\$ 26,850	\$ 47,186
Working capital	65,971	68,874	61,587	21,126	43,249
Total assets	96,174	87,189	74,284	35,104	55,361
Long-term debt	5,735	7,655	6,575	5,437	6,847
Accumulated deficit	(247,098)	(191,616)	(156,043)	(136,317)	(108,474)
Stockholders' equity	71,378	67,440	59,326	21,852	43,093

## 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 "Selected Financial Data" and our consolidated financial statements and the related notes included elsewhere in this report.*

### Overview

We are engaged in the discovery and development of breakthrough medicines to treat cancers by regulating cell signaling with small molecules. We are developing a comprehensive approach to patients with cancer that addresses the greatest medical need – aggressive and advanced-stage cancers for which current treatments are inadequate. Our goal is to build a fully integrated oncology company focused on novel, molecularly targeted therapies to treat solid tumors and hematologic cancers, as well as the spread of primary tumors to distant sites.

Our lead cancer product candidate, AP23573, has been or is being studied in multiple clinical trials in patients with various types of cancers, including sarcomas, hormone refractory prostate cancer, endometrial cancer, brain cancer and leukemias and lymphomas. Medinol Ltd. is also developing stents to deliver AP23573 to prevent reblockage at sites of vascular injury following stent-assisted angioplasty.

We have a focused drug discovery program centered on small-molecule, molecularly targeted therapies and cell-signaling pathways implicated in cancer. We also have an exclusive license to pioneering technology and patents related to certain NF- $\kappa$ B cell-signaling activity, which may be useful in treating certain diseases. Additionally, we have developed a proprietary portfolio of cell-signaling regulation technologies, our ARGENT technology, to control intracellular processes with small molecules, which may be useful in the development of therapeutic vaccines and gene and cell therapy products, and which provide versatile tools for applications in cell biology, functional genomics and drug discovery research.

Since our inception in 1991, we have devoted substantially all of our resources to our research and development programs. We receive no revenue from the sale of pharmaceutical products, and most of our revenue to date was received in connection with a joint venture we had with a major pharmaceutical company from 1997 to 1999. Except for the gain on the sale of our fifty percent interest in that joint venture in December 1999, which resulted in net income for fiscal 1999, we have not been profitable since inception. We expect to incur substantial and increasing operating losses for the foreseeable future, primarily due to costs associated with our pharmaceutical product development programs, including costs for clinical trials and product manufacturing, personnel and our intellectual property. We expect that losses will fluctuate from quarter to quarter and that these fluctuations may be substantial. As of December 31, 2005, we had an accumulated deficit of \$247.1 million and cash, cash equivalents and marketable securities of \$81.5 million and working capital of \$66.0 million.

### General

Our operating losses are primarily due to the costs associated with our pharmaceutical product development programs, personnel and intellectual property protection and enforcement. As our product development programs progress, we incur significant costs for toxicology and pharmacology studies, product development, manufacturing, clinical trials and regulatory support. These costs can vary significantly from quarter to quarter depending on the number of product candidates in development, the stage of development of each product candidate, the number of patients enrolled in and complexity of clinical trials and other factors. Costs associated with our intellectual property include legal fees and other costs to prosecute, maintain, protect and enforce our intellectual property, which can fluctuate from quarter to quarter depending on the status of patent issues being pursued.

Because we currently receive no revenue from the sale of pharmaceutical products and receive only limited license revenue, we have relied primarily on the capital markets as our source of funding. In March 2004 and August 2005, we raised approximately \$40.0 million and \$57.9 million, respectively, through underwritten public offerings of our common stock. We also utilize long-term debt to supplement our funding, particularly as a means to fund investment in property and equipment and infrastructure needs. In addition, we may seek funding from collaborations with pharmaceutical, biotechnology and/or medical device companies for development and commercialization of our product candidates. These collaborations may take the form of licensing arrangements, co-development or joint venture arrangements or other structures. If funding from these various sources is unavailable on reasonable terms, we may be required to reduce our operating expenses in order to conserve cash and capital by delaying, scaling back or eliminating one or more of our product development programs.

### **Critical Accounting Policies and Estimates**

Our financial position and results of operations are affected by subjective and complex judgments, particularly in the areas of the carrying value of intangible assets, deferred compensation benefits for executives, and stock-based compensation to consultants.

At December 31, 2005, we reported \$4.6 million of intangible assets consisting of capitalized costs related primarily to purchased and issued patents, patent applications and licenses, net of accumulated amortization. These costs are being amortized over the estimated useful lives of the underlying patents or licenses. Changes in these lives or a decision to discontinue using the technologies could result in material changes to our balance sheet and statements of operations. For example, during 2005 and 2004, we expensed \$43,000 and \$87,000, respectively, of unamortized costs related to certain intangible assets which we are not actively pursuing any longer. We have concluded that the carrying value of our remaining intangible assets is not currently impaired because such assets are utilized in our product development programs and/or continue to be viable technologies for collaborations or licensing efforts which we continue to pursue. If we were to abandon the underlying technologies or terminate our efforts to pursue collaborations or license agreements, we may be required to write off a portion of the carrying value of our intangible assets. The net book value as of December 31, 2005 of intangible assets related to our NF- $\kappa$ B technology is \$456,000. If the patentability of our NF- $\kappa$ B patents is successfully challenged and such patents are subsequently narrowed, invalidated or circumvented, we may be required to write off some or all of the net book value related to such technology.

In determining expense related to stock-based compensation to consultants, recorded balances are adjusted at each reporting period to reflect fair value utilizing the Black-Scholes option pricing model that takes into account, among other things, the price and volatility of our common stock, a risk-free discount rate, and an estimate of the life of the option contract. In addition, under our deferred executive compensation plans, we are required to adjust our recorded obligations to our employees on a periodic basis to reflect fair value based on the value of certain underlying mutual funds. Fluctuations in those factors can result in uneven expense charges or credits to our statements of operations. If, for example, the market prices of the underlying securities in our deferred executive compensation plans were 10% higher at December 31, 2005, we would have recognized an additional \$133,000 in compensation expense in 2005. Similarly, if the price and volatility of our common stock were 10% greater as of December 31, 2005, we would have recognized an increase of \$4,000 in stock-based compensation to consultants in 2005.

## Results of Operations

### *Years Ended December 31, 2005 and 2004*

#### *Revenue*

We recognized license revenue of \$1.2 million for the year ended December 31, 2005 compared to \$742,000 for the year ended December 31, 2004. The increase in license revenue was due primarily to a license agreement we signed in January 2005 with Medinol to develop and commercialize stents and other medical devices to deliver our lead product candidate, AP23573, to prevent reblockage of injured vessels following stent-assisted angioplasty.

#### *Operating Expenses*

##### *Research and Development Expenses*

Research and development expenses increased by \$18.2 million, or 66%, from \$27.7 million in 2004 to \$45.9 million in 2005. The research and development process necessary to develop a pharmaceutical product for commercialization is subject to extensive regulation by numerous governmental authorities in the United States and other countries. This process typically takes years to complete and requires the expenditure of substantial resources. Current requirements include:

- preclinical toxicology, pharmacology and metabolism studies, as well as *in vivo* efficacy studies in relevant animal models of disease;
- manufacturing of drug product for preclinical studies and clinical trials and ultimately for commercial supply;
- submission of the results of preclinical studies and information regarding manufacturing and control and proposed clinical protocol to the FDA in an Investigational New Drug application, or IND, (or similar filings with regulatory agencies outside the United States);
- conduct of clinical trials designed to provide data and information regarding the safety and efficacy of the product candidate in humans; and
- submission of all the results of testing to the FDA in a New Drug Application, or NDA, (or similar filings with regulatory agencies outside the United States).

Upon approval by the appropriate regulatory authorities, including in some countries approval of product pricing, we may commence commercial marketing and distribution of the product.

We group our research and development, or R&D, expenses into two major categories: direct external expenses and all other R&D expenses. Direct external expenses consist of costs of outside parties to conduct laboratory studies, to develop manufacturing processes and manufacture product candidates, to conduct and manage clinical trials and similar costs related to our clinical and preclinical studies. These costs are accumulated and tracked by product candidate. All other R&D expenses consist of costs to compensate personnel, to purchase lab supplies and services, to lease, operate and maintain our facility, equipment and overhead and similar costs of our research and development efforts. These costs apply to work on our clinical and preclinical candidates as well as our discovery research efforts. These costs are not tracked by product candidate because the number of product candidates and projects in R&D may vary from time to time and because we utilize internal resources across multiple projects at the same time.

Direct external expenses are further categorized as costs for clinical programs and costs for preclinical programs. Preclinical programs include product candidates undergoing toxicology, pharmacology, metabolism and efficacy studies and manufacturing process development required before testing in humans can begin. Product candidates are designated as clinical programs once we have filed an IND with the FDA, or a similar filing with regulatory agencies outside the United States, for the purpose of commencing clinical trials in humans.

Our R&D expenses for 2005 as compared to 2004 were as follows:

<i>In thousands</i>	Year ended December 31,		Increase/ (decrease)
	2005	2004	
Direct external expenses:			
Clinical programs	\$ 26,311	\$ 11,542	\$ 14,769
Preclinical programs	1,142	3,494	(2,352)
All other R&D expenses	18,463	12,675	5,788
	<u>\$ 45,916</u>	<u>\$ 27,711</u>	<u>\$ 18,205</u>

AP23573, our lead product candidate which is in Phase 2 clinical trials, was our only clinical program in 2005 and 2004. Direct external expenses for AP23573 increased by \$14.8 million in 2005 as compared to 2004 due primarily to increases in clinical trial costs (\$10.9 million) and manufacturing-related costs (\$3.5 million). In 2005, we continued to enroll patients in our existing clinical trials of AP23573 and initiated new clinical trials in additional disease indications, including prostate and endometrial cancer. The increase in clinical trial costs is directly related to the increased enrollment, the costs of evaluating enrolled patients, the costs of managing the trials, laboratory costs and the costs of compiling and analyzing results obtained in the trials. Manufacturing costs include product and process development work, as well as the costs to produce drug product. Manufacturing costs for AP23573 increased in 2005 as compared to 2004 due to an increase in the quantities of drug product manufactured for the clinical trials and investments in manufacturing process development. Through December 31, 2005, we have incurred a total of approximately \$40.4 million in direct external expenses for AP23573 from the date it became a clinical program. We expect that our direct external costs for AP23573 will increase in 2006 as we continue to manage our clinical trials and incur the related costs of manufacturing and other costs to support such trials for this product candidate.

Preclinical programs consist primarily of our oncogenic kinase inhibitor program and our bone-targeted mTOR inhibitor program. Direct external expenses on preclinical programs will increase or decrease over time depending on the status and number of programs in this stage of development and the mix between external and internal efforts applied to such programs. Direct external expenses for preclinical programs decreased by \$2.4 million in 2005 as compared to 2004 due primarily to the completion of certain pharmacology and toxicology studies conducted by outside contract laboratories in 2004, as well as expansion of internal efforts on these programs in 2005. We expect that our direct external expenses for preclinical programs will increase in 2006, as resources allow, as we continue to move these programs forward in development.

All other R&D expenses increased by \$5.8 million in 2005 as compared to 2004 due to higher personnel and related costs (\$2.6 million) as a result of an increase in the number of personnel and salary adjustments, an increase in depreciation and amortization costs related to our property and equipment (\$1.9 million) due to the impact of capital improvements and purchases in 2004 and 2005, an increase in laboratory supplies and services (\$506,000) related to ongoing development of our clinical and preclinical programs and miscellaneous increases in costs related to our facility, including maintenance and utility costs. We expect that all other R&D expenses will increase in 2006 in support of the expanding activity in our clinical and preclinical programs.

The successful development of our products is uncertain and subject to a number of risks. We cannot be certain that any of our product candidates will prove to be safe and effective or will meet all of the applicable regulatory requirements needed to receive and maintain marketing approval. Data from preclinical studies and clinical trials are susceptible to varying interpretations that could delay, limit or prevent regulatory clearance. We, the FDA or other regulatory authorities may suspend clinical trials at any time if we or they believe that the subjects participating in such trials are being exposed to unacceptable risks or if such regulatory agencies find deficiencies in the conduct of the trials or other problems with our products under development. Delays or rejections may be encountered based on additional governmental regulation, legislation, administrative action or changes in FDA or other regulatory policy during development or the review process. Other risks associated with our product development programs are described in Part I, Item 1A: Risk Factors. Due to these uncertainties, accurate and meaningful estimates of the ultimate cost to bring a product to market, the timing of completion of any of our drug development programs and the period in which material net cash inflows from any of our drug development programs will commence are unavailable.

#### *General and Administrative Expenses*

General and administrative expenses increased by \$2.8 million, or 30%, from \$9.4 million in 2004 to \$12.3 million in 2005. Professional fees increased by \$3.2 million to \$7.4 million in 2005 as compared to \$4.2 million in 2004 due primarily to costs related to expansion of business and commercial development initiatives and to our patent infringement litigation with Lilly. This increase was offset in part by a decrease in expenses related to a restricted stock grant to our chief executive officer in January 2004 which was fully amortized by December 31, 2004. We expect that our general and administrative expenses will increase in 2006 as necessary to support our research and development programs.

We expect that our operating expenses in total will increase in 2006 for the reasons described above, and such increase could be substantial. In addition, we expect that our R&D expenses and our general and administrative expenses will increase in 2006 due to the adoption of SFAS No. 123(R), *Share-Based Payment*, pursuant to which we will begin to recognize expenses in 2006 related to stock options and other share-based payments to employees. Operating expenses may fluctuate from quarter to quarter. The actual amount of any increase in operating expenses will depend on the progress of our product development programs, including preclinical and clinical studies and product manufacturing, the status of our patent infringement litigation with Lilly and our ability to raise funding through equity offerings, collaborations, licensing, joint ventures or other sources.

#### *Interest Income/Expense*

Interest income increased by 71% to \$1.9 million in 2005 from \$1.1 million in 2004, as a result of higher interest yields from our securities, offset in part by a lower average balance of funds invested in 2005.

Interest expense increased by 55% to \$422,000 in 2005 from \$272,000 in 2004, as a result of higher interest rates and higher average loan balances in 2005.

#### *Operating Results*

We reported a loss from operations of \$57.0 million in 2005 compared to a loss from operations of \$36.4 million in 2004, an increase in loss of \$20.5 million, or 56%. We expect that our loss from operations will increase in 2006 due to the expected increases in R&D expenses and general and administrative expenses described above. Losses may fluctuate depending on the extent to which, if at all, we enter into collaborations or partnerships for one or more of our product candidates or licenses for our technologies. The extent of operating losses will also depend on our ability to raise funds from other sources, such as

the capital markets, which will influence the amount we will spend on research and development and the development timelines for our product candidates.

We reported a net loss of \$55.5 million in 2005 compared to a net loss of \$35.6 million in 2004, an increase in net loss of \$19.9 million or 56%, and a net loss per share of \$0.99 and \$0.69 in 2005 and 2004, respectively.

*Years Ended December 31, 2004 and 2003*

*Revenue*

We recognized license revenue of \$742,000 for the year ended December 31, 2004 compared to \$660,000 for the year ended December 31, 2003. The increase in license revenue was due to license agreements into which we entered during this period related to our NF-κB technology and our ARGENT cell-signaling regulation technology.

*Operating Expenses*

*Research and Development Expenses*

R&D expenses increased by \$12.8 million, or 86%, from \$14.9 million in 2003 to \$27.7 million in 2004. Our R&D expenses for 2004 as compared to 2003 were as follows:

<i>In thousands</i>	<u>Year ended December 31,</u>		<u>Increase/ (decrease)</u>
	<u>2004</u>	<u>2003</u>	
Direct external expenses:			
Clinical programs	\$ 11,542	\$ 2,540	\$ 9,002
Preclinical programs	3,494	1,246	2,248
All other R&D expenses	12,675	11,103	1,572
	<u>\$ 27,711</u>	<u>\$ 14,889</u>	<u>\$ 12,822</u>

AP23573 was our only clinical program in 2004 and 2003. Direct external expenses for AP23573 increased by \$9.0 million in 2004 as compared to 2003 due primarily to increases in clinical trial costs (\$3.3 million) and manufacturing-related costs (\$4.6 million). In 2004, we continued to manage our ongoing Phase 1 trials of AP23573, initiated additional Phase 1 trials and commenced enrollment of patients in Phase 2 trials. The increase in clinical trial costs is directly related to the initiation of trials, increased enrollment, the costs of evaluating enrolled patients, the costs of managing the trials, laboratory costs and the costs of compiling and analyzing results obtained in the trials. Manufacturing costs include product and process development work, as well as the costs to produce drug product. Manufacturing costs for AP23573 increased significantly in 2004 due to an increase in the quantities of drug product manufactured for the clinical trials and investments in manufacturing process development.

Preclinical programs consist primarily of our oncogenic kinase inhibitor program and our bone-targeted mTOR inhibitor program. Direct external expenses on preclinical programs will increase or decrease over time depending on the status and number of programs in this stage of development. Direct external expenses for preclinical programs increased by \$2.2 million in 2004 as compared to 2003 due to pharmacology and toxicology studies conducted by outside contract laboratories, particularly in the first half of 2004, as well as product and process development efforts for these product candidates.

All other R&D expenses increased by \$1.6 million in 2004 as compared to 2003 due to higher personnel and related costs (\$1.4 million) as a result of an increase in the number of personnel and salary adjustments, and miscellaneous increases in supplies, consulting fees, equipment maintenance costs and

travel-related expenses in support of our research and development programs. Increases in these expenses were partially offset by decreases in write-offs of capitalized license and patent costs (\$433,000) and termination or buy-out of equipment leases in 2003 (\$229,000).

#### *General and Administrative Expenses*

General and administrative expenses increased 70% to \$9.4 million in 2004 from \$5.5 million in 2003. Professional fees increased by \$2.3 million to \$4.2 million in 2004 as compared to \$1.9 million in 2003 due primarily to costs related to our patent infringement litigation with Lilly and to business development and other corporate initiatives, including compliance with the internal control requirements of the Sarbanes-Oxley Act of 2002. The increase in general and administrative expenses was also due to the awarding in January 2004 of restricted stock grants, to our chief executive officer and each of the other members of our Board of Directors. In 2004, we recorded an expense of \$1.3 million related to these awards. Other increases in general and administrative expenses included salary adjustments, the cost of awards under our deferred executive compensation plan, and miscellaneous increases in insurance, state taxes and travel-related expenses.

#### *Interest Income/Expense*

Interest income increased by 214% to \$1.1 million in 2004 from \$353,000 in 2003, primarily as a result of a higher level of funds invested in 2004.

Interest expense decreased by 10% to \$272,000 in 2004 from \$303,000 in 2003, primarily as a result of lower average loan balances in 2004.

#### *Operating Results*

We reported a loss from operations of \$36.4 million in 2004 compared to a loss from operations of \$19.8 million in 2003, an increase in loss of \$16.6 million, or 84%.

We reported a net loss of \$35.6 million in 2004 compared to a net loss of \$19.7 million in 2003, an increase in net loss of \$15.9 million or 80%, and a net loss per share of \$0.69 and \$0.51 in 2004 and 2003, respectively.

#### **Selected Quarterly Financial Data**

Summarized unaudited quarterly financial data are as follows:

*In thousands, except per share amounts*

	<u>2005 Quarters</u>			
	<u>First</u>	<u>Second</u>	<u>Third</u>	<u>Fourth</u>
Total license revenue	\$ 304	\$ 350	\$ 321	\$ 242
Net loss	(12,346)	(14,083)	(14,594)	(14,459)
Net loss per share	(0.23)	(0.27)	(0.25)	(0.23)

	<u>2004 Quarters</u>			
	<u>First</u>	<u>Second</u>	<u>Third</u>	<u>Fourth</u>
Total license revenue	\$ 190	\$ 188	\$ 185	\$ 179
Net loss	(6,235)	(9,245)	(9,379)	(10,714)
Net loss per share	(0.13)	(0.18)	(0.18)	(0.20)

## Liquidity and Capital Resources

We have financed our operations and investments primarily through offerings of our common stock and, to a lesser extent, through issuances of our common stock pursuant to our stock option and employee stock purchase plans, supplemented by the issuance of long-term debt. We sell securities and incur debt when the terms of such transactions are deemed favorable by us and as necessary to fund our current and projected cash needs. We seek to balance the level of cash, cash equivalents and marketable securities on hand with our projected needs and to allow us to withstand periods of uncertainty relative to the availability of funding on favorable terms.

### Sources of Funds

During the years ended December 31, 2005, 2004 and 2003, our sources of funds were as follows:

<i>In thousands</i>	Year ended December 31,		
	2005	2004	2003
Sales/issuances of common stock:			
In common stock offerings	\$ 57,860	\$ 40,001	\$ 56,180
Pursuant to stock option and employee stock purchase plans	970	2,382	964
Proceeds from long-term borrowings	-	3,000	9,500
	<u>\$ 58,830</u>	<u>\$ 45,383</u>	<u>\$ 66,644</u>

The amount of funding we raise through sales of our common stock depends on many factors, including, but not limited to, the status and progress of our product development programs, projected cash needs, availability of funding from other sources, our stock price and the status of the capital markets. In 2003, we completed three offerings of our common stock and realized net proceeds of \$56.2 million. In 2004 and 2005, we completed underwritten offerings of our common stock for net proceeds of \$40.0 million and \$57.9 million, respectively. The following table details our common stock offerings in 2003, 2004 and 2005:

	Number of Shares	Price Per Share	Net Cash Proceeds <i>In thousands</i>
<b>2003</b>			
May	4,000,000	\$ 2.50	\$ 9,338
October	6,438,113	6.35	38,094
December	<u>1,175,375</u>	8.00	<u>8,748</u>
	<u>11,613,488</u>		<u>\$ 56,180</u>
<b>2004</b>			
March	<u>5,060,000</u>	8.50	<u>\$ 40,001</u>
<b>2005</b>			
August	<u>8,625,000</u>	7.20	<u>\$ 57,860</u>

We have filed shelf registration statements with the SEC, from time to time, to ensure that we have registered shares of our common stock available for sale, giving us the opportunity to raise funding when terms are favorable. On December 19, 2003, we filed a shelf registration statement with the SEC for the issuance of up to 7,000,000 shares of our common stock, which was declared effective on January 9, 2004. As of December 31, 2005, after selling 5,060,000 of these shares in our March 2004 offering, we have 1,940,000 shares available for issuance under this shelf registration. On February 18, 2005, we filed another shelf registration statement with the SEC which was amended on March 11, 2005 for the issuance of up to 9,500,000 shares of our common stock. This filing was declared effective on March 14, 2005. As

of December 31, 2005, after selling 8,625,000 of these shares in our August 2005 offering, we have 875,000 shares available for issuance under this shelf registration.

In March 2003, we entered into a term loan agreement with a bank for \$7.5 million, the proceeds of which were used to repay existing long-term debt, to pay off our obligations under certain operating leases for equipment and for general working capital purposes. The loan is secured by all of our assets excluding intellectual property, which we have agreed not to pledge to any other party. The loan carries interest at the bank's prime rate or LIBOR plus 2%. We amended the terms of the loan on December 31, 2003 and December 31, 2004, receiving another \$2.0 million and \$3.0 million, respectively, in loan proceeds. The amended loan is payable in monthly installments of \$160,000 plus interest beginning in January 2005 with a final payment of \$3.5 million due in March 2008. The terms of the loan require us to maintain at least \$13.0 million in unrestricted cash, cash equivalents and investments. The agreement also contains certain covenants that restrict additional indebtedness, additional liens, and sales of assets, and dividends, distributions or repurchases of common stock. The balance outstanding as of December 31, 2005 was \$7,655,000.

### *Uses of Funds*

The primary uses of our cash are to fund our operations and working capital requirements and, to a lesser degree, to repay our long-term borrowings and invest in intellectual property and property and equipment as needed for our business. Our uses of cash during the years ended December 31, 2005, 2004 and 2003 were as follows:

<i>In thousands</i>	<b>Year ended December 31,</b>		
	<b>2005</b>	<b>2004</b>	<b>2003</b>
Net cash used in operating activities	\$ 44,556	\$ 31,559	\$ 18,014
Repayment of long-term borrowings	1,920	1,800	8,040
Investment in intangible assets	675	730	507
Investment in property and equipment	6,538	2,743	307
	<u>\$ 53,689</u>	<u>\$ 36,832</u>	<u>\$ 26,868</u>

The net cash used in operating activities is comprised of our net losses and working capital requirements. As noted above, our net loss increased in 2004 and 2005 due primarily to the increased costs of advancing our product candidates through preclinical and clinical phases of development. Also as noted above, we expect that our loss from operations will increase in 2006 due to continued progress in development of our product candidates, and we expect that our net cash used in operations will increase accordingly. We expect that our investment in intangible assets, consisting of our intellectual property, will increase in 2006 in support of our product development activities. Our investment in property and equipment increased in 2005 primarily due to a renovation project to create more useable space in our facility and an upgrade to our information technology infrastructure. We expect that our investment in property and equipment will decrease in 2006.

### **Contractual Obligations**

We have substantial fixed contractual obligations under various research and licensing agreements, consulting and employment agreements, lease agreements and long-term debt instruments. These contractual obligations were comprised of the following as of December 31, 2005:

*In thousands*

	<u>Total</u>	<u>Payments Due By Period</u>			
		<u>In 2006</u>	<u>2007 through 2009</u>	<u>2010 through 2011</u>	<u>After 2011</u>
Long-term debt	\$ 7,655	\$ 1,920	\$ 5,735	\$	\$
Operating leases	871	550	321		
Other long-term obligations	<u>14,948</u>	<u>4,800</u>	<u>8,527</u>	<u>1,226</u>	<u>395</u>
	<u>\$ 23,474</u>	<u>\$ 7,270</u>	<u>\$ 14,583</u>	<u>\$ 1,226</u>	<u>\$ 395</u>

Long-term debt consists of scheduled principal payments on such debt. Interest on our long-term debt is based on variable interest rates. Assuming a constant interest rate of 6.28%, our average interest rate on our debt at December 31, 2005, over the remaining term of the debt, our interest expense would total approximately \$420,000 in 2006 and \$357,000 in the period 2007 through 2009.

Other long-term obligations are comprised primarily of employment agreements, obligations under our deferred executive compensation plans and license agreements. The license agreements generally provide for payment by us of annual license fees, milestone payments and royalties upon successful commercialization of products. All license agreements are cancelable by us. The above table reflects remaining license fees for the lives of the agreements but excludes milestone and royalty payments, as such amounts are not probable or estimable at this time.

### **Liquidity**

At December 31, 2005, we had cash, cash equivalents and marketable securities totaling \$81.5 million and working capital of \$66.0 million, compared to cash, cash equivalents and marketable securities totaling \$75.5 million and working capital of \$68.9 million at December 31, 2004.

We will require substantial additional funding for our research and development programs, including preclinical development and clinical trials, for operating expenses including intellectual property protection and enforcement, for the pursuit of regulatory approvals, and for establishing manufacturing, marketing and sales capabilities. In order to fund our needs, we may (1) sell common stock through public or private offerings as market conditions permit, (2) enter into partnerships for our product candidates, and/or (3) license our cell-signaling technologies, including our ARGENT and NF- $\kappa$ B intellectual property. We have available 2,815,000 shares of our common stock under currently effective shelf registration statements, which may be sold to raise funding.

We believe that our cash, cash equivalents and marketable securities should be sufficient to satisfy our capital and operating requirements into mid 2007. However, there are numerous factors that are likely to affect our spending levels, including the timing of the start of the initial registration trial for AP23573, the timing of product and process development work for AP23573, the manufacture of drug product for clinical trials and potential product launch, if approved, developments in our ongoing clinical trials, the timing and terms of a partnership, if any, to commercialize AP23573 outside of the U.S., the status of our in-house efforts to prepare for the potential launch of AP23573 in the U.S., the progress of our preclinical programs, and developments in our NF- $\kappa$ B litigation, among other factors. These variables could result in earlier depletion of our current funds. In any event, we expect to need additional funding in order to pursue our business plan, which we will seek to raise through the sale of additional securities, collaborative partnerships, and possible additional credit arrangements. There can be no assurance, however, that adequate resources will be available when needed or on terms acceptable to us.

## Recently Issued Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board, or FASB, issued SFAS No. 123(R), *Share-Based Payment*, which revised SFAS No. 123 and superseded APB Opinion No. 25, *Accounting for Stock Issued to Employees*. SFAS No. 123(R) requires that companies recognize compensation expense associated with grants of stock options and other equity instruments to employees in the financial statements, effective as of the first annual reporting period that begins after June 15, 2005. Compensation cost will be measured based on the fair value of the instrument on the grant date and will be recognized over the vesting period. This pronouncement applies to all grants after the effective date and to the unvested portion of stock options outstanding as of the effective date. SFAS No. 123(R) eliminates the ability to account for such transactions using the intrinsic method currently used by us. We are required to adopt SFAS No. 123(R) as of January 1, 2006. We expect to adopt SFAS 123(R) using the modified prospective application method. Assuming the continuation of current programs, our estimate of stock compensation expense for 2006 is in the range of \$4.5 million to \$5.0 million. SFAS No. 123(R) also requires that companies recognize compensation expense associated with purchases of shares of common stock by employees at a discount to market value under employee stock purchase plans that meet certain criteria. The impact of this requirement on the Company's consolidated financial statements is not expected to be material.

## ITEM 7A: QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We invest our available funds in accordance with our investment policy to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. Our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure to any single issue, issuer or type of investment.

We invest cash balances in excess of operating requirements first in short-term, highly liquid securities, with original maturities of 90 days or less, and money market accounts. Depending on our level of available funds and our expected cash requirements, we may invest a portion of our funds in marketable securities, consisting generally of corporate debt and U.S. government and agency securities. Maturities of our marketable securities are generally limited to periods necessary to fund our liquidity needs and may not in any case exceed three years. These securities are classified as available-for-sale. Available-for-sale securities are recorded on the balance sheet at fair market value with unrealized gains or losses reported as a separate component of stockholders' equity (accumulated other comprehensive income or loss). Realized gains and losses on marketable security transactions are reported on the specific-identification method. Interest income is recognized when earned. A decline in the market value of any available-for-sale security below cost that is deemed other than temporary results in a charge to earnings and establishes a new cost basis for the security.

Our investments are sensitive to interest rate risk. We believe, however, that the effect, if any, of reasonably possible near-term changes in interest rates on our financial position, results of operations and cash flows generally would not be material due to the current short-term nature of these investments. In particular, at December 31, 2005, because our available funds were invested solely in cash equivalents and short-term marketable securities with maturities of 12 months or less, our risk of loss due to changes in interest rates is not material.

We have an executive compensation plan which provides participants an option to purchase certain designated mutual funds at a discount. These deferred compensation arrangements are accounted for as derivatives under SFAS No. 133. The fair value of the derivatives is reflected as a liability on our balance sheet. Effective October 1, 2005, we adopted a new executive compensation plan that defers the payment of annual bonus awards to future periods as specified in each award. We accrue a liability based on the fair value of the awards ratably over the vesting period. The fair value of such awards is increased or

decreased based on the actual total return of certain underlying mutual funds. As of December 31, 2005, in the event of a hypothetical 10% increase (decrease) in the fair market value of the underlying mutual funds, we would incur approximately \$133,000 of additional (reduced) compensation expense.

At December 31, 2005, we had \$7.7 million outstanding under a bank term note which bears interest at prime or, alternatively, LIBOR +2%. This note is sensitive to changes in interest rates. In the event of a hypothetical 10% increase in the interest rate on which the loan is based (63 basis points at December 31, 2005), we would incur approximately \$42,000 of additional interest expense in 2006.

### **Certain Factors That May Affect Future Results of Operations**

The SEC encourages companies to disclose forward-looking information so that investors can better understand a company's future prospects and make informed investment decisions. This Annual Report on Form 10-K contains such "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be made directly in this Annual Report, and they may also be made a part of this Annual Report by reference to other documents filed with the SEC, which is known as "incorporation by reference."

Such statements in connection with any discussion of future operating or financial performance may be identified by use of words such as "may," "anticipate," "estimate," "expect," "project," "intend," "plan," "believe," and other words and terms of similar meaning. Such statements are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such forward-looking statements. These risks include, but are not limited to, risks and uncertainties regarding our ability to accurately estimate the timing and actual R&D expenses and other costs associated with the preclinical and clinical development and manufacture of our product candidates, the adequacy of our capital resources and the availability of additional funding, risks and uncertainties regarding our ability to manufacture or have manufactured our product candidates on a commercial scale, risks and uncertainties regarding our ability to successfully enroll and conduct clinical studies of product candidates, risks and uncertainties that clinical trial results at any phase of development may be adverse or may not be predictive of future results or lead to regulatory approval of any of our or any partner's product candidates, risks and uncertainties of third-party intellectual property claims relating to our and any partner's product candidates, and risks and uncertainties relating to regulatory oversight, the timing, scope, cost and outcome of legal proceedings, including litigation concerning our NF- $\kappa$ B patent portfolio, future capital needs, key employees, dependence on collaborators and manufacturers, markets, economic conditions, products, services, prices, reimbursement rates, competition and other factors. Please also see the discussion under Part I, Item 1A: Risk Factors appearing elsewhere in this Annual Report for more details regarding these and other risks.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this Annual Report or in any document incorporated by reference might not occur. Stockholders are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this report or the date of the document incorporated by reference in this Annual Report. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

## ITEM 8: FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

### Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of  
ARIAD Pharmaceuticals, Inc.:

We have audited the accompanying consolidated balance sheets of ARIAD Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2005. 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, such consolidated financial statements present fairly, in all material respects, the financial position of ARIAD Pharmaceuticals, Inc. and subsidiaries as of December 31, 2005 and 2004, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2005, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of the Company's internal control over financial reporting as of December 31, 2005, based on the criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission, and our report dated March 13, 2006 expressed an unqualified opinion on management's assessment of the effectiveness of the Company's internal control over financial reporting and an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts  
March 13, 2006

**ARIAD PHARMACEUTICALS, INC. AND SUBSIDIARIES**  
**CONSOLIDATED BALANCE SHEETS**

	December 31,	
	2005	2004
<i>In thousands, except share and per share data</i>		
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 25,453	\$ 18,556
Marketable securities	56,063	56,950
Inventory and other current assets	2,225	1,965
Total current assets	83,741	77,471
Property and equipment:		
Leasehold improvements	17,840	12,693
Equipment and furniture	9,908	6,525
Construction in progress		2,049
Total	27,748	21,267
Less accumulated depreciation and amortization	(20,022)	(18,031)
Property and equipment, net	7,726	3,236
Intangible and other assets, net	4,707	6,482
Total assets	\$ 96,174	\$ 87,189
 <b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 3,961	\$ 2,129
Current portion of long-term debt	1,920	1,920
Accrued compensation and benefits	497	310
Accrued product development expenses	8,444	2,934
Other accrued expenses	2,097	591
Current portion of deferred revenue	851	713
Total current liabilities	17,770	8,597
Long-term debt	5,735	7,655
Deferred revenue	24	404
Deferred executive compensation	1,267	3,093
Commitments, contingent liabilities and minority interest (Notes 1, 6, 7, 10)		
Stockholders' equity:		
Preferred stock, authorized, 10,000,000 shares, none issued and outstanding		
Common stock, \$.001 par value, authorized, 145,000,000 shares, issued and outstanding, 61,698,129 shares in 2005, 52,688,673 shares in 2004	62	53
Additional paid-in capital	318,684	259,122
Deferred compensation	(246)	(58)
Accumulated other comprehensive loss	(24)	(61)
Accumulated deficit	(247,098)	(191,616)
Total stockholders' equity	71,378	67,440
Total liabilities and stockholders' equity	\$ 96,174	\$ 87,189

See notes to consolidated financial statements.

**ARIAD PHARMACEUTICALS, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**

<i>In thousands, except share and per share data</i>	Years Ended December 31,		
	2005	2004	2003
License revenue	\$ <u>1,217</u>	\$ <u>742</u>	\$ <u>660</u>
Operating expenses:			
Research and development	45,916	27,711	14,889
General and administrative	<u>12,261</u>	<u>9,442</u>	<u>5,547</u>
Operating expenses	<u>58,177</u>	<u>37,153</u>	<u>20,436</u>
Loss from operations	<u>(56,960)</u>	<u>(36,411)</u>	<u>(19,776)</u>
Other income (expense):			
Interest income	1,900	1,110	353
Interest expense	<u>(422)</u>	<u>(272)</u>	<u>(303)</u>
Other income, net	<u>1,478</u>	<u>838</u>	<u>50</u>
Net loss	\$ <u>(55,482)</u>	\$ <u>(35,573)</u>	\$ <u>(19,726)</u>
Net loss per share	\$ <u>(0.99)</u>	\$ <u>(0.69)</u>	\$ <u>(0.51)</u>
Weighted average number of shares of common stock outstanding	56,283,948	51,294,160	39,036,073

See notes to consolidated financial statements.

**ARIAD PHARMACEUTICALS, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
For the Years Ended December 31, 2003, 2004 and 2005

<i>In thousands, except share data</i>	Common Stock		Additional Paid-in Capital	Deferred Compensation	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Shareholders' Equity
	Shares	Amount					
Balance, December 31, 2002	34,828,689	\$ 35	\$ 158,147	\$ (13)	\$ --	\$ (136,317)	\$ 21,852
Issuance of common stock, net of issuance costs	11,613,488	12	56,168				56,180
Issuance of shares pursuant to ARIAD stock plans	374,855		964	(64)			964
Stock-based compensation to consultants			64	55			55
Amortization of stock-based compensation							
Comprehensive loss:							
Net loss						(19,726)	(19,726)
Other comprehensive income (loss)					1		1
Net unrealized losses on marketable securities							(19,725)
Comprehensive loss					1	(156,043)	59,326
Balance, December 31, 2003	46,817,032	47	215,343	(22)			40,001
Issuance of common stock, net of issuance costs	5,060,000	5	39,996				3,690
Issuance of shares pursuant to ARIAD stock plans	811,641	1	3,689	(94)			
Stock-based compensation to consultants			94	58			58
Amortization of stock-based compensation							
Comprehensive loss:							
Net loss						(35,573)	(35,573)
Other comprehensive income (loss)							
Net unrealized gains on marketable securities					(62)		(62)
Comprehensive loss					(61)	(191,616)	(35,635)
Balance, December 31, 2004	52,688,673	53	259,122	(58)			67,440
Issuance of common stock, net of issuance costs	8,625,000	9	57,851				57,860
Issuance of shares pursuant to ARIAD stock plans	384,456		1,512				1,512
Stock-based compensation to consultants			213	(213)			
Amortization of stock-based compensation			(14)	25			11
Comprehensive loss:							
Net loss						(55,482)	(55,482)
Other comprehensive income (loss)					37		37
Net unrealized losses on marketable securities							(55,445)
Comprehensive loss					(24)	(247,098)	(55,445)
Balance, December 31, 2005	61,698,129	62	\$ 318,684	\$ (246)	\$ (24)	\$ (247,098)	\$ 71,378

See notes to consolidated financial statements.

**ARIAD PHARMACEUTICALS, INC. AND SUBSIDIARIES**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

<i>In thousands</i>	Years Ended December 31,		
	2005	2004	2003
<b>Cash flows from operating activities:</b>			
Net loss	\$ (55,482)	\$ (35,573)	\$ (19,726)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,970	911	1,602
Stock-based compensation	554	1,366	55
Deferred executive compensation expense	374	800	444
Increase (decrease) from:			
Inventory and other current assets	(260)	(1,431)	313
Other assets	6	15	21
Accounts payable	1,832	1,376	(1,391)
Accrued compensation and benefits	187	(156)	67
Accrued product development expenses	5,510	2,054	(126)
Other accrued expenses	1,506	(454)	(265)
Deferred revenue	(242)	(216)	1,100
Deferred executive compensation paid	(511)	(251)	(108)
Net cash used in operating activities	(44,556)	(31,559)	(18,014)
<b>Cash flows from investing activities:</b>			
Acquisitions of marketable securities	(58,888)	(58,259)	(32,296)
Proceeds from sales and maturities of marketable securities	60,644	16,590	17,344
Investment in property and equipment	(6,538)	(2,743)	(307)
Investment in intangible assets	(675)	(730)	(507)
Net cash used in investing activities	(5,457)	(45,142)	(15,766)
<b>Cash flows from financing activities:</b>			
Proceeds from long-term debt borrowings		3,000	9,500
Repayment of long-term debt borrowings	(1,920)	(1,800)	(8,040)
Proceeds from issuance of common stock, net of issuance costs	57,860	40,001	56,180
Proceeds from issuance of common stock pursuant to stock option and purchase plans	970	2,382	964
Net cash provided by financing activities	56,910	43,583	58,604
Net increase (decrease) in cash and cash equivalents	6,897	(33,118)	24,824
Cash and cash equivalents, beginning of year	18,556	51,674	26,850
Cash and cash equivalents, end of year	\$ 25,453	\$ 18,556	\$ 51,674
Interest paid, net of amounts capitalized	\$ 333	\$ 273	\$ 256

See notes to consolidated financial statements.

**ARIAD PHARMACEUTICALS, INC. AND SUBSIDIARIES**  
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Nature of Business and Summary of Significant Accounting Policies**

*Nature of Business*

The Company is engaged in the discovery and development of breakthrough medicines to treat cancers by regulating cell signaling with small molecules. The Company is developing a comprehensive approach to patients with cancer that addresses the greatest medical need – aggressive and advanced-stage cancers for which current treatments are inadequate. The Company’s goal is to build a fully integrated oncology company focused on novel, molecularly targeted therapies to treat solid tumors and hematologic cancers, as well as the spread of primary tumors to distant sites. The Company’s lead cancer product candidate, AP23573, has been or is being studied in multiple clinical trials in patients with various types of cancers, including sarcomas, hormone refractory prostate cancer, endometrial cancer, brain cancer and leukemias and lymphomas. Medinol Ltd. is also developing stents to deliver AP23573 to prevent reblockage at sites of vascular injury following stent-assisted angioplasty.

The Company has a focused drug discovery program centered on small molecule, molecularly targeted therapies and cell-signaling pathways implicated in cancer. The Company also has an exclusive license to pioneering technology and patents related to certain NF- $\kappa$ B cell-signaling activity, which may be useful in treating certain diseases. Additionally, the Company has developed a proprietary portfolio of cell-signaling regulation technologies, the Company’s ARGENT technology, to control intracellular processes with small molecules, which may be useful in the development of therapeutic vaccines and gene and cell therapy products, and which provide versatile tools for use in cell biology, functional genomics and drug discovery research.

*Principles of Consolidation*

The consolidated financial statements include the accounts of ARIAD Pharmaceuticals, Inc., its wholly-owned subsidiaries, ARIAD Corporation and ARIAD Pharma S.A., and its 80%-owned subsidiary ARIAD Gene Therapeutics, Inc. (“AGTI”) (Note 7). The Company’s research and development relating to product candidates based on its ARGENT cell-signaling regulation technology and its small molecule mTOR inhibitors derived from the ARGENT programs are conducted on behalf of AGTI. Intercompany accounts and transactions have been eliminated in consolidation. AGTI is a research and development company and its accumulated deficit exceeds its total paid-in capital at December 31, 2005. Because the Company funds all losses of AGTI and the minority interest holders of AGTI common stock are not obligated to fund such losses, no minority interest income/ gain or asset is recorded in the Company’s consolidated financial statements.

*Fair Value of Financial Instruments*

The carrying amounts of cash, cash equivalents, accounts payable and accrued liabilities approximate fair value because of their short-term nature. Marketable securities are recorded in the consolidated financial statements at aggregate fair value (Note 2). The carrying amount of the Company’s bank term note of \$7.7 million at December 31, 2005 approximates fair value due to its variable interest rate (Note 4). The Company’s obligation under its executive compensation plans (Note 5) is based in part on the current fair market value of underlying securities, which is therefore stated at its estimated current fair value.

### *Accounting Estimates*

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

### *Cash Equivalents*

Cash equivalents include short-term, highly liquid investments, which consist principally of United States government and agency securities, purchased with remaining maturities of 90 days or less, and money market accounts.

### *Marketable Securities*

The Company has classified its marketable securities as "available-for-sale" and, accordingly, carries such securities at aggregate fair value. The difference between fair value and original cost is reflected as a component of accumulated other comprehensive income (loss). Fair value has been determined based on quoted market prices, in a dealer market, at the closing bid for each individual security held.

### *Inventory*

Inventory consists of bulk pharmaceutical material to be used for multiple development programs. Inventories are carried at cost using the first-in, first-out method and are charged to research and development expense when consumed. The carrying value of inventory amounted to \$1.7 million and \$1.3 million at December 31, 2005 and 2004, respectively.

### *Property and Equipment*

Property and equipment are recorded at cost. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets (3 to 10 years). Leasehold improvements are amortized over the shorter of their useful lives or lease term using the straight-line method (4 to 10 years). Costs classified as construction in progress are accumulated and are not amortized or depreciated until placed in service. The Company capitalized approximately \$42,000 of interest costs related to construction in progress in 2005. No interest was capitalized in 2004 or 2003.

### *Intangible and Other Assets*

Intangible and other assets consist primarily of capitalized patent and license costs, deposits and the unvested portion of the fair value of certain outstanding grants under the Company's executive compensation plan (Note 5). The cost of purchased patents and patent applications, costs incurred in filing patents and certain license fees are capitalized. Capitalized costs related to issued patents are amortized over a period not to exceed seventeen years or the remaining life of the patent, whichever is shorter, using the straight-line method. Capitalized license fees are amortized over the periods to which they relate. In addition, capitalized costs are expensed when it becomes determinable that such patent applications or technology will not be pursued.

### *Impairment of Long-Lived Assets*

The Company reviews its long-lived assets, including the above-mentioned intangible assets, for impairment when events or changes in circumstances indicate that the carrying amount of a long-lived asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison

of the carrying amount of an asset to future net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets.

#### *Revenue Recognition*

The Company recognizes revenue in accordance with the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") No. 101, *Revenue Recognition in Financial Statements*, SAB No. 104, *Revenue Recognition*, and Emerging Issues Task Force ("EITF"), No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables*. Revenue is principally comprised of license fees received under agreements that provide the licensee with access to and/or the right to review and evaluate certain technology owned or controlled by the Company. Upfront and annual license fees are recorded as deferred revenue upon receipt and recognized as revenue on a systematic basis over the period of time they are earned in accordance with the terms of the agreements. Such agreements may also include milestone and royalty payments. Such payments are recognized as revenue when earned in accordance with the terms of the related agreements.

#### *Income Taxes*

The Company accounts for income taxes in accordance with Statement of Financial Accounting Standard ("SFAS") No. 109, *Accounting for Income Taxes*, which requires an asset and liability approach to financial accounting and reporting for income taxes. Deferred income tax assets and liabilities are computed annually for differences between financial statement basis and the income tax basis of assets and liabilities that will result in taxable or deductible amounts in the future. Such deferred income tax computations are based on enacted tax laws and rates applicable to the years in which the differences are expected to affect taxable income. A valuation allowance is established when it is necessary to reduce deferred income tax assets to the expected realized amounts (Note 9).

#### *Segment Reporting*

The Company organizes itself into one segment reporting to the chief executive officer. No significant revenues from product sales or services occurred in 2005, 2004 or 2003.

#### *Stock-Based Compensation*

SFAS No. 123, *Accounting for Stock-Based Compensation*, addresses the financial accounting and reporting standards for stock or other equity-based compensation arrangements. The Company accounts for stock or other equity-based compensation for non-employees under the fair value-based method as required by SFAS No. 123 and EITF No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* and other related interpretations. Under this method, the equity-based instrument is valued at either the fair value of the consideration received or the equity instrument issued on the date of grant. The resulting compensation cost is recognized and charged to operations over the service period, which is usually the vesting period. The unearned portion of these awards is classified as a component of stockholders' equity and is listed as "deferred compensation" on the consolidated balance sheet.

The Company uses the intrinsic value method to measure compensation expense associated with grants of stock options to employees. Since options are granted to employees with exercise prices equal to the fair market value of the Company's common stock on the date of grant, there was no expense included in the statement of operations for the years ended December 31, 2005, 2004 and 2003 related to employee stock options. On a *pro forma* basis, had the Company used the fair value method to measure compensation, the net loss and net loss per share would have been reported as follows:

<i>In thousands (except per share data)</i>	<u>Years ended December 31,</u>		
	<u>2005</u>	<u>2004</u>	<u>2003</u>
Net loss, as reported	\$ (55,482)	\$ (35,573)	\$ (19,726)
Effect of stock options if valued at fair value	(4,159)	(4,026)	(3,564)
<i>Pro forma</i> net loss	<u>\$ (59,641)</u>	<u>\$ (39,599)</u>	<u>\$ (23,290)</u>
Net loss per share, as reported	\$ (0.99)	\$ (0.69)	\$ (0.51)
Effect of stock options if valued at fair value	(.07)	(0.08)	(0.09)
<i>Pro forma</i> net loss per share	<u>\$ (1.06)</u>	<u>\$ (0.77)</u>	<u>\$ (0.60)</u>

The above disclosure, required by SFAS No. 123, includes only the effect of grants made subsequent to January 1, 1996. For purposes of calculating the above disclosure, the fair value of options on their grant date was measured using the Black-Scholes option pricing model. Key assumptions used to apply this pricing model included a risk-free interest rate of 4.17% for 2005, 3.71% for 2004 and 3.42% for 2003, expected lives of the option grants ranging from one to eight years and expected rates of volatility for the underlying stock of 101% for 2005, 112% for 2004 and 115% for 2003. Using this model, the weighted average fair value per option for all options granted to employees in 2005, 2004 and 2003 was \$5.46, \$6.02 and \$2.88, respectively.

#### *Earnings Per Share*

Basic earnings per common share are computed using the weighted average number of common shares outstanding during each year. Diluted earnings per common share reflect the effect of the Company's outstanding options using the treasury stock method, except where such items would be anti-dilutive. In years in which a net loss is reported, basic and diluted per share amounts are the same. In 2005, 2004 and 2003, options amounting to 6,826,644, 5,889,532 and 5,647,839 shares of common stock, respectively, were not included in the computation of dilutive earnings per share, because the effect would be anti-dilutive. There were no warrants or convertible securities outstanding at December 31, 2005, 2004 or 2003.

#### *Executive Compensation Plan*

The Company maintains a deferred executive compensation plan, established in 1997 (the "1997 Plan"), which provides participants, in lieu of a cash bonus, an option to purchase certain designated mutual funds at a discount. EITF No. 02-8, *Accounting for Options Granted to Employees in Unrestricted, Publicly Traded Shares of an Unrelated Party*, and SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities* require that the Company account for such benefits as derivatives. Under these pronouncements, the Company records the fair value of the awards as an asset and a liability and amortizes the asset to expense over the vesting period of the awards. Subsequent changes in the fair value of the liability are included in the determination of net income or loss.

Effective October 1, 2005, the Company adopted a new deferred executive compensation plan (the "2005 Plan") that defers the payment of annual bonus awards to future periods as specified in each award. The Company accrues a liability based on the fair value of the awards ratably over the vesting period. The recorded balances of such awards are increased or decreased based on the actual total return of specified mutual funds.

## *Recently Issued Accounting Pronouncements*

In December 2004, the Financial Accounting Standards Board ("FASB") issued SFAS No. 123(R), *Share-Based Payment*, which revised SFAS No. 123 and superseded Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*. SFAS No. 123(R) requires that companies recognize compensation expense associated with grants of stock options and other equity instruments to employees in the financial statements, effective as of the first annual reporting period that begins after June 15, 2005. Compensation cost will be measured based on the fair value of the instrument on the grant date and will be recognized over the vesting period. This pronouncement applies to all grants after the effective date and to the unvested portion of stock options outstanding as of the effective date. SFAS No. 123(R) eliminates the ability to account for such transactions using the intrinsic method currently used by the Company. The Company will be required to adopt SFAS No. 123(R) as of January 1, 2006. The Company expects to adopt SFAS No. 123(R) using the modified prospective application method. Assuming the continuation of current programs, the preliminary estimate of stock compensation expense for 2006 is in the range of \$4.5 million to \$5.0 million.

SFAS No. 123(R) also requires that companies recognize compensation expense associated with purchases of shares of common stock by employees at a discount to market value under employee stock purchase plans that meet certain criteria. The impact of this requirement on the Company's consolidated financial statements is not expected to be material.

## **2. Marketable Securities**

The Company has classified its marketable securities as available-for-sale and, accordingly, carries such securities at aggregate fair value. At December 31, 2005 and 2004, all of the Company's marketable securities consisted of United States Treasury or agency securities.

At December 31, 2005, the aggregate fair value and amortized cost of the Company's marketable securities were \$56,063,000 and \$56,087,000, respectively. Gross unrealized gains and losses were \$9,000 and \$33,000, respectively, at December 31, 2005. The gross unrealized losses of \$33,000 pertain to fourteen marketable securities with an aggregate fair value of \$35.6 million, all of which have been in a continuous loss position for less than twelve months.

At December 31, 2004, the aggregate fair value and amortized cost of the Company's marketable securities were \$56,950,000 and \$57,011,000, respectively. Gross unrealized gains and losses were \$0 and \$61,000, respectively, at December 31, 2004. The gross unrealized losses of \$61,000 pertain to eighteen marketable securities with an aggregate fair value of \$51.5 million, all of which have been in a continuous loss position for less than twelve months.

The Company's marketable securities with unrealized losses consist of U.S. Treasury and agency securities that are guaranteed by the U.S. government or an agency thereof. The unrealized losses were caused by increased interest rates. Because the Company has the intent and ability to hold the securities to maturity which should result in a recovery of the fair value, the Company does not consider the investments to be other-than-temporarily impaired.

Realized gains and losses on investment security transactions are reported on the specific-identification method. Realized gains and losses on sales of marketable securities were not material in 2005, 2004 and 2003. Changes in market values resulted in a decrease (increase) in net unrealized losses of \$37,000, (\$62,000) and \$1,000 in 2005, 2004 and 2003, respectively.

### 3. Intangible and Other Assets, Net

Intangible and other assets, net, were comprised of the following at December 31:

<i>In thousands</i>	<u>2005</u>	<u>2004</u>
Capitalized patent and license costs	\$ 9,433	\$ 8,796
Less accumulated amortization	<u>(4,784)</u>	<u>(4,067)</u>
	4,649	4,729
Unvested deferred executive compensation (Note 5)	0	1,690
Other	<u>58</u>	<u>63</u>
	<u>\$ 4,707</u>	<u>\$ 6,482</u>

Amortization expense for intangible assets amounted to \$717,000, \$697,000 and \$692,000 in 2005, 2004 and 2003 respectively. In addition, the Company expensed unamortized patent and license costs of \$43,000, \$87,000 and \$520,000 in 2005, 2004 and 2003, respectively, related to patent applications or technology no longer being pursued. The estimated future amortization expenses for capitalized patent and license costs are \$720,000 for 2006, \$690,000 for 2007, \$444,000 for 2008, \$354,000 for 2009 and \$349,000 for 2010.

### 4. Long-Term Debt

Long-term debt was comprised of the following at December 31:

<i>In thousands</i>	<u>2005</u>	<u>2004</u>
Bank term note at prime rate or LIBOR +2% (average interest rate of 6.28% at December 31, 2005) payable in monthly installments of \$160,000 plus interest, through March 2008	\$ 7,655	\$ 9,575
Less current portion	<u>(1,920)</u>	<u>(1,920)</u>
	<u>\$ 5,735</u>	<u>\$ 7,655</u>

In March 2003, the Company entered into a term loan agreement with a bank for \$7.5 million, the proceeds of which were used to pay off then outstanding loans as well as remaining obligations under certain operating leases. Such repayments totaled \$6.9 million in the aggregate. The loan is secured by a lien on all assets of the Company excluding intellectual property, which the Company has agreed not to pledge to any other party. This term loan agreement was amended on December 31, 2003 and on December 31, 2004 pursuant to which the Company received another \$5.0 million in loan proceeds in the aggregate. The loan, as amended, is repayable in monthly installments of \$160,000 plus interest with a balloon payment of \$3.5 million in March 2008. The loan, as amended, requires the Company to maintain a minimum of \$13.0 million in unrestricted cash, cash equivalents and investments. The agreement also contains certain covenants that restrict additional indebtedness, additional liens and sales of assets, and dividends, distributions or repurchases of common stock.

The annual aggregate future principal payments of the above loan, as amended, are \$1.9 million in each of 2006 and 2007, and \$3.8 million in 2008.

### 5. Executive Compensation Plans

Under the Company's deferred executive compensation plan established in 1997 (the "1997 Plan"), the Company recorded an asset and a liability on the date of grant equal to the fair value of awards granted

under the 1997 Plan. The fair value of awards made in 2004 and 2003 under the 1997 Plan were \$1.0 million and \$930,000, respectively. The asset is amortized to expense over the vesting period and the liability is revalued and adjusted to fair value at each reporting period. Under the Company's 2005 Plan, the Company accrues a liability for the fair value of awards ratably over the vesting period. The value of awards made in 2005 under the 2005 Plan was \$962,000.

Pursuant to an amendment to the 1997 Plan in 2005, the unvested balances as of December 31, 2004 of awards under the 1997 Plan were cancelled. The value of such unvested balances was transferred to the 2005 Plan and will be accounted for accordingly. The recorded asset and liability balances attributable to the 1997 Plan were adjusted to reflect the cancellation and transfer of unvested awards. The net expense for these plans was \$374,000, \$800,000 and \$440,000 in 2005, 2004 and 2003, respectively. The estimated future expenses for awards made through December 31, 2005 are \$858,000, \$637,000, \$372,000 and \$183,000 for 2006, 2007, 2008 and 2009, respectively.

## **6. Leases, Licensed Technology and Other Commitments**

### *Facility Lease*

The Company conducts its operations in a 100,000 square foot office and laboratory facility under a non-cancelable operating lease. The original ten-year term of the lease expired in July 2002, and the Company has extended the lease for the first of two five-year extension periods. The Company currently subleases approximately 34,000 square feet of space to one tenant. Rent expense, net of sublease income of \$1.3 million, \$1.4 million and \$1.4 million in 2005, 2004 and 2003 respectively, amounted to \$620,000, \$509,000 and \$446,000 respectively. Future minimum annual rental payments through July 2007, the expiration of the first extension period, are \$550,000 in 2006 and \$321,000 in 2007, which are net of expected sublease income of \$1.1 million in 2006 and \$654,000 in 2007.

### *Licensed Technology*

The Company and AGTI have entered into agreements with several universities under the terms of which the Company and/or AGTI have received exclusive licenses to technology and intellectual property. The agreements, which are generally cancelable by the Company and/or AGTI, provide for the payment of license fees and/or minimum payments, which are generally creditable against future royalties. Fees paid by the Company on behalf of the Company and/or AGTI amounted to \$145,000, \$238,000 and \$165,000 in 2005, 2004 and 2003, respectively, and are expected to amount to approximately \$145,000 annually in 2006 through 2010. In addition, the agreements provide for payments upon the achievement of certain milestones in product development. The agreements also require the Company to fund certain costs associated with the filing and prosecution of patent applications.

### *Other Commitments*

The Company has entered into various employment agreements with 15 senior officers. The agreements provide for aggregate annual base salaries of \$10.4 million and remaining terms of employment of up to three years.

## **7. Stockholders' Equity**

### *Preferred Stock*

The Company has authorized 10,000,000 shares of preferred stock which the Board of Directors is empowered to designate and issue in different series. At December 31, 2005, the Board of Directors had designated 500,000 shares as series A preferred stock, and 9,500,000 shares remained undesignated.

### *Common Stock*

On May 19, 2003, the Company sold 4,000,000 registered shares of its common stock to institutional investors at a price of \$2.50 per share and received gross proceeds of \$10.0 million before commissions and expenses of \$662,000. These shares were sold pursuant to previously filed shelf registration statements and under a related registration statement pursuant to SEC rules. No shares remain available for sale under those shelf registrations.

On July 3, 2003, the Company filed a shelf registration statement with the SEC for the issuance of up to 7,500,000 shares of its common stock. On October 8, 2003, the Company sold 6,438,113 registered shares of its common stock, registered pursuant to this shelf registration, to institutional investors at a price of \$6.35 per share and received gross proceeds of \$40.9 million before commissions and expenses of \$2.8 million. On December 3, 2003, the Company sold 1,175,375 registered shares of its common stock, including 113,489 shares registered under a related registration statement pursuant to SEC rules, to institutional investors at a price of \$8.00 per share and received gross proceeds of \$9.4 million before commissions and expenses of \$652,000. Following this sale, no shares remain available for sale under this shelf registration.

On December 19, 2003, the Company filed a shelf registration statement with the SEC for the issuance of up to 7,000,000 shares of its common stock. This filing was declared effective on January 9, 2004. On March 29, 2004, the Company sold 5,060,000 of these registered shares in an underwritten public offering at a price of \$8.50 per share for net proceeds of \$40.0 million. As of December 31, 2005, the Company has 1,940,000 shares available for issuance under this shelf registration.

On February 18, 2005, the Company filed a shelf registration statement with the SEC, which was amended on March 11, 2005, registering 9,500,000 shares of common stock. The filing was declared effective on March 14, 2005. On August 10, 2005 and August 18, 2005, the Company sold an aggregate of 8,625,000 of these registered shares in an underwritten public offering at a price of \$7.20 per share for net proceeds of approximately \$57.9 million. At December 31, 2005, the Company had 875,000 shares that remain available for issuance under this shelf registration.

### *Stockholder Rights Plan*

The Board of Directors of the Company adopted a Rights Agreement, dated as of June 8, 2000 (the "2000 Rights Agreement"), between the Company and State Street Bank and Trust Company, as Rights Agent, and approved the declaration of a dividend distribution of one Preferred Share Purchase Right (a "Right") on each outstanding share of its Common Stock. In general, the Rights become exercisable if a person or group hereafter acquires 15% or more of the Common Stock of the Company or announces a tender offer for 15% or more of the Common Stock. The Board of Directors will, in general, be entitled to redeem the Rights at one cent per Right at any time before any such person hereafter acquires 15% or more of the outstanding Common Stock. The plan is designed to protect the Company's stockholders in the event that an attempt is made to acquire the Company without an offer of fair value.

If a person hereafter acquires 15% or more of the outstanding Common Stock of the Company (the "Acquiring Person"), each Right will entitle its holder to purchase, for an initial exercise price of \$65, a number of shares of Common Stock having a market value at that time of twice the Right's exercise price. Rights held by the Acquiring Person will become void. If the Company is acquired in a merger or other business combination transaction after a person acquires 15% or more of the Company's Common Stock, each Right will entitle its holder to purchase, at the Right's then-current exercise price, a number of the acquiring company's common shares having a market value at that time of twice the Right's exercise price.

The dividend distribution of Rights was payable on July 19, 2000 to shareholders of record on June 19, 2000. The Rights will expire in ten years. The Rights distribution is not taxable to the Company's stockholders.

The Board of Directors also adopted two amendments to the Rights Agreement dated December 15, 1994, (the "1994 Rights Agreement"), between the Company and State Street Bank and Trust Company, as Rights Agent. As a result of these amendments, the adoption of the 2000 Rights Agreement and the setting of a record date to distribute new Rights, the 1994 Rights Agreement is no longer in effect.

#### *Minority Interest in Subsidiary*

At December 31, 2003, AGTI had 5,195,779 shares of its common stock outstanding. Of this amount, the Company owned 4,157,143 shares or 80%, which allows it to consolidate for tax purposes the results of operations of AGTI with those of the Company. On January 17, 2004, stock options for a total of 87,428 shares of AGTI common stock held by minority interest holders were exercised prior to their expiration on that date. In order to maintain its 80% ownership interest in AGTI, the Company acquired an additional 351,909 shares of AGTI common stock on January 13, 2004. The purchase price of such shares was approximately \$8.8 million, effected through the reduction of intercompany debt representing the estimated fair value of such shares, subject to adjustment in certain circumstances.

After taking into account the above transactions, AGTI has a total of 5,635,116 shares of its common stock outstanding of which 80% are owned by ARIAD, 14% are owned by Stanford University, Harvard University, consultants and inventors, and 6% are owned by certain current members of the Company's management and Board of Directors. Approximately 75% of the shares of common stock owned by the minority interest holders are subject to restrictions on transfer and a right of first refusal held by AGTI to repurchase such shares of AGTI common stock before sale of such shares to another purchaser. There are currently no outstanding options to purchase AGTI common stock and no shares available for grant of additional options.

## **8. Stock Plans**

#### *ARIAD Stock Option and Stock Plans*

The Company's 1991, 1994 and 2001 stock option and stock plans (the "Plans") provide for the awarding of nonqualified and incentive stock options, stock grants and restricted stock units to officers, directors, employees and consultants of the Company. Stock options become exercisable as specified in the related option certificate, typically over a four-year period, and expire ten years from the date of grant. Stock grants and restricted stock units provide the recipient with ownership of common stock subject to any rights the Company may have to repurchase the shares granted or other restrictions. The 1991 and 1994 Plans have expired according to their terms, although existing stock options granted under these Plans remain outstanding. As of December 31, 2005, there are 696,046 shares available awards under the 2001 Plan.

Stock option transactions under the Plans for the years ended December 31, 2003, 2004 and 2005 are as follows:

	Number Of Shares	Weighted Average Exercise Price Per Share
Options outstanding, January 1, 2003	5,392,311	\$ 4.51
Granted	781,220	3.90
Forfeited	(239,473)	5.16
Exercised	(286,219)	2.94
Options outstanding, December 31, 2003	5,647,839	4.48
Granted	1,192,150	6.02
Forfeited	(320,114)	6.17
Exercised	(630,343)	3.62
Options outstanding, December 31, 2004	5,889,532	4.80
Granted	1,310,875	7.30
Forfeited	(132,444)	7.16
Exercised	(241,319)	3.52
Options outstanding, December 31, 2005	6,826,644	\$ 5.28
Options exercisable, December 31, 2003	3,605,255	\$ 4.27
December 31, 2004	4,078,371	\$ 4.65
December 31, 2005	4,345,848	\$ 4.70

In addition to the above stock option transactions, in 2005 and 2004, the Company awarded grants of its common stock totaling 120,000 and 170,000 shares, respectively, to its directors and chief executive officer. The 2005 stock grant to the chief executive officer remains subject to the right of the Company to repurchase the shares in certain circumstances until January 2007. The Company recognized expense of \$548,000 and \$1.3 million in 2005 and 2004, respectively, related to these grants, based on the fair market value of the common stock on the date of grant.

The following table sets forth information regarding options outstanding at December 31, 2005:

Range of Exercise Prices	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (years)	Number of Option Shares Currently Exercisable	Weighted Average Exercise Price for Currently Exercisable
\$.75 - 1.25	392,396	\$ 0.78	3.8	392,396	\$ 0.78
1.34 - 2.31	624,308	1.59	4.5	528,942	1.62
2.68 - 4.88	2,149,875	4.14	5.3	1,968,312	4.13
4.89 - 8.00	3,345,565	6.46	8.0	1,144,886	6.07
9.65 - 14.63	314,500	13.40	4.6	311,312	13.44
	6,826,644	\$ 5.28	6.4	4,345,848	\$ 4.70

### ARIAD Gene Therapeutics, Inc. Stock Option Plan

The Company's subsidiary, AGTI, adopted a stock option plan in 1993, which was approved by the Company's stockholders and which has now expired according to its terms. At December 31, 2003, there were 87,428 options outstanding all of which were exercised on January 17, 2004 for proceeds to AGTI of approximately \$37,000 (Note 7). There were no other options exercised nor any options granted under this plan in 2005, 2004 or 2003. At December 31, 2005, there are no outstanding options to purchase AGTI common stock under this plan.

### Employee Stock Purchase Plan

In 1997, the Company adopted the 1997 Employee Stock Purchase Plan and reserved 500,000 shares of common stock for issuance under this plan. Under this plan, substantially all of its employees may, through payroll withholdings, purchase shares of the Company's stock at a price of 85% of the lesser of the fair market value at the beginning or end of each three-month withholding period. In 2005, 2004 and 2003, 23,137, 11,298 and 88,636 shares of common stock were issued under the plan, respectively.

## 9. Income Taxes

At December 31, 2005, the Company had available, for federal tax reporting purposes, net operating loss carryforwards of approximately \$250.0 million, which expire commencing in 2009 and, for state tax reporting purposes, net operating loss carryforwards of approximately \$156.3 million, which expire commencing in 2006. The Company also had federal research and development credit carryovers of approximately \$9.3 million, which expire commencing in 2006, and state research and development credit carryovers of \$5.1 million, which expire commencing in 2007. Both the net operating loss carryforwards and credits are subject to certain limitations under federal tax law.

The components of deferred income taxes were as follows at December 31:

<i>In thousands</i>	<u>2005</u>	<u>2004</u>
Deferred tax liabilities:		
Intangible and other assets	\$ 1,860	\$ 1,891
Deferred tax assets:		
Net operating loss carryforwards	94,345	73,863
Federal and State tax credit carryovers	16,451	14,804
Depreciation	3,800	3,489
Other	1,344	1,478
Total deferred tax assets	<u>115,940</u>	<u>93,634</u>
Deferred tax assets, net	114,080	91,742
Valuation allowance	<u>(114,080)</u>	<u>(91,742)</u>
Total deferred taxes	<u>\$ 0</u>	<u>\$ 0</u>

Since the Company has not yet achieved sustained profitable operations, management believes the tax benefits as of December 31, 2005 and 2004 do not satisfy the realization criteria set forth in SFAS No. 109 and has recorded a valuation allowance for the entire net deferred tax asset. The increase in the valuation allowance of \$22.3 million in 2005 and \$16.8 million in 2004 resulted primarily from net operating loss carryforwards and tax credit carryovers from operations in those years and that were not benefited.

## 10. Litigation

### NF- $\kappa$ B Patent Infringement Litigation and Reexamination

In 2002, the Company, together with Massachusetts Institute of Technology, The Whitehead Institute for Biomedical Research and Harvard University (collectively, the "Plaintiffs") filed a lawsuit in the United States District Court for the District of Massachusetts (the "U.S. District Court") against Eli Lilly and Company ("Lilly") alleging infringement of certain claims ("the NF- $\kappa$ B '516 Claims") of the Plaintiffs' U.S. Patent No. 6,410,516 (the "'516 Patent") covering methods of treating human disease by regulating NF- $\kappa$ B cell-signaling activity through sales of Lilly's osteoporosis drug, Evista®, and Lilly's septic shock drug, Xigris®, and seeking monetary damages from Lilly.

#### *Re-examination Proceedings in PTO*

On April 4, 2005, Lilly filed an *ex parte* request in the United States Patent and Trademark Office ("PTO") to reexamine the patentability of certain claims of the '516 Patent. On June 8, 2005, the PTO mailed to counsel for the patentees of the '516 Patent its Order granting a reexamination of all of the claims of the '516 Patent. On August 4, 2005, counsel for the patentees of the '516 Patent filed a Petition requesting the PTO to vacate its Order granting reexamination of the '516 Patent and a Petition requesting the PTO to stay its reexamination ("Patentee's Petitions"). On October 6, 2005, the PTO mailed to counsel for patentees of the '516 Patent its Decision denying Patentee's Petitions ("PTO's October 6 Decision"), whereupon, on November 25, 2005, counsel for the patentees filed a Request for Reconsideration of the PTO's October 6 Decision. On February 8, 2006, the PTO mailed to counsel for the patentees of the '516 Patent its Decision granting patentee's Request for Reconsideration and denying the relief sought by patentees there under.

In addition, an unrelated third party filed an *ex parte* request in the PTO on December 2, 2005 to reexamine the patentability of certain claims of the '516 Patent ("Second Request"). On December 12, 2005, the PTO mailed to counsel for the patentees of the '516 Patent its Order granting a reexamination based on this Second Request. On February 13, 2006, counsel for the patentees of the '516 Patent filed Petitions requesting the PTO to vacate its Order granting reexamination of the '516 Patent based on this Second Request and requesting the PTO to stay this reexamination.

#### *Motions to Stay Litigation*

In connection with its request for reexamination of the '516 patent, Lilly filed a motion in the U.S. District Court on April 4, 2005 requesting a stay of the NF- $\kappa$ B patent infringement litigation by the Court pending reexamination of the '516 Patent by the PTO. On June 6, 2005, the U.S. District Court denied Lilly's motion. On January 17, 2006, Lilly filed a renewed motion to stay pending reexamination of the '516 patent by the PTO, which was denied by the U.S. District Court on February 13, 2006.

#### *Trial and Pre-Trial Motions*

On December 23, 2005, Lilly filed two motions for summary judgment of invalidity. At a status conference held on March 9, 2006, the U.S. District Court confirmed that the trial would begin on April 10, 2006 and gave no indication as to when it would rule on the pending summary judgment motions. A pre-trial conference in this case is scheduled for April 5, 2006, with trial scheduled to commence on April 10, 2006.

The ultimate outcome of the request for reexamination and litigation cannot be determined at this time, and, as a result, no determination can be made with respect to the PTO's allowance of the claims of the '516 patent in the reexamination, nor can any determination be made with respect to the validity or infringement of the claims of the '516 patent in the Lilly litigation, nor can an estimate of a damage award or range of awards in the Lilly litigation, if any, be made. If the Company prevails at trial in the Lilly

litigation, any damages it may be awarded by the jury could be subsequently eliminated or limited by an adverse finding upon appeal or in the event that the claims of the '516 Patent are invalidated by the PTO.

#### **11. Related Party Transactions**

For the Company's March 2004 and August 2005 public offerings of common stock, Lehman Brothers served as the sole-book running manager for which it received underwriting discounts and commissions of \$1,399,090 and \$2,018,250, respectively. In addition, Lehman Brothers provided assistance to the Company in connection with its January 2005 transaction with Medinol Ltd. for the development of drug-eluting stents for which Lehman Brothers earned a fee of \$200,000. The spouse of a member of our Board of Directors is a vice chairman of Lehman Brothers. We believe the transactions with Lehman Brothers were entered into on terms no less favorable to us than we could have obtained from unaffiliated third parties.

**ITEM 9: CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

Not applicable.

**ITEM 9A: CONTROLS AND PROCEDURES**

(a) *Evaluation of Disclosure Controls and Procedures.* Our principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were adequate and effective to ensure that material information relating to us, including our consolidated subsidiaries, was made known to them by others within those entities, particularly during the period in which this Annual Report on Form 10-K was being prepared.

In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

(b) *Changes in Internal Controls.* There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during our last fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**Management's Report On Internal Control Over Financial Reporting**

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended. The Company's internal control system was designed to provide reasonable assurance to the Company's management and board of directors regarding the preparation and fair presentation of published financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. 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.

The Company's management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2005. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework. Based on our assessment we believe that, as of December 31, 2005, the Company's internal control over financial reporting is effective based on those criteria.

The Company's independent auditors have issued an audit report on our assessment of the Company's internal control over financial reporting. This report appears below.

## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of  
ARIAD Pharmaceuticals, Inc.:

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that ARIAD Pharmaceuticals, Inc. and subsidiaries (the "Company") maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company'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 opinions.

A company's internal control over financial reporting is a process designed by, or under the supervision of, the company's principal executive and principal financial officers, or persons performing similar functions, and effected by the company's board of directors, management, and other personnel 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 the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the 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 the Company maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements as of and for the year ended December 31, 2005 of the Company and our report dated March 13, 2006 expressed an unqualified opinion on those financial statements.

/s/ DELOITTE & TOUCHE LLP  
Boston, Massachusetts  
March 13, 2006

**ITEM 9B: OTHER INFORMATION**

Not applicable.

### **PART III**

#### **ITEM 10: DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Board of Directors," "Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Code of Conduct and Ethics" in the Company's Proxy Statement for the 2006 Annual Meeting of Stockholders.

#### **ITEM 11: EXECUTIVE COMPENSATION**

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Executive Compensation" and "Board of Directors" in the Company's Proxy Statement for the 2006 Annual Meeting of Stockholders.

#### **ITEM 12: SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Executive Compensation-Equity Compensation Plan Information" in the Company's Proxy Statement for the 2006 Annual Meeting of Stockholders.

#### **ITEM 13: CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Transactions" and "Executive Compensation-Employment Agreements, Termination of Employment and Change in Control Arrangements" in the Company's Proxy Statement for the 2006 Annual Meeting of Stockholders.

#### **ITEM 14: PRINCIPAL ACCOUNTING FEES AND SERVICES**

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Proposal 2: Ratification of Selection of Independent Registered Public Accounting Firm" in the Company's Proxy Statement for the 2006 Annual Meeting of Stockholders.

#### PART IV

#### ITEM 15: EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

- (a)(1) The following Consolidated Financial Statements, Notes thereto and Report of Independent Registered Public Accounting Firm have been presented in Item 8:

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations

Consolidated Statements of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

- (a)(2) Financial Statement Schedules:

Schedules have been omitted because of the absence of conditions under which they are required or because the required information is included in the financial statements or notes thereto.

- (a)(3) The Exhibits listed in the Exhibit Index are filed herewith in the manner set forth therein.
- (b) See (a) (3) above.
- (c) See (a) (2) above.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge and Commonwealth of Massachusetts on the 14th of March, 2006.

### ARIAD PHARMACEUTICALS, INC.

By: /s/ Harvey J. Berger, M.D.  
Name: Harvey J. Berger, M.D.  
Title: Chairman, Chief Executive Officer and President

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 and on the dates indicated.

Signature	Title	Date
<u>/s/ Harvey J. Berger, M.D.</u> Harvey J. Berger, M.D.	Chairman of the Board of Directors, Chief Executive Officer and President (Principal Executive Officer)	March 14, 2006
<u>/s/ Sandford D. Smith</u> Sandford D. Smith	Vice Chairman of the Board of Directors	March 14, 2006
<u>/s/ Edward M. Fitzgerald</u> Edward M. Fitzgerald	Senior Vice President, Finance and Corporate Operations, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 14, 2006
<u>/s/ Michael D. Kishbauch</u> Michael D. Kishbauch	Director	March 14, 2006
<u>/s/ Jay R. LaMarche</u> Jay R. LaMarche	Director	March 14, 2006
_____ Athanasios Lavidas, Ph.D	Director	
<u>/s/ Peter J. Nelson</u> Peter J. Nelson	Director	March 14, 2006
<u>/s/ Burton E. Sobel, M.D.</u> Burton E. Sobel, M.D.	Director	March 14, 2006
<u>/s/ Mary C. Tanner</u> Mary C. Tanner	Director	March 14, 2006
<u>/s/ Elizabeth H.S. Wyatt</u> Elizabeth H.S. Wyatt	Director	March 14, 2006

## EXHIBIT INDEX

Exhibit No.	Title
3.1	Certificate of Incorporation of the Company, as amended. (16)
3.2	Restated By-laws of the Company, as amended. (5)
4.1	Rights Agreement, dated as of June 8, 2000, between the Company and State Street Bank and Trust Company, which includes the Form of Certificate of Designations in respect of the Series A Preferred Stock, as Exhibit A, the Form of Right Certificate as Exhibit B and the Summary of Rights to Purchase Series A Preferred Stock as Exhibit C. Pursuant to the Rights Agreement, Right Certificates will not be mailed until after the Separation Date (as defined therein). (3)
10.1	Lease Agreement, dated January 8, 1992, between ARIAD Pharmaceuticals, Inc. and Forest City Cambridge, Inc. (1)
10.2+	Executive Employment Agreement, dated as of January 1, 1992, between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D. (1)
10.3+	ARIAD Pharmaceuticals, Inc. 1991 Stock Option Plan for Employees and Consultants, as amended. (4)
10.4+	ARIAD Pharmaceuticals, Inc. 1991 Stock Option Plan for Directors. (1)
10.5+	ARIAD Retirement Savings Plan. (1)
10.6**	Amended and Restated Agreement, dated as of December 12, 1997, between The Board of Trustees of The Leland Stanford Junior University and ARIAD Gene Therapeutics, Inc. (6)
10.7+	Amendment, dated April 19, 1994, to Executive Employment Agreement between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D. (2)
10.8+	Amendment No. 2, dated June 30, 1994, to Executive Employment Agreement between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D. (4)
10.9+	ARIAD Pharmaceuticals, Inc. 1994 Stock Option Plan for Non-Employee Directors. (4)
10.10+	Amendment, dated January 1, 1997, to Executive Employment Agreement between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D. (11)
10.11+	ARIAD Pharmaceuticals, Inc. 1997 Employee Stock Purchase Plan. (11)
10.12+	Amendment to the 1991 Stock Option Plan for Employees and Consultants. (11)
10.13+	Amendment to the 1994 Stock Option Plan for Non-Employee Directors. (11)
10.14+	ARIAD Pharmaceuticals, Inc. 1997 Executive Compensation Plan. (6)
10.15+	Executive Employment Agreement, dated May 1, 1992, Fourth Amendment to Employment Agreement dated June 8, 2000, Third Amendment to Employment Agreement dated January 1, 1999, and Amendments to Employment Agreements dated January 1, 1997 and March 2, 1994 between ARIAD Pharmaceuticals, Inc. and John Iuliucci, Ph.D. (7)
10.16+	Executive Employment Agreement, dated August 1, 1993, Third Amendment to Employment Agreement dated June 8, 2000, and Amendments to Employment Agreements dated January 1, 1997 and March 2, 1994 between ARIAD Pharmaceuticals, Inc. and David L. Berstein, J.D. (7)
10.17+	Amendment, dated as of January 1, 2001, to Executive Employment Agreement with John Iuliucci, Ph.D. (8)
10.18+	Amendment, dated as of January 1, 2001, to Executive Employment Agreement with David Berstein, Esq. (8)
10.19+	ARIAD Pharmaceuticals, Inc. 2001 Stock Plan, as amended. (16)
10.20	Revised and Restated Research and Development Agreement, dated as of March 15, 2002, by and between ARIAD Pharmaceuticals, Inc. and ARIAD Corporation. (9)
10.21	Revised and Restated Research and Development Agreement, dated as of March 15, 2002, by and between ARIAD Gene Therapeutics, Inc. and ARIAD Corporation. (9)
10.22+	Executive Employment Agreement, dated as of March 4, 2002, between ARIAD Pharmaceuticals, Inc. and Laurie A. Allen, Esq. (9)
10.23	Stock Transfer Agreement between ARIAD Gene Therapeutics, Inc. and the individuals listed on Exhibit A thereto. (9)
10.24	Notice of Extension of Lease, dated October 2, 2001, from ARIAD Corporation to Forest City Commercial Group. (9)
10.25+	Executive Employment Agreement, dated May 6, 2002, between ARIAD Pharmaceuticals, Inc. and Edward M. Fitzgerald (10)
10.26+	Executive Employment Agreement, dated June 8, 2000, between ARIAD Pharmaceuticals, Inc. and Timothy Clackson, Ph.D.(12)

- 10.27+ Amendment to Employment Agreement, dated July 1, 2001, between ARIAD Pharmaceuticals, Inc. and Timothy Clackson, Ph.D. (12)
- 10.28+ Amendment to Employment Agreement, dated July 12, 2002, between ARIAD Pharmaceuticals, Inc. and Timothy Clackson, Ph.D. (12)
- 10.29 Agreement of Sublease, dated December 31, 1999, between ARIAD Corporation and Aventis Pharmaceuticals Inc. (12)
- 10.30 First Amendment to Sublease, dated July 26, 2002, between ARIAD Corporation and Aventis Pharmaceuticals Inc. (12)
- 10.31 Credit Agreement, dated as of March 12, 2003, by and among ARIAD Pharmaceuticals, Inc., ARIAD Corporation and ARIAD Gene Therapeutics, Inc. and Citizens Bank of Massachusetts. (13)
- 10.32 Security Agreement - All Assets, dated as of March 12, 2003, by and between ARIAD Pharmaceuticals, Inc. and Citizens Bank of Massachusetts. (13)
- 10.33 Security Agreement - All Assets, dated as of March 12, 2003, by and between ARIAD Corporation and Citizens Bank of Massachusetts. (13)
- 10.34 Security Agreement - All Assets, dated as of March 12, 2003, by and between ARIAD Gene Therapeutics, Inc. and Citizens Bank of Massachusetts. (13)
- 10.35+ Amendment to Employee Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D. (14)
- 10.36+ Amendment to Employee Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc. and Laurie A. Allen, Esq. (14)
- 10.37+ Amendment to Employee Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc. and David Berstein, Esq. (14)
- 10.38+ Amendment to Employee Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc. and Timothy P. Clackson, Ph.D. (14)
- 10.39+ Amendment to Employee Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc. and Edward M. Fitzgerald. (14)
- 10.40+ Amendment to Employee Agreement, dated September 2, 2003 between ARIAD Pharmaceuticals, Inc. and John D. Iulucci, Ph.D. (14)
- 10.41 Amendment No. 1 to Credit Agreement, dated as of December 31, 2003, by and among ARIAD Pharmaceuticals, Inc., ARIAD Corporation and ARIAD Gene Therapeutics, Inc. and Citizens Bank of Massachusetts. (15)
- 10.42 Stock Issuance Agreement, dated January 13, 2004, between ARIAD Gene Therapeutics, Inc. and ARIAD Pharmaceuticals, Inc. (15)
- 10.43 Stock Transfer Agreement, dated January 17, 2004, between ARIAD Gene Therapeutics, Inc. and the individuals listed on Exhibit A thereto. (15)
- 10.44 Amendment No. 2 to Credit Agreement dated as of December 31, 2004 by and among ARIAD Pharmaceuticals, Inc., ARIAD Corporation and ARIAD Gene Therapeutics, Inc. and Citizens Bank of Massachusetts. (17)
- 10.45 Second Amended and Restated Term Note, dated December 31, 2004, issued ARIAD Pharmaceuticals, Inc., ARIAD Corporation and ARIAD Gene Therapeutics, Inc. to Citizens Bank of Massachusetts. (17)
- 10.46\*\* License Agreement, effective January 26, 2005, by and between ARIAD Pharmaceuticals, Inc. and Medinol Ltd. (19)
- 10.47\*\* Supply Agreement, entered into as of January 26, 2005, by and between ARIAD Pharmaceuticals, Inc. and Medinol Ltd. (19)
- 10.48+ Executive Employment Agreement, dated August 19, 2002, and First Amendment to Employment Agreement, dated September 2, 2003, between ARIAD Pharmaceuticals, Inc., and Camille L. Bedrosian, M.D. (18)
- 10.49+ ARIAD Pharmaceuticals, Inc. 2005 Executive Compensation Plan. (20)
- 10.50+ Amendment to ARIAD Pharmaceuticals, Inc. 1997 Executive Compensation Plan. (20)
- 10.51+ ARIAD Pharmaceuticals, inc. Amended and Restated 2001 Stock Plan. (20)
- 10.52+ Executive Bonus and Stock Option Arrangements. (20)
- 10.53+ Director Compensation Arrangements. (20)
- 10.54+\* Executive Compensation Arrangements
- 10.55+ Amendment to Executive Employment Agreements, as of October 4, 2005, between ARIAD Pharmaceuticals, Inc. and each of Laurie A. Allen, Esq., Camille L. Bedrosian, M.D., David L. Berstein, Esq., Timothy P. Clackson, Ph.D., Edward M. Fitzgerald and John D. Iulucci, Ph.D. (20)

- 10.56+\* Amendment to Executive Employment Agreement, dated as of January 1, 2006 between ARIAD Pharmaceuticals, Inc. and Harvey J. Berger, M.D.
- 10.57+\* Executive Employment Agreement, dated as of September 25, 2005 between ARIAD Pharmaceuticals, Inc. and Richard W. Pascoe.
- 21.1 Subsidiaries of the Company. (17)
- 23.1\* Consent of Deloitte & Touche LLP.
- 31.2\* Certification of the Chief Executive Officer.
- 31.3\* Certification of the Chief Financial Officer.
- 32.1\* Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

**Notes to Exhibits:**

- (+) Management Contract or Compensatory Plan or Arrangement
- (\*) Filed Herewith.
- (\*\*) Confidential treatment has been granted by the Securities and Exchange Commission as to certain portions.
- (1) Incorporated by reference to Registration Statement on Form 10 of the Company filed with the Securities and Exchange Commission on June 25, 1993.
- (2) Incorporated by reference to Registration Statement on Form S-1 of the Company (No. 33-76414) filed with the Securities and Exchange Commission on March 11, 1994.
- (3) Incorporated by reference to Form 8-A of the Company filed with the Securities and Exchange Commission on June 19, 2000.
- (4) Incorporated by reference to Form 10-K of the Company for the fiscal year ended December 31, 1994 filed with the Securities and Exchange Commission on March 31, 1995.
- (5) Incorporated by reference to Amendment No. 1 to the Registration Statement on Form S-3 of the Company (No. 333-38664) filed with the Securities and Exchange Commission on June 23, 2000.
- (6) Incorporated by reference to Form 10-K of the Company for the fiscal year ended December 31, 1997 filed with the Securities and Exchange Commission on March 10, 1998.
- (7) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on August 10, 2000.
- (8) Incorporated herein by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on May 14, 2001.
- (9) Incorporated by reference to Form 10-K of the Company for the fiscal year ended December 31, 2001 filed with the Securities and Exchange Commission on March 22, 2002.
- (10) Incorporated herein by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on May 9, 2002.
- (11) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on August 12, 1997.
- (12) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission in March 14, 2003.
- (13) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission in May 13, 2003.
- (14) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission in November 4, 2003.
- (15) Incorporated by reference to Form 10-K of the Company filed with the Securities and Exchange Commission on March 2, 2004.
- (16) Incorporated by reference to Registration Statement on Form S-8 of the Company (No. 333-116996) filed with the Securities and Exchange Commission on June 30, 2004.
- (17) Incorporated by reference to Form 10-K of the Company filed with the Securities and Exchange Commission on February 18, 2005.

- (18) Incorporated by reference to Form 10-K/A of the Company filed with the Securities and Exchange Commission on March 11, 2005.
- (19) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on May 10, 2005.
- (20) Incorporated by reference to Form 10-Q of the Company filed with the Securities and Exchange Commission on November 9, 2005.

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