Ardea Biosciences, Inc./DE
Form 10-K
March 13, 2009

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

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2008

or

o **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: 1-33734
Ardea Biosciences, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	**94-3200380**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
4939 Directors Place **San Diego, CA** *(Address of principal executive offices)*	**92121** *(Zip Code)*

Registrant s telephone number, including area code:
(858) 652-6500

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

Title of Each Class:	**Name of Each Exchange on Which Registered:**
Common Stock, par value $0.001 per share	**The Nasdaq Global Market**

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No þ

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 þ No o

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. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.:

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No þ

The aggregate market value of voting and non-voting common stock held by non-affiliates of the registrant as of June 30, 2008 totaled approximately $92,000,000 based on the closing price of $12.82 as reported by the Nasdaq Global Market. As of March 6, 2009, there were 17,854,549 shares of the Company s common stock ($0.001 par value) outstanding.

Documents Incorporated by Reference

Portions of the proxy statement for the registrant s 2009 annual meeting of stockholders are incorporated by reference into Part III.

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FORWARD-LOOKING STATEMENTS

This annual report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. These statements include, but are not limited to, statements regarding our development programs, our capabilities, our goals, the expected timeline for achievement of our clinical milestones, the expected properties and benefits of RDEA806, RDEA594, RDEA427, RDEA119, RDEA436 and our other compounds, the results of clinical and other studies, the size of the market for our products and our financial results. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as anticipate, estimate, plan, project, continuing, ongoi expect, management believes, we believe, we intend and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed or implied in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed in this report or incorporated by reference.

Because the factors discussed in this report, and even factors of which we are not yet aware, could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by or on behalf of us you should not place undue reliance on any such forward-looking statements. These statements are subject to risks and uncertainties, known and unknown, which could cause actual results and developments to differ materially from those expressed or implied in such statements. We have included important factors in the cautionary statements included in this report, particularly under Item 1A. Risk Factors, and in our SEC filings that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. These and other risks are also detailed and occasionally modified or updated in our reports filed from time to time under the Securities Act and/or the Exchange Act. You are encouraged to read these filings as they are made.

Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

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PART I

In this report, all references to Ardea, we, our, and us, refer to Ardea Biosciences, Inc., a Delaware corporation, and our wholly owned subsidiary. In December 2006, Ardea changed its name from IntraBiotics Pharmaceuticals, Inc.

ITEM 1. *BUSINESS.*

Overview and Business Strategy

Ardea Biosciences, Inc., of San Diego, California, is a biotechnology company focused on the discovery and development of small-molecule therapeutics for the treatment of gout, human immunodeficiency virus, or HIV, cancer and inflammatory diseases. We are currently pursuing multiple development programs, including the following:

Product Portfolio

Product Candidate	Target Indication	Development Status
RDEA594	Gout	Phase 1 ongoing
RDEA806	HIV	Phase 2a completed
RDEA427	HIV	Phase 0* completed
RDEA119	Cancer	Phase 1 and Phase 1/2 ongoing
RDEA119	Inflammation	Phase 1 completed
RDEA436	Inflammation	Phase 0* completed

* First-in-human micro-dose pharmacokinetic study in normal healthy volunteers.

GOUT

RDEA594

RDEA594 is an inhibitor of URAT1, a transporter in the kidney which regulates uric acid excretion from the body. RDEA594 has been well tolerated in Phase 1 studies to date in normal healthy volunteers and has demonstrated significant dose-related decreases in serum uric acid of up to 30% over the first 24 hours after administration of single ascending doses. We are currently evaluating RDEA594 in a multiple ascending dose Phase 1 study in normal healthy volunteers. We plan to complete this study in the first quarter of 2009. We also plan to initiate a Phase 2 dose-ranging study of RDEA594 in gout patients in the first half of 2009, with the goal of completing that study by the end of 2009. We are also conducting a pilot Phase 2a proof-of-concept study of RDEA806, RDEA594 s prodrug, in gout patients to provide an early confirmation of RDEA594 s activity in the target population. In Phase 1 studies of RDEA806 in normal healthy volunteers, increased urinary excretion of uric acid was observed in the first 24 hours after dosing, with statistically significant, exposure-dependent decreases in serum uric acid of 35% to 50% observed during multiple dosing out to 14 days. We plan to complete the Phase 2a study in the first quarter of 2009 and do not plan any further studies of RDEA806 in gout.

HIV

RDEA806

RDEA806 is our lead non-nucleoside reverse transcriptase inhibitor, or NNRTI, for the treatment of HIV. *In vitro* preclinical tests have shown RDEA806 to be a potent inhibitor of a wide range of HIV viral isolates, including isolates that are resistant to efavirenz (SUSTIVA®/Stocrin® from Bristol-Myers Squibb Company and Merck & Co., Inc.), the most widely prescribed NNRTI, in addition to other currently available NNRTIs. *In vitro* preclinical tests have also shown RDEA806 to have a high genetic barrier to resistance. *In vivo* preclinical tests suggest that RDEA806 does not pose a risk of reproductive toxicity. Based on both preclinical and clinical data, we anticipate that RDEA806 could be amenable to a once-daily oral dosing regimen, may have limited pharmacokinetic interactions with other drugs and may be readily co-formulated in a single pill with other HIV antiviral

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drugs, such as Truvada® (emtricitabine and tenofovir from Gilead Sciences, Inc.), which is important for patient compliance and efficacy.

RDEA806 has successfully completed Phase 1 and Phase 2a studies and has been evaluated in over 250 subjects. Results from a Phase 2a monotherapy proof-of-concept study of RDEA806 demonstrated placebo-adjusted plasma viral load reductions of up to 2.0 $\log_{10}$ on day 8 with once-daily dosing of RDEA806. In addition, all dosing regimens tested were well tolerated. We have continued preparing RDEA806 for further clinical development by obtaining additional regulatory approvals to conduct our planned international Phase 2b HIV trial and by successfully completing a number of important preparatory safety and supportive toxicology studies including a Thorough QT study. Results from the Thorough QT study demonstrated that QTc intervals were not increased by any dose of RDEA806 tested. In addition, the study provided information on the lack of pharmacokinetic differences between Caucasians and African-Americans. These results provide further support for RDEA806 s cardiac safety profile as well as its potential to improve current standard-of-care therapy as ethnicity-based differences in metabolism, which can lead to increased side effects in African-Americans, have been documented with efavirenz (Sustiva®, Bristol-Myers Squibb).

RDEA427

The lead compound in our next generation NNRTI program, RDEA427, is from a chemical class that is distinct from the RDEA806 chemical class. Based on early preclinical data, we believe that RDEA427 may share certain of the positive attributes of RDEA806, but may also have even greater activity against a wide range of drug-resistant viral isolates. We have evaluated RDEA427, in a human micro-dose pharmacokinetic study and have selected it for clinical development based on a plasma half-life of greater than 40 hours. The timing of future studies of RDEA806 and RDEA427 will be determined in part by the results of our partnering efforts.

CANCER

RDEA119

RDEA119, our lead mitogen-activated ERK kinase, or MEK, inhibitor for the treatment of cancer, is a potent and selective inhibitor of MEK, which is believed to play an important role in cancer cell proliferation, apoptosis and metastasis. *In vivo* preclinical tests have shown RDEA119 to have potent anti-tumor activity.

Data from an ongoing Phase 1 study of RDEA119 in advanced cancer patients suggests that RDEA119 has a pharmacokinetic profile allowing for convenient once-daily oral dosing. Once the maximum tolerated dose is determined, we plan to evaluate the activity of RDEA119 in advanced cancer patients with selected tumor types, such as hepatocellular, sarcoma, glioma, non-small cell lung, colon, pancreatic or thyroid cancer or melanoma.

In addition, preclinical *in vitro* and *in vivo* studies of RDEA119 have demonstrated synergistic activity across multiple tumor types when RDEA119 is used in combination with other anti-cancer agents, including sorafenib (Nexavar® from Onyx Pharmaceuticals, Inc. and Bayer HealthCare AG). We are currently conducting a Phase 1/2 study of RDEA119 in combination with sorafenib in advanced cancer patients to evaluate the safety, tolerability, pharmacokinetics and anti-tumor activity of this combination therapy.

INFLAMMATION

RDEA119

In vivo preclinical tests have also shown RDEA119 to significantly inhibit production of inflammatory cytokines. Results from a completed Phase 1 study in normal healthy volunteers demonstrated that RDEA119 was well tolerated with a pharmacokinetic profile allowing for convenient once-daily oral dosing.

RDEA436

The lead compound in our next generation MEK inhibitor program, RDEA436, is from a chemical class that is distinct from the RDEA119 chemical class. Based on early preclinical data, we believe that RDEA436 may potentially share certain of the positive attributes of RDEA119, and may have even greater potency than RDEA119.

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We have evaluated RDEA436 in a Phase 0 study and have selected it for clinical development. We received regulatory approval in December 2008 to initiate a Phase 1 study of RDEA436 evaluating safety, pharmacokinetics and inflammatory disease biomarkers in normal healthy volunteers. The timing of future studies of RDEA119 and RDEA436 for inflammatory diseases will be determined in part by the results of our partnering efforts.

Market Opportunity

We believe that there is a significant market opportunity for our products, should they be successfully developed, approved and commercialized.

We believe that there is a significant need for new products for the treatment and prevention of gout, a painful and debilitating disease caused by abnormally elevated levels of uric acid. There has been only one new drug approved in the United States for the treatment of gout in the last 40 years. According to the National Arthritis Data Workgroup, an estimated 6.1 million adults in the United States in 2005 had experienced at least one episode of gout. The incidence and severity of gout is increasing in the United States. According to the Annals of Rheumatic Diseases there was a 288% increase in gout-related hospitalizations from 1988-2005 and over $11.2 billion in gout-related hospital costs were incurred in 2005 in the United States. In addition, according to a 2008 Nerac Inc. survey, approximately 5.0 million patients in the European Union suffer from gout. Many chronic gout sufferers are unable to achieve target reductions in uric acid with current treatments. Approximately 80% to 90% of gout patients are under excretors of uric acid. Scientists have recently discovered defects in multiple transporters in the kidney that play important roles in uric acid transport and are genetically linked to a higher risk of gout. URAT1 has been identified as the most important transporter for uric acid. We are developing products for the treatment of hyperuricemia and gout that inhibit URAT1, thereby increasing the excretion of uric acid and lowering serum uric acid levels. In addition, we believe there may be opportunities to develop uric acid-lowering agents to treat diseases other than gout. Evidence suggests that the chronic elevation of uric acid associated with gout, known as hyperuricemia, may also have systemic consequences, including an increased risk for kidney dysfunction, elevated CRP, hypertension and possibly other cardiovascular risk factors.

In 2007, sales of HIV antivirals in the seven major drug markets (the United States, Japan, France, Germany, Italy, Spain and the United Kingdom) were approximately $9.3 billion and are expected to reach $15.1 billion in 2017, according to Datamonitor. While the treatment of HIV has improved dramatically over the past decade, we believe that there remains a significant need for new treatments that are effective against drug-resistant virus, safer for women and African-Americans, well tolerated and convenient to take. According to the Centers for Disease Control and Prevention (CDC), 56,300 people were newly infected with HIV in 2006, 40% more than estimated previously. African-Americans accounted for more than 45% of the new infections. Women account for 27% of the new infections. We are developing products for the treatment of HIV that are highly active against resistant strains, have a high genetic barrier to resistance, have a better safety profile than current drugs in African-Americans and women, can be taken once a day, and are easy to formulate in a combination pill with current drugs.

We also believe that there is growing interest in the potential for targeted therapies, including kinase inhibitors, for the treatment of both cancer and inflammatory disease. Sales of products used in the treatment of cancer were expected to exceed $45.0 billion in 2008, according to IMS Health Incorporated, fueled by strong acceptance of innovative and effective targeted therapies. The failure rate of kinase inhibitor compounds in clinical development in oncology is only 53% versus 82% in the oncology field as a whole. In 2007, the worldwide market for targeted therapies for inflammatory diseases was more than $8.6 billion. Given the role that MEK appears to play in cancer and inflammatory diseases and the increasing preference for oral therapies, we believe that RDEA119 and our next generation MEK inhibitors, if successfully developed, approved and commercialized, could participate in these growing markets.

Valeant Relationship

On December 21, 2006, we acquired intellectual property and other assets from Valeant Research & Development, Inc. related to RDEA806 and our next generation NNRTI program, and RDEA119 and our next generation MEK inhibitor program. Concurrent with the closing of the acquisition from Valeant, we hired a new senior management team and changed our name from IntraBiotics Pharmaceuticals, Inc. to Ardea Biosciences, Inc.

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In consideration for the assets purchased from Valeant and subject to the satisfaction of certain conditions, Valeant has the right to receive development-based milestone payments and sales-based royalty payments from us. There is one set of milestones for RDEA806 and the next generation NNRTI program and a separate set of milestones for RDEA119 and the next generation MEK inhibitor program. In the event of the successful commercialization of a product incorporating RDEA806 or a compound from the next generation NNRTI program, resulting milestone payments could total up to $25.0 million. In the event of the successful commercialization of a product incorporating RDEA119 or a compound from the next generation MEK inhibitor program, resulting milestone payments could total up to $17.0 million. Milestones are paid only once for each program, regardless of how many compounds are developed or commercialized. The first milestone payments of $2.0 million and $1.0 million in the NNRTI program and the MEK inhibitor program, respectively, would be due after the first patient is dosed in the first Phase 2b study, and approximately 80% of the total milestone payments in each program would be due upon United States Food and Drug Administration acceptance and approval of a New Drug Application, or NDA. The royalty rates on all products are in the mid-single digits. We agreed to further develop these compounds with the objective of obtaining marketing approval in the United States, the United Kingdom, France, Spain, Italy and Germany.

Valeant also has the right to exercise a one-time option to repurchase commercialization rights in territories outside the United States and Canada (the Valeant Territories) to the first NNRTI compound derived from the acquired intellectual property to complete a Phase 2b study in HIV. If Valeant exercises this option, which it can do following the completion of a Phase 2b HIV study, but prior to the initiation of a Phase 3 study, we would be responsible for completing Phase 3 studies and for registration of the product in the United States and the European Union. Valeant would pay us a $10.0 million option fee, up to $21.0 million in milestone payments based on regulatory approvals, and a mid-single-digit royalty on product sales in the Valeant Territories.

Research and Development Expenses

Our research and development expenses for the three years ended December 31, 2008, 2007 and 2006 were $44.9 million, $23.1 million and $0.1 million, respectively. Research and development expenses increased substantially in 2008 and 2007 primarily due to continued development and progression of our clinical and preclinical programs.

Clinical Supplies and Manufacturing

We have no in-house manufacturing capabilities. We rely on third-party contract manufacturers to produce our product candidates to support our development activities. Our clinical trial material, critical to our operations, is purchased from various companies and suppliers.

Sales and Marketing

We do not currently have sales or marketing capabilities. In order to commercially market any pharmaceutical product that we successfully advance through preclinical and clinical development and for which we obtain regulatory approval, we must either develop a sales and marketing infrastructure or collaborate with third parties with sales and marketing capabilities. Because of the early stage of our pharmaceutical development programs, we have not yet developed a sales and marketing strategy for any pharmaceutical products that we may develop.

Customers and Distribution

We do not currently sell or distribute pharmaceutical products.

Competition

The biotechnology and pharmaceutical industries are extremely competitive. Our potential competitors in the field are many in number and include major pharmaceutical and specialized biotechnology companies. Many of our potential competitors have significantly more financial, technical and other resources than we do, which may allow them to have a competitive advantage. In addition, they may have substantially more experience in effecting strategic combinations, in-licensing technology, developing drugs, obtaining regulatory approvals and

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manufacturing and marketing products. We cannot give any assurances that we can effectively compete with these other biotechnology and pharmaceutical companies.

Any products that we may develop or discover will compete in highly competitive markets. Our potential competitors in these markets may succeed in developing products that could render our products and those of our collaborators obsolete or non-competitive. In addition, many of our competitors have significantly greater experience than we do in the fields in which we compete.

Intellectual Property

Our success will depend in large part on our ability to:

- obtain and maintain international and domestic patent and other legal protections for the proprietary technology, inventions and improvements we consider important to our business;
- prosecute and defend our patents;
- preserve our trade secrets; and
- operate without infringing the patents and proprietary rights of third parties.

We intend to continue to seek appropriate patent protection for the lead product candidates in our research and development programs and their uses by filing patent applications in the United States and other selected countries. We intend for these patent applications to cover, where possible, claims for composition of matter, medical uses, processes for preparation and formulations.

We own a total of two issued United States patents, 16 pending United States non-provisional applications, seven pending United States provisional applications, eight pending international applications and 80 pending foreign patent applications.

Although we believe that our rights under patent applications we own provide a competitive advantage, the patent positions of pharmaceutical and biotechnology companies are highly uncertain and involve complex legal and factual questions. We may not be able to develop patentable products or processes, and may not be able to obtain patents from pending applications. Even if patent claims are allowed, the claims may not issue, or in the event of issuance, may not be sufficient to protect the technology owned by or licensed to us. Any patents or patent rights that we obtain may be circumvented, challenged or invalidated by our competitors.

We also rely on trade secrets, proprietary know-how and continuing innovation to develop and maintain our competitive position, especially when we do not believe that patent protection is appropriate or can be obtained. We seek protection of these trade secrets, proprietary know-how and any continuing innovation, in part, through confidentiality and proprietary information agreements. However, these agreements may not provide meaningful protection for, or adequate remedies to protect, our technology in the event of unauthorized use or disclosure of information. Furthermore, our trade secrets may otherwise become known to, or be independently developed by, our competitors.

Government Regulation

Pharmaceutical Regulation

If and when we market any pharmaceutical products, they would be subject to extensive government regulation in the United States. Additionally, if we seek to market and distribute any such products abroad, they would also be subject to extensive foreign government regulation.

In the United States, the Food and Drug Administration, or FDA, regulates pharmaceutical products. FDA regulations govern the testing, manufacturing, advertising, promotion, labeling, sale and distribution of pharmaceutical products, and generally require approval of new drugs through a rigorous process. We also may be subject to foreign regulatory requirements governing clinical trials and drug product sales if products are studied or marketed abroad. The approval process outside the United States varies from jurisdiction to jurisdiction and the time required may be longer or shorter than that required for FDA approval.

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Regulation in the United States

The FDA testing and approval process requires substantial time, effort and money. We cannot assure you that any of our products will ever obtain approval. The FDA approval process for new drugs includes, without limitation:

preclinical studies;

submission of an Investigational New Drug application, or IND, for clinical trials;

adequate and well-controlled human clinical trials to establish safety and efficacy of the product;

review of a NDA; and

inspection of the facilities used in the manufacturing of the drug to assess compliance with the FDA s current Good Manufacturing Practices, or cGMP, regulations.

A NDA must include comprehensive and complete descriptions of the preclinical testing, clinical trials and the chemical, manufacturing and control requirements of a drug that enable the FDA to determine the drug s safety and efficacy. A NDA must be submitted, filed and approved by the FDA before any product that we may successfully develop can be marketed commercially in the United States.

Preclinical studies include laboratory evaluation of the product, as well as animal studies to assess the potential safety and effectiveness of the product. Most of these studies must be performed according to good laboratory practices. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Clinical trials may begin 30 days after an IND is received, unless the FDA raises concerns or questions about the conduct of the clinical trials. If concerns or questions are raised, an IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. We have filed and received approval for INDs for our lead clinical candidates, RDEA806, RDEA119 and RDEA594, and we may file additional INDs during 2009. We are required to file an IND before we can commence any clinical trials for our product candidates in the United States.

We cannot assure you that submission of an IND for any of our preclinical product candidates will result in authorization to commence clinical trials. Nor can we assure you that any of our current or future clinical trials will result in approval to market our products. Clinical trials involve the administration of the product candidate that is the subject of the trial to volunteers or patients under the supervision of a qualified principal investigator. Each clinical trial must be reviewed and approved by an independent institutional review board at each institution at which the study will be conducted. The institutional review board will consider, among other things, ethical factors, safety of human subjects and the possible liability of the institution arising from the conduct of the proposed clinical trial. Also, clinical trials must be performed according to good clinical practices which are enumerated in FDA regulations and guidance documents.

Clinical trials typically are conducted in sequential phases: Phases 1, 2, 3 and 4. The phases may overlap. The FDA may require that we suspend clinical trials at any time on various grounds, including if the FDA makes a finding that the subjects are being exposed to an unacceptable health risk.

In Phase 1 clinical trials, a drug is usually tested on a small number of healthy volunteers to determine safety, any adverse effects, proper dosage, absorption, metabolism, distribution, excretion and other drug effects.

In Phase 2 clinical trials, a drug is usually tested on a limited number of subjects (generally up to several hundred) to preliminarily evaluate the efficacy of the drug for specific, targeted indications, determine dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.

In Phase 3 clinical trials, a drug is usually tested on a larger number of subjects (up to several thousand), in an expanded patient population and at multiple clinical sites.

In Phase 4 clinical trials or other post-approval commitments, additional studies and patient follow-up are conducted to gain experience from the treatment of patients in the intended therapeutic indication. Additional studies and follow-up are also conducted to document a clinical benefit where drugs are approved under accelerated approval regulations and based on surrogate endpoints. In clinical trials, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable

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clinical symptoms. Failure to promptly conduct Phase 4 clinical trials and follow-up could result in expedited withdrawal of products approved under accelerated approval regulations.

The facilities, procedures and operations for any of our contract manufacturers must be determined to be adequate by the FDA before product approval. Manufacturing facilities are subject to inspections by the FDA for compliance with cGMP, licensing specifications and other FDA regulations before and after a NDA has been approved. Foreign manufacturing facilities are also subject to periodic FDA inspections or inspections by foreign regulatory authorities. Among other things, the FDA may withhold approval of NDAs or other product applications if deficiencies are found at the facility. Vendors that may supply us with finished products or components used to manufacture, package and label products are also subject to similar regulations and periodic inspections.

In addition, the FDA imposes a number of complex regulatory requirements on entities that advertise and promote pharmaceuticals, including, but not limited to, standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities, and promotional activities involving the Internet.

Failure to comply with FDA and other governmental regulations can result in fines, unanticipated compliance expenditures, recall or seizure of products, total or partial suspension of production and/or distribution, suspension of the FDA s review of NDAs, injunctions and criminal prosecution. Any of these actions could have a material adverse effect on us.

Regulation Outside the United States

If we market drugs in foreign countries, we also will be subject to foreign regulatory requirements governing human clinical trials and marketing approval for pharmaceutical products. The requirements governing the conduct of clinical trials, product approval, pricing and reimbursement vary widely from country to country. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained before manufacturing or marketing the product in those countries. The approval process varies from country to country and the time required for such approvals may differ substantially from that required for FDA approval. There is no assurance that any future FDA approval of any of our clinical trials or drugs will result in similar foreign approvals or vice versa.

Additional Regulation

Third-Party Reimbursement

In the United States, physicians, hospitals and other healthcare providers that purchase pharmaceutical products generally rely on third-party payers, principally private health insurance plans, Medicare and, to a lesser extent, Medicaid, to reimburse all or part of the cost of the product and procedure for which the product is being used. Even if a product is approved for marketing by the FDA, there is no assurance that third-party payers will cover the cost of the product and related medical procedures. If they do not, end-users of the drug would not be eligible for any reimbursement of the cost, and our ability to market any such drug would be materially and adversely impacted.

Reimbursement systems in international markets vary significantly by country and, within some countries, by region. Reimbursement approvals must be obtained on a country-by-country basis. In many foreign markets, including markets in which we hope to sell our products, the pricing of prescription pharmaceuticals is subject to government pricing control. In these markets, once marketing approval is received, pricing negotiations could take significant additional time. As in the United States, the lack of satisfactory reimbursement or inadequate government pricing of any of our products would limit their widespread use and lower potential product revenues.

Fraud and Abuse Laws

Federal and state anti-kickback and anti-fraud and abuse laws, as well as the federal Civil False Claims Act may apply to certain drug and device research and marketing practices. The Civil False Claims Act prohibits knowingly presenting or causing to be presented a false, fictitious or fraudulent claim for payment to the United States. Actions under the Civil False Claims Act may be brought by the Attorney General or by a private individual

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acting as an informer or whistleblower in the name of the government. Violations of the Civil False Claims Act can result in significant monetary penalties. The federal government is using the Civil False Claims Act, and the threat of significant liability, in its investigations of healthcare providers, suppliers and drug and device manufacturers throughout the country for a wide variety of drug and device marketing and research practices, and has obtained multi-million dollar settlements. The federal government may continue to devote substantial resources toward investigating healthcare providers , suppliers and drug and device manufacturers compliance with the Civil False Claims Act and other fraud and abuse laws. We may have to expend significant financial resources and management attention if we ever become the focus of such an investigation, even if we are not guilty of any wrong doings.

HIPAA

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, requires the use of standard transactions, privacy and security standards and other administrative simplification provisions by covered entities, which include many healthcare providers, health plans and healthcare clearinghouses. HIPAA instructs the Secretary of the Department of Health and Human Services to promulgate regulations implementing these standards in the United States.

Other Laws

We are also subject to other federal, state and local laws of general applicability, such as laws regulating working conditions, and various federal, state and local environmental protection laws and regulations, including those governing the discharge of material into the environment.

Employees

As of March 6, 2009, we employed 81 regular full-time employees (including 28 people who have a Ph.D. and one person who has a Pharm.D.), 64 of whom are involved full-time in research, clinical and development activities. All members of our senior management team have had prior experience with pharmaceutical or biotechnology companies. We believe that we have been successful in attracting skilled and experienced personnel, but competition for personnel is intense and there can be no assurance that we will be able to attract and retain the individuals needed. None of our employees are covered by a collective bargaining agreements and management considers relations with our employees to be good.

Company Information

We were incorporated in the State of Delaware in January 1994. Our corporate offices are located at 4939 Directors Place, San Diego, CA 92121. Our telephone number is (858) 652-6500. Our website address is www.ardeabio.com. We make available free of charge through our Internet website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

ITEM 1A. *RISK FACTORS.*

You should carefully consider the following information about risks and uncertainties that may affect us or our business, together with the other information appearing elsewhere in this annual report on Form 10-K. If any of the following events described as risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment in our securities. An investment in our

securities is speculative and involves a high degree of risk. You should not invest in our securities if you cannot bear the economic risk of your investment for an indefinite period of time and cannot afford to lose your entire investment.

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Risks Related to Our Business

Development of our products will take years; we may never attain product sales; and we expect to continue to incur net operating losses.

We have incurred, and expect to continue to incur, substantial operating losses for the foreseeable future. We expect that most of our resources for the foreseeable future will be dedicated to research and development and preclinical and clinical testing of compounds. The amounts paid to advance the preclinical and clinical development of our product candidates, including RDEA806, RDEA594, RDEA427, RDEA119, RDEA436 and our other compounds, may continue to increase. Any compounds we advance through preclinical and clinical development will require extensive and costly development, preclinical testing and clinical trials prior to seeking regulatory approval for commercial sales. Our most advanced product candidates, RDEA806, RDEA594, RDEA427, RDEA119, RDEA436, and any other compounds we advance further into development, may never be approved for commercial sales. The time required to achieve product sales and profitability is lengthy and highly uncertain and we cannot assure you that we will be able to achieve or maintain product sales.

We are not currently profitable and may never become profitable.

To date, we have generated limited revenues and we do not anticipate generating significant revenues for at least several years, if ever. We may increase our operating expenses over at least the next several years as we plan to advance our product candidates, including RDEA806, RDEA594, RDEA427, RDEA119, RDEA436, into further preclinical testing and clinical trials, and may expand our research and development activities and acquire or license new technologies and product candidates. As a result, we expect to continue to incur significant and potentially increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with our research and product development efforts, we are unable to predict the extent of any future losses or when we will become profitable, if ever. Even if we do achieve profitability, we may not be able to sustain or increase profitability on an ongoing basis.

Because the results of preclinical studies are not necessarily predictive of future results, we can provide no assurances that, even if our product candidates are successful in preclinical studies, such product candidates will have favorable results in clinical trials or receive regulatory approval.

Positive results from preclinical studies should not be relied upon as evidence that clinical trials will succeed. Even if our product candidates achieve positive results in clinical studies, we will be required to demonstrate through clinical trials that these product candidates are safe and effective for use in a diverse population before we can seek regulatory approvals for their commercial sale. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through clinical trials. If any product candidate fails to demonstrate sufficient safety and efficacy in any clinical trial, then we would experience potentially significant delays in, or be required to abandon, development of that product candidate. If we delay or abandon our development efforts of any of our product candidates, then we may not be able to generate sufficient revenues to become profitable, and our reputation in the industry and in the investment community would likely be significantly damaged, each of which would cause our stock price to decrease significantly.

Delays in the commencement of clinical testing of our current and potential product candidates could result in increased costs to us and delay our ability to generate revenues.

Our product candidates will require preclinical testing and extensive clinical trials prior to submission of any regulatory application for commercial sales. Delays in the commencement of clinical testing of our product candidates could significantly increase our product development costs and delay product commercialization. In addition, many of

the factors that may cause, or lead to, a delay in the commencement of clinical trials may also ultimately lead to denial of regulatory approval of a product candidate.

The commencement of clinical trials can be delayed for a variety of reasons, including:

- delays in demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial;

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delays in reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;

delays in manufacturing quantities of a product candidate sufficient for clinical trials;

delays in obtaining approval of a IND from the FDA or similar foreign approval;

delays in obtaining institutional review board approval to conduct a clinical trial at a prospective site; and

insufficient financial resources.

In addition, the commencement of clinical trials may be delayed due to insufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, and the eligibility criteria for the clinical trial.

Delays in the completion of, or the termination of, clinical testing of our current and potential product candidates could result in increased costs to us and delay or prevent us from generating revenues.

Once a clinical trial for any current or potential product candidate has begun, it may be delayed, suspended or terminated by us or the FDA, or other regulatory authorities due to a number of factors, including:

ongoing discussions with the FDA or other regulatory authorities regarding the scope or design of our clinical trials;

failure to conduct clinical trials in accordance with regulatory requirements;

lower than anticipated retention rate of patients in clinical trials;

the imposition of a clinical hold;

lack of adequate funding to continue clinical trials;

negative results of clinical trials;

insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials; or

serious adverse events or other undesirable drug-related side effects experienced by clinical trial participants.

Many of these factors that may lead to a delay, suspension or termination of clinical testing of a current or potential product candidate may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays in the completion of, or termination of, clinical testing, our financial results and the commercial prospects for our product candidates will be harmed, and our ability to generate revenues from those products will be delayed.

If our internal discovery and development efforts are unsuccessful, we will be required to obtain rights to new products or product candidates from third parties, which we may not be able to do.

Our long-term ability to earn product revenue depends on our ability to successfully advance our product candidates through clinical development and regulatory approval and to identify and obtain new products or product candidates through internal development or licenses from third parties. If the development programs we acquired from Valeant and our internal development programs are not successful, we will need to obtain rights to new products or product candidates from third parties. We may be unable to obtain suitable product candidates or products from third parties for a number of reasons, including:

- we may be unable to purchase or license products or product candidates on terms that would allow us to make a sufficient financial return from resulting products;

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competitors may be unwilling to assign or license products or product candidate rights to us (in particular, if we are not able to successfully advance the further development of the product candidates we acquired from Valeant); or

we may be unable to identify suitable products or product candidates within, or complementary to, our areas of interest relating to the treatment of gout, HIV, cancer and inflammatory diseases.

If we are unable to obtain rights to new products or product candidates from third parties, our ability to generate product revenues and achieve profitability may suffer.

Even if we successfully initiate and complete clinical trials for any product candidate, there are no assurances that we will be able to submit or obtain regulatory approval of a new drug application.

There can be no assurance that if our clinical trials of any potential product candidate are successfully initiated and completed, we will be able to submit an NDA to the FDA in the U.S. or similar application to other regulatory authorities elsewhere in the world, or that any applications we submit will be approved by these regulatory authorities in a timely manner, if at all. If we are unable to submit an NDA or similar application with respect to any future product candidate, or if any NDA or similar application we submit is not approved by the FDA or other regulatory authorities elsewhere in the world, we will be unable to commercialize that product. These authorities can and do reject new drug application and require additional clinical trials, even when product candidates have performed well or have achieved favorable results in clinical trials. If we fail to commercialize any future product candidate in clinical trials, we may be unable to generate sufficient revenues to attain profitability and our reputation in the industry and in the investment community would likely be damaged, each of which would cause our stock price to decrease.

If we successfully develop products, but those products do not achieve and maintain market acceptance, our business will not be profitable.

Even if any of our product candidates are approved for commercial sale by the FDA or other regulatory authorities, our profitability and growth will depend on the degree of market acceptance of any approved product candidate by physicians, healthcare professionals and third-party payors, which will in turn depend on a number of factors, including:

our ability to provide acceptable evidence of safety and efficacy of our products;

relative convenience and ease of administration of products;

the prevalence and severity of any adverse side effects from the products;

the availability of alternative treatments;

pricing and cost effectiveness of products; and

our ability to obtain sufficient third-party insurance coverage or reimbursement.