

Ardea Biosciences, Inc./DE  
Form S-3  
January 13, 2009

**Table of Contents**

**As filed with the Securities and Exchange Commission on January 13, 2009**

**Registration No. 333-**

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

**Form S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**ARDEA BIOSCIENCES, INC.**

*(Exact Name of Registrant as Specified in its Charter)*

**Delaware**  
*(State or Other Jurisdiction of  
Incorporation or Organization)*

**94-3200380**  
*(I.R.S. Employer  
Identification No.)*

**4939 Directors Place  
San Diego, CA 92121  
(858) 652-6500**  
*(Address, Including Zip Code and Telephone Number, Including  
Area Code, of Registrant's Principal Executive Offices)*

**Barry D. Quart, Pharm.D.  
Chief Executive Officer  
Ardea Biosciences, Inc.  
4939 Directors Place  
San Diego, CA 92121  
(858) 652-6500**  
*(Name, Address, Including Zip Code and Telephone Number, Including  
Area Code, of Agent for Service)*

***With a Copy to:*  
Ethan E. Christensen, Esq.  
Cooley Godward Kronish LLP  
4401 Eastgate Mall  
San Diego, CA 92121  
(858) 550-6000**

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

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

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

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

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

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

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

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. (Check one):

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

**CALCULATION OF REGISTRATION FEE**

<b>Title of Each Class of Securities to be Registered</b>	<b>Amount to be Registered(1)</b>	<b>Proposed Maximum Offering Price per Share(2)</b>	<b>Proposed Maximum Aggregate Offering Price</b>	<b>Amount of Registration Fee</b>
Common Stock, \$0.001 par value per share	3,421,668	\$12.01	\$41,094,233	\$1,615
<b>Total</b>	<b>3,421,668</b>	<b>\$12.01</b>	<b>\$41,094,233</b>	<b>\$1,615</b>

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (sometimes referred to herein as the Securities Act), this registration statement also covers such additional shares as may hereafter be offered or issued with respect to the shares registered hereby resulting from stock splits, stock dividends, recapitalizations or certain other capital adjustments.

(2) Estimated solely for purposes of calculating the amount of the registration fee pursuant to Rule 457(c) of the Securities Act of 1933, as amended, based upon the average of the high and low sales prices of the registrant's common stock as reported on The NASDAQ Global Market on January 6, 2009.

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

**Table of Contents**

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

**SUBJECT TO COMPLETION, DATED JANUARY 13, 2009**

**PROSPECTUS**

**3,421,668 Shares  
Ardea Biosciences, Inc.  
Common Stock**

This prospectus relates to the resale from time to time of up to 3,421,668 shares of our common stock by the selling stockholders named in this prospectus and the selling stockholders transferees. Of the shares, 2,737,336 were issued pursuant to a private placement that closed on December 19, 2008, and an additional 684,332 shares are issuable upon the exercise of warrants sold in the private placement which are first exercisable beginning June 17, 2009 and expire on December 19, 2013. The private placement is more fully described on pages 18-20 of this prospectus under the heading Selling Stockholders. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholders.

The selling stockholders may sell the common stock being offered by this prospectus from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under Plan of Distribution. The selling stockholders may sell the shares in negotiated transactions or otherwise, at the prevailing market price for the shares or at negotiated prices. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is listed on The NASDAQ Global Market under the symbol RDEA. On January 12, 2009, the last reported sale price of our common stock on The NASDAQ Global Market was \$13.00 per share.

**Investing in our common stock involves a high degree of risk. You are urged to read the section entitled Risk Factors beginning on page 5; of this prospectus, which describes specific risks and other information that should be considered before you make an investment decision.**

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

The date of this prospectus is January \_\_, 2009.

**TABLE OF CONTENTS**

	<b>Page</b>
<u>Summary</u>	1
<u>Risk Factors</u>	5
<u>Forward-Looking Statements</u>	16
<u>Use of Proceeds</u>	17
<u>Selling Stockholders</u>	18
<u>Plan of Distribution</u>	20
<u>Legal Matters</u>	22
<u>Experts</u>	22
<u>Where You Can Find More Information</u>	23
<u>Incorporation of Certain Information by Reference</u>	23
<u>EX-5.1</u>	
<u>EX-23.1</u>	

You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. We have not, and the selling stockholders have not, authorized anyone to provide you with different information. Neither we nor the selling stockholders are making an offer to sell or seeking an offer to buy shares of our common stock under this prospectus or any applicable prospectus supplement in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, any applicable prospectus supplement and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since that date.

---

**Table of Contents****SUMMARY**

To understand this offering fully and for a more complete description of the legal terms of this offering as well as our company and the common stock being sold in this offering, you should read carefully the entire prospectus and the other documents to which we may refer you, including Risk Factors included below in this prospectus and our consolidated financial statements and notes to those statements incorporated by reference in this prospectus. Reference to we, us, our, our company, the Company, and RDEA refers to Ardea Biosciences, Inc. and its subsidiaries, unless the context requires otherwise.

The following description of our business contains forward-looking statements that involve risks, uncertainties and assumptions. The actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those set forth under Risk Factors. All forward-looking statements included in this document are based on information available to us on the date of this document and we assume no obligation to update any forward-looking statements contained herein.

**ARDEA BIOSCIENCES, INC.****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 ( HIV ), cancer and inflammatory diseases. We believe that we are well-positioned to create stockholder value through our development activities, given our ability to achieve clinical proof-of-concept relatively quickly and cost-effectively in these disease areas. We are currently pursuing multiple development programs, including the following:

**Product Portfolio**

<b>Product Candidate</b>	<b>Target Indication</b>	<b>Development Status</b>
RDEA806 (a prodrug of RDEA594)	Gout	Phase 2a ongoing
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****RDEA806**

RDEA806, a prodrug of RDEA594, is currently being evaluated in a Phase 2a proof-of-concept study to provide an early confirmation of RDEA594's activity in the target population of gout patients. We plan to complete this study in the first quarter of 2009.

**RDEA594**

RDEA594, our lead product candidate for the treatment of hyperuricemia and gout, is a major metabolite of RDEA806. RDEA594 does not have antiviral activity and is responsible for the lowering of serum uric acid levels observed following administration of RDEA806 to over 100 subjects in Phase 1 and Phase 2 studies. In October 2008, we reported positive preliminary data from a single ascending dose Phase 1 study of RDEA594 in normal healthy volunteers. In this study, RDEA594 demonstrated a significant increase in urinary excretion of uric acid, confirming that RDEA594 is responsible for the uric acid-lowering effects observed in previous clinical studies of RDEA806. 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 study of RDEA594 in gout patients in the first half of 2009, with the goal of completing that study by the end of 2009.

**Table of Contents****HIV****RDEA806**

RDEA806 is our lead non-nucleoside reverse transcriptase inhibitor ( 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 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 100 subjects. Results from a Phase 2a monotherapy proof-of-concept study of RDEA806 demonstrated up to 2.0 log placebo-adjusted reduction in plasma viral load on Day 8 with once-daily dosing of RDEA806. In addition, all dosing regimens tested were well tolerated.

We have received regulatory approval from the Medicines and Healthcare Products Regulatory Agency in the United Kingdom to conduct a Phase 2b study comparing RDEA806 to efavirenz in anti-retroviral treatment naïve patients without transmitted resistance receiving background treatment with Truvada. We expect to dose the first patient in this study in 2009, the timing of which will be determined by the results of ongoing partnering discussions.

**RDEA427**

The lead compound in our 2<sup>nd</sup> 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 Phase 0 study and have selected it for clinical development. We plan to initiate a Phase 1 study of RDEA427 in normal healthy volunteers in the first quarter of 2009, the timing of which will be determined by the results of ongoing partnering discussions.

**CANCER****RDEA119**

RDEA119, our lead mitogen-activated ERK kinase ( 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 have initiated 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.

## **Table of Contents**

### **INFLAMMATION**

#### **RDEA119**

*In vivo* preclinical tests have shown RDEA119 to significantly inhibit production of inflammatory cytokines. We have completed a Phase 1 study of RDEA119 in normal healthy volunteers. Data from the Phase 1 study suggests that RDEA119 has a pharmacokinetic profile allowing for convenient once-daily oral dosing. All dosing regimens tested were well tolerated.

#### **RDEA436**

The lead compound in our 2<sup>nd</sup> 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. We have evaluated RDEA436 in a Phase 0 study and have selected RDEA436 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. We plan to initiate this study in the first half of 2009, the timing of which will be determined by the results of ongoing partnering discussions.

We plan to initiate a Phase 2a clinical study of RDEA119 or RDEA436 in patients with inflammatory disease in the first half of 2009, the timing of which will be determined by the results of ongoing partnering discussions.

### **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. Approximately three-to-five million Americans suffer from gout, many of whom do not achieve a target reduction in uric acid with current treatments.

In 2007, the worldwide market for HIV antivirals was approximately \$8.1 billion, according to Decision Resources. 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, well-tolerated and convenient to take.

We also believe that there is a 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 billion in 2008, according to IMS Health Incorporated, fueled by strong acceptance of innovative and effective targeted therapies. 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 2<sup>nd</sup> 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. ( Valeant ) related to RDEA806 and our 2<sup>nd</sup> generation NNRTI program, and RDEA119 and our 2<sup>nd</sup> 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.

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 2<sup>nd</sup> generation NNRTI program and a separate set of milestones for RDEA119 and the 2<sup>nd</sup> generation MEK inhibitor program. In the event of the successful commercialization of a product incorporating RDEA806 or a compound from the 2<sup>nd</sup> 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 2<sup>nd</sup> 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 ( 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.

**Table of Contents**

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.

**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](http://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. Information contained on our website, unless specifically referenced herein, does not constitute part of this prospectus or any prospectus supplement.

**Table of Contents**

**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 prospectus. 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.*

**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. We expect that the amounts paid to advance the preclinical and clinical development of our product candidates, including RDEA806, RDEA427, RDEA594, RDEA119, RDEA436 and our other compounds, will 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, RDEA427, RDEA594, RDEA119 and RDEA436, and any other compounds we advance into further 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 expect to increase our operating expenses over at least the next several years as we plan to advance our product candidates, including RDEA806, RDEA427, RDEA594, RDEA119 and RDEA436, into further preclinical testing and clinical trials, 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 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;

**Table of Contents**

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 an Investigational New Drug Application ( IND ) from the United States Food and Drug Administration ( 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:



**Table of Contents**

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;

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 HIV, gout, 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 FDA 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 or that any NDA we submit will be approved by the FDA in a timely manner, if at all. If we are unable to submit an NDA with respect to any future product candidate, or if any NDA we submit is not approved by the FDA, we will be unable to commercialize that product. The FDA can and does reject NDAs and requires additional clinical trials, even when product candidates performed well or 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.

In addition, even if any of our potential products achieve market acceptance, we may not be able to maintain that market acceptance over time if:

new products or technologies are introduced that are more favorably received than our potential future products, are more cost effective or render our potential future products obsolete; or

complications arise with respect to use of our potential future products.

***We will need substantial additional funding and may be unable to raise capital when needed, or at all, which would force us to delay, reduce or eliminate our research and development programs or commercialization efforts.***

Based on current projections, excluding any funds that we may receive from future business development activities, we believe that our existing cash, cash equivalents and short-term investments and interest earned thereon, including the funds received from our recent growth capital loan, will be adequate to fund our anticipated levels of

operations into the second quarter of 2010. However, our business and operations may change in a manner that would consume available resources at a greater rate than anticipated. In particular, because most of our resources for the foreseeable future will be used to advance our product candidates, we

**Table of Contents**

may not be able to accurately anticipate our future research and development funding needs. We will need to raise substantial additional capital in the future to, among other things:

fund our research, discovery and development programs;

advance our product candidates into and through clinical trials and the regulatory review and approval process;

establish and maintain manufacturing, sales and marketing operations;

commercialize our product candidates, if any, that receive regulatory approval; and

acquire rights to products or product candidates, technologies or businesses.

Our future funding requirements will depend on, and could increase significantly as a result of, many factors, including:

the rate of progress and cost of our research and development activities;

the scope, prioritization and number of preclinical studies and clinical trials we pursue;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the costs and timing of regulatory approval;

the costs of establishing or contracting for manufacturing, sales and marketing capabilities;

the effects of competing technological and market developments;

the terms and timing of any collaborative, licensing and other arrangements that we may establish; and

the extent to which we acquire or license new technologies, products or product candidates.

We do not anticipate that we will generate significant continuing revenues for at least several years, if ever. Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through public or private equity offerings, debt financings and corporate collaboration and licensing arrangements, as well as through interest income earned on cash balances. We cannot be certain that additional funding will be available to us on acceptable terms, or at all. Our ability to obtain new financing may be constrained by the current unprecedented volatile economic conditions affecting financial markets. If funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts.

***Raising additional funds 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 raise additional funds through public or private equity offerings, debt financings or corporate collaborations and licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. To the extent that we raise additional capital by issuing equity securities, our stockholders ownership will be diluted. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants would likely include, among other things, limitations on borrowing, specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens, pay dividends, redeem capital stocks or make investments. In addition, if we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. For example, we might be required to relinquish all or a portion of our sales and marketing rights with respect to potential products or license intellectual property that enables licensees to

develop competing products in order to complete any such transaction.

**Table of Contents**

***The investment of our cash balance and investments in marketable securities are subject to risks which may cause losses and affect the liquidity of these investments.***

Our short-term investments consist of securities of the United States government, its federal agencies, entities controlled by the federal government and municipal bonds. These investments are subject to general credit, liquidity, market and interest rate risks, which may further be exacerbated by United States sub-prime mortgage defaults and other factors, which have affected various sectors of the financial markets and caused credit and liquidity issues. During the quarter ended September 30, 2008, we determined that any declines in the fair value of our investments were temporary. There may be further declines in the value of these investments, which we may determine to be other-than-temporary. These market risks associated with our investment portfolio may have a negative adverse effect on our results of operations, liquidity and financial condition.

***We do not have internal manufacturing capabilities, and if we fail to develop and maintain internal capabilities or supply relationships with collaborators or other outside manufacturers, we may be unable to develop or commercialize any products.***

Our ability to develop and commercialize any products we may develop will depend in part on our ability to manufacture, or arrange for collaborators or other parties to manufacture, our products at a competitive cost, in accordance with regulatory requirements, and in sufficient quantities for clinical testing and eventual commercialization. We currently do not have any significant manufacturing arrangements or agreements, as our current product candidates will not require commercial-scale manufacturing for at least several years, if ever. Our inability to enter into or maintain manufacturing agreements with collaborators or capable contract manufacturers on acceptable terms could delay or prevent the development and commercialization of our products, which would adversely affect our ability to generate revenues and would increase our expenses.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop, we may be unable to generate product revenue.***

We do not currently have a sales organization for the sales, marketing and distribution of pharmaceutical products. In order to commercialize any products, we must build our sales, marketing, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We have not definitively determined whether we will attempt to establish internal sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop. The establishment and development of our own sales force to market any products we may develop will be expensive and time consuming and could delay any product launch, and we cannot be certain that we would be able to successfully develop this capacity. If we are unable to establish our sales and marketing capability or any other non-technical capabilities necessary to commercialize any product we may develop, we will need to contract with third parties to market and sell any products we may develop. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable.

***We will need to increase the size of our organization, and we may encounter difficulties managing our growth, which could adversely affect our results of operations.***

We will need to expand and effectively manage our managerial, operational, financial and other resources in order to successfully pursue our research, development and commercialization efforts and secure collaborations to market and distribute our products. If we continue to grow, it is possible that our management, accounting and scientific personnel, systems and facilities currently in place may not be adequate to support this future growth. To manage any growth, we will be required to continue to improve our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. We may be unable to successfully manage the expansion of our operations or operate on a larger scale and, accordingly, may not achieve our research, development and commercialization goals.

***If we are unable to attract and retain key management and scientific staff, we may be unable to successfully develop or commercialize our product candidates.***

We are a small company, and our success depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. In particular, our research and drug discovery and development

programs depend on our ability to attract and retain highly skilled chemists, biologists and preclinical personnel, especially in the fields of HIV, gout, cancer and inflammatory diseases. If we are unable to hire or retain these employees, we may not be able to advance our research and development programs at the pace we anticipate. We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for qualified personnel among biotechnology and pharmaceutical businesses, particularly in the San Diego, California area. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will impede significantly the achievement of our research and development objectives. In addition, all of our employees are at will employees, which means that any employee may quit at any time and we may terminate any employee at any time. Currently, we do not have employment agreements with any employees or members of senior management that provide us any guarantee of their continued employment. If we lose members of our senior management team, we may not be able to find suitable replacements and our business may be harmed as a result.

**Table of Contents**

***Our quarterly results and stock price may fluctuate significantly.***

We expect our results of operations and future stock price to continue to be subject to significant quarterly fluctuations. The level of our revenues, if any, our results of operations and our stock price at any given time will be based primarily on the following factors:

whether or not we achieve specified research or commercialization milestones under any agreement that we enter into with collaborators and the timely payment by potential commercial collaborators of any amounts payable to us or by us to Valeant or any other party, including the milestone payments that we may make to Valeant;

the addition or termination of research or development programs or funding support;

the status of development of our product candidates, including results of preclinical studies and any future clinical trials;

variations in the level of expenses related to our product candidates or potential product candidates during any given period;

our execution of collaborative, licensing or other arrangements, and the timing and accounting treatment of payments we make or receive under these arrangements;

our recommendation of additional compounds for preclinical development; and

fluctuations in the stock prices of other companies in the biotechnology and pharmaceuticals industries and in the financial markets generally.

These factors, some of which are not within our control, may cause the price of our stock to fluctuate substantially. In particular, if our quarterly operating results fail to meet or exceed the expectations of securities analysts or investors, our stock price could drop suddenly and significantly. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

***If we engage in any acquisition, we will incur a variety of costs, and we may never realize the anticipated benefits of the acquisition.***

In 2006, we acquired pharmaceutical research and development programs, including our most advanced product candidates, from Valeant, and there is no guarantee that we will be able to successfully develop the acquired product candidates. We may attempt to acquire businesses, technologies, services or other products or in-license technologies that we believe are a strategic fit with our existing development programs, at the appropriate time and as resources permit. In any acquisition, the process of integrating the acquired business, personnel, technology, service or product may result in unforeseen operating difficulties and expenditures and may divert significant management attention from our ongoing business operations. These operational and financial risks include:

**Table of Contents**

assumption and exposure to unknown liabilities;

disruption of our business and diversion of our management's time and attention to acquiring and developing acquired products or technologies;

incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;

higher than expected acquisition and integration costs;

increased amortization expenses;

negative effect on our earnings (or loss) per share;

difficulty and cost in combining and integrating the operations and personnel of any acquired businesses with our operations and personnel;

impairment of relationships with key suppliers, contractors or customers of any acquired businesses due to changes in management and ownership; and

inability to retain key employees of any acquired businesses.

We may fail to realize the anticipated benefits of any acquisition or devote resources to potential acquisitions that are never completed. If we fail to successfully identify strategic opportunities, complete strategic transactions or integrate acquired businesses, technologies, services or products, then we may not be able to successfully expand our product candidate portfolio to provide adequate revenue to attain and maintain profitability.

***Earthquake damage to our facilities could delay our research and development efforts and adversely affect our business.***

Our research and development facility in San Diego, California, is located in a seismic zone, and there is the possibility of an earthquake, which could be disruptive to our operations and result in delays in our research and development efforts. In the event of an earthquake, if our facilities or the equipment in our facilities are significantly damaged or destroyed for any reason, we may not be able to rebuild or relocate our facility or replace any damaged equipment in a timely manner and our business, financial condition and results of operations could be materially and adversely affected.

***Valeant's exercise of its option to repurchase commercialization rights in territories outside the United States and Canada could limit the market for our first NNRTI product and adversely affect our business.***

Under the asset purchase agreement that we entered into with Valeant on December 21, 2006, Valeant retains a one-time option to repurchase commercialization rights in the Valeant Territories for our first NNRTI product derived from the acquired intellectual property to advance to a Phase 2b HIV clinical trial. If Valeant exercises this option, which it can do following the completion of a Phase 2b clinical trial, but prior to the initiation of a Phase 3 clinical trial, 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. However, Valeant would then own all commercialization rights in the Valeant Territories, which may adversely impact the amount of aggregate revenue we may be able to generate from sales of our NNRTI product and may negatively impact our potential for long-term growth. Also, if Valeant exercises its option to repurchase commercialization rights in the Valeant Territories and experiences difficulties in commercializing our NNRTI product in the Valeant Territories, then our commercialization efforts in the United States and Canada may be adversely impacted.

***Failure to comply with our minimum commitments under the asset purchase agreement with Valeant could expose us to potential liability or otherwise adversely affect our business.***

We agreed to use reasonable efforts to develop the product candidates in the pharmaceutical research and development programs we acquired from Valeant, with the objective of obtaining marketing approval for RDEA806,

RDEA119 and the lead product candidates from the 2<sup>nd</sup> generation NNRTI and MEK inhibitor programs in the United States, the United Kingdom, France, Spain, Italy and Germany. Our efforts will be designed to consistently advance the program with the goal of achieving the first milestone event within 24 months of the closing of the transaction with Valeant. If we fail to make sufficient effort to develop the product candidates, then we may be subject to a potential lawsuit or lawsuits from Valeant under the asset purchase agreement. If such a lawsuit were filed, our reputation within the pharmaceutical research and development community may be negatively impacted and our business may suffer.

**Table of Contents**

***Failure to achieve and maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and stock price.***

Section 404 of the Sarbanes-Oxley Act requires on-going management assessments, beginning with the year ended December 31, 2007, of the effectiveness of our internal controls over financial reporting and, beginning with the year ending December 31, 2008, will further require a report by our independent auditors that provides our independent auditor's assessment of the effectiveness of our internal controls. Testing and maintaining internal controls involves significant costs and can divert our management's attention from other matters that are important to our business. We and our auditors may not be able to conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404. Failure to achieve and maintain an effective internal control environment could harm our operating results and could cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the price of our stock.

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our internal controls over financial reporting will prevent all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations on all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud involving a company have been, or will be, detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and we cannot assure you that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in cost-effective control systems, misstatements due to error or fraud may occur and not be detected. We cannot assure you that we or our independent registered public accounting firm will not identify a material weakness in our internal controls in the future. A material weakness in our internal controls over financial reporting would require management and our independent registered public accounting firm to evaluate our internal controls as ineffective. If our internal controls over financial reporting are not considered effective, we may experience a loss of public confidence, which could have an adverse effect on our business and on the price of our stock.

**Risks Related to Our Industry**

***Because our product candidates and development and collaboration efforts depend on our intellectual property rights, adverse events affecting our intellectual property rights will harm our ability to commercialize products.***

Our commercial success depends on obtaining and maintaining patent protection and trade secret protection of our product candidates and their uses, as well as successfully defending these patents against third-party challenges. We will only be able to protect our product candidates and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or effectively protected trade secrets cover them.

Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to obtain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our product candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Even with respect to patents that have issued or will issue, we cannot guarantee that the claims of these patents are, or will be valid, enforceable or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us. For example:

we might not have been the first to make, conceive or reduce to practice the inventions covered by any or all of our pending patent applications;

we might not have been the first to file patent applications for these inventions;

others may independently develop similar or alternative technologies or duplicate any of our technologies;

it is possible that none of our pending patent applications will result in issued patents;

our issued or acquired patents may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or may be challenged by third parties;

our issued patents may not be valid or enforceable; or

the patents of others may have an adverse effect on our business.

## **Table of Contents**

Patent applications in the United States are maintained in confidence for at least 18 months after their filing. Consequently, we cannot be certain that the patent applications we are pursuing will lead to the issuance of any patent or be free from infringement or other claims from third parties. In the event that a third party has also filed a United States patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the United States Patent Office to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our United States patent position. Furthermore, we may not have identified all United States and foreign patents or published applications that affect our business either by blocking our ability to commercialize our product candidates or by covering similar technologies that affect our market.

In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our product candidates.

Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us.

Other companies may obtain patents and/or regulatory approvals to use the same drugs to treat diseases, other than HIV, gout, cancer and inflammatory diseases. As a result, we may not be able to enforce our patents effectively because we may not be able to prevent healthcare providers from prescribing, administering or using another company's product that contains the same active substance as our products when treating patients with HIV, gout, cancer or inflammatory diseases.

### ***Our business depends upon not infringing the rights of others.***

If we are sued for infringing intellectual property rights of others, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business. Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. We may be exposed to future litigation by third parties based on claims that our product candidates or activities infringe the intellectual property rights of others. There are numerous United States and foreign issued patents and pending patent applications owned by others in HIV, gout, cancer, inflammatory diseases and the other fields in which we may develop products. We cannot assure you that third parties holding any of these patents or patent applications will not assert infringement claims against us for damages or seek to enjoin our activities. We also cannot assure you that, in the event of litigation, we will be able to successfully assert any belief we may have as to non-infringement, invalidity or immateriality, or that any infringement claims will be resolved in our favor.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. Any litigation or claims against us, with or without merit, may cause us to incur substantial costs, could place a significant strain on our financial resources, divert the attention of management from our core business and harm our reputation. In addition, intellectual property litigation or claims could result in substantial damages and force us to do one or more of the following if a court decides that we infringe on another party's patent or other intellectual property rights:

- cease selling, incorporating or using any of our product candidates that incorporate the challenged intellectual property;

- obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or

- redesign our processes so that they do not infringe, which could be costly and time-consuming and may not be possible.

If we find during clinical evaluation that our product candidates for the treatment of HIV, gout, cancer or inflammatory diseases should be used in combination with a product covered by a patent held by another company or institution, and that a labeling instruction is required in product packaging recommending that combination, we could be accused of, or held liable for, infringement of the third-party patents covering the product recommended for co-administration with our product. In that case, we may be required to obtain a license from the other company or institution to use the required or desired package labeling, which may not be available on reasonable terms, or at all.

If we fail to obtain any required licenses or make any necessary changes to our technologies, we may be unable to develop or commercialize some or all of our product candidates.

**Table of Contents**

***Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property.***

We also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. In order to protect our proprietary technology and processes, we also rely in part on confidentiality and intellectual property assignment agreements with our employees, consultants and other advisors. These agreements may not effectively prevent disclosure of confidential information or result in the effective assignment to us of intellectual property, and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information, and in such case we could not assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

***Many of our competitors have significantly more resources and experience, which may harm our commercial opportunity.***

The biotechnology and pharmaceutical industries are subject to intense competition and rapid and significant technological change. We have many potential competitors, including major drug and chemical companies, specialized biotechnology firms, academic institutions, government agencies and private and public research institutions. Many of our competitors have significantly greater financial resources, experience and expertise in:

research and development;

preclinical testing;

clinical trials;

regulatory approvals;

manufacturing; and

sales and marketing of approved products.

Smaller or early stage companies and research institutions may also prove to be significant competitors, particularly through collaborative arrangements with large and established pharmaceutical companies. We will also face competition from these parties in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, and acquiring and in-licensing technologies and products complementary to our programs or potentially advantageous to our business. If any of our competitors succeed in obtaining approval from the FDA or other regulatory authorities for their products sooner than we do or for products that are more effective or less costly than ours, our commercial opportunity could be significantly reduced.

***If our competitors develop treatments for HIV, gout, cancer or inflammatory diseases that are approved faster, marketed better or demonstrated to be safer or more effective than any products that we may develop, our commercial opportunity will be reduced or eliminated.***

We believe that a significant number of drugs are currently under development and may become available in the future for the treatment of HIV, gout, cancer and inflammatory diseases. Potential competitors may develop treatments for HIV, gout, cancer or inflammatory diseases or other technologies and products that are safer, more effective or less costly than our product candidates or that would make our technology and product candidates obsolete or non-competitive. Some of these products may use therapeutic approaches that compete directly with our most advanced product candidates.

## **Table of Contents**

***If we cannot establish pricing of our product candidates acceptable to the government, insurance companies, managed care organizations and other payors, or arrange for favorable reimbursement policies, any product sales will be severely hindered.***

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect our ability to set a price we believe is fair for any products we may develop and our ability to generate adequate revenues and gross margins. Our ability to commercialize any product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate reimbursement levels for the cost of any products and related treatments.

In certain foreign markets, the pricing of prescription pharmaceuticals is subject to government control. In the United States, given recent federal and state government initiatives directed at lowering the total cost of health care, the United States Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. The trend toward managed health care in the United States, which could significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care, control pharmaceutical prices or reduce government insurance programs, may result in lower prices for our product candidates. While we cannot predict whether any legislative or regulatory proposals affecting our business will be adopted, the announcement or adoption of these proposals could have a material and adverse effect on our potential revenues and gross margins.

***Product liability claims may damage our reputation and, if insurance proves inadequate, the product liability claims may harm our results of operations.***

We face an inherent risk of product liability exposure when we test our product candidates in human clinical trials, and we will face an even greater risk if we sell our product candidates commercially. If we cannot successfully defend ourselves against product liability claims, we will incur substantial liabilities, our reputation may be harmed and we may be unable to commercialize our product candidates.

***Any claims relating to our improper handling, storage or disposal of biological, hazardous and radioactive materials could be time-consuming and costly.***

Our research and development involves the controlled use of hazardous materials, including chemicals that cause cancer, volatile solvents, radioactive materials and biological materials that have the potential to transmit disease. Our operations also produce hazardous waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials and waste products. If we fail to comply with these laws and regulations or with the conditions attached to our operating licenses, the licenses could be revoked, and we could be subjected to criminal sanctions and substantial financial liability or be required to suspend or modify our operations. Although we believe that our safety procedures for handling and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of contamination or injury, we could be held liable for damages or penalized with fines in an amount exceeding our resources. In addition, we may have to incur significant costs to comply with future environmental laws and regulations. We do not currently have a pollution and remediation insurance policy.

***Our business and operations would suffer in the event of system failures.***

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our research and drug discovery and development programs. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability as a result, our research and drug discovery and development programs may be adversely affected and the further development of our product candidates may be delayed. In addition, we may incur additional costs to remedy the damages caused by these disruptions or security breaches.

**Risks Related to Our Common Stock**

***Directors, executive officers, principal stockholders and affiliated entities beneficially own or control a significant majority of our outstanding voting common stock and together control our activities.***

Our directors, executive officers, principal stockholders and affiliated entities currently beneficially own or control a significant majority of our outstanding securities. These stockholders, if they determine to vote in the same manner, would control the outcome of any matter requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions or terms of any liquidation.

**Table of Contents**

***Future sales of our common stock may cause our stock price to decline.***

Our principal stockholders and affiliated entities hold a substantial number of shares of our common stock that they are able to sell in the public market. In addition, they currently own outstanding warrants exercisable as of June 17, 2009 for approximately 685,000 shares of our common stock. The exercise of these warrants or the sale by our current stockholders of a substantial number of shares, or the expectation that such exercises or sales may occur, could significantly reduce the market price of our common stock.

***Anti-takeover provisions in our charter documents and under Delaware law may make it more difficult to acquire us.***

Provisions in our certificate of incorporation and bylaws could make it more difficult for a third party to acquire us, even if doing so would be beneficial to our stockholders. These provisions:

allow the authorized number of directors to be changed only by resolution of our Board of Directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;

establish advance notice requirements for nominations to our Board of Directors or for proposals that can be acted on at stockholder meetings;

authorize our Board of Directors to issue blank check preferred stock to increase the number of outstanding shares; and

limit who may call stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit large stockholders from consummating a merger with, or acquisition of us. These provisions may prevent a merger or acquisition that would be attractive to stockholders and could limit the price that investors would be willing to pay in the future for our common stock.

***We have never paid cash dividends on our common stock and we do not anticipate paying dividends in the foreseeable future.***

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any future debt or credit facility may preclude us from paying any dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of potential gain for the foreseeable future.

**FORWARD-LOOKING STATEMENTS**

This prospectus, the documents that we incorporate by reference herein and the applicable prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the 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 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, ongoing, 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 in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed in this prospectus, in the applicable prospectus supplement or incorporated by reference.

Because the factors discussed in this prospectus, incorporated by reference herein or discussed in the applicable prospectus supplement, 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 prospectus, in the applicable prospectus supplement, particularly under the heading 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 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.

**Table of Contents**

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.

**USE OF PROCEEDS**

We will not receive any proceeds from the sale of shares of our common stock by the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees and fees and expenses of our counsel and our accountants.

**Table of Contents****SELLING STOCKHOLDERS**

On December 17, 2008, we entered into a securities purchase agreement with the selling stockholders named below and other investors, pursuant to which we sold an aggregate of 2,737,336 shares of our common stock, along with warrants to purchase an additional 684,332 shares of our common stock, in a private placement transaction otherwise referred to in this prospectus as the Private Placement. The warrants are first exercisable on June 17, 2009 and expire on December 19, 2013. We received aggregate gross proceeds of approximately \$30.6 million in connection with the Private Placement before deduction of transaction expenses. This prospectus covers, among other things, the offer and sale by the selling stockholders listed below of up to the total number of shares of common stock issued to the selling stockholders pursuant to the securities purchase agreement and issuable to the selling stockholders upon exercise of the warrants.

We are registering the above-referenced shares to permit the selling stockholders listed below and their pledgees, donees, transferees or other successors-in-interest that receive their shares after the date of this prospectus to resell the shares in the manner contemplated under the Plan of Distribution.

The selling stockholders may sell some, all or none of their shares. We do not know how long the selling stockholders will hold the shares before selling them. We currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares other than the securities purchase agreement and the warrants. The shares offered by this prospectus may be offered from time to time by the selling stockholders.

The following table sets forth the name of each selling stockholder, the number of shares owned by each of the respective selling stockholders, the number of shares that may be offered under this prospectus by such selling stockholders and the number of shares of our common stock to be owned by the selling stockholders after this offering is completed, assuming that all offered shares are sold as contemplated herein. The number of shares in the column Number of Shares Being Offered represents all of the shares that such selling stockholders may offer under this prospectus. Except as otherwise disclosed in this prospectus (or as disclosed in any document incorporated by reference) including information incorporated herein by reference, none of the selling stockholders has, or within the past three fiscal years has had, any position, office or other material relationship with us. These selling stockholders have advised us that they may enter into short sales in the ordinary course of their business of investing and trading securities. These selling stockholders have also advised us that no short sales in our securities were entered into by them during the period beginning when the selling stockholders obtained knowledge that we were contemplating a private placement and ending upon the public announcement of the Private Placement.

Ownership is based upon information provided by each respective selling stockholder, Schedules 13D and 13G and other public documents filed with the SEC up to, and including, December 31, 2008. The percentages of shares owned after the offering are based on 17,835,734 shares of our common stock outstanding as of December 31, 2008. In computing the number of shares beneficially owned by a person and the percentage ownership of that person, shares of common stock that could be issued upon the exercise of outstanding options and warrants held by that person that are currently exercisable or exercisable within 60 days of December 31, 2008 are considered outstanding. These shares, however, are not included in the shares outstanding as of December 31, 2008 when computing the percentage ownership of each other person.

The selling stockholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act of 1933, some or all of their shares since the date on which the information in the table is presented. Information about the selling stockholders may change over time.

Name	Shares of Common Stock	Number of Shares Being Offered	Shares Owned After Offering	
	Owned Prior to Offering(1)		Number	Percent
Baker Tisch Investments, L.P.(2)	99,636	4,988	95,646	*
Baker Bros. Investments II, L.P.(3)	75,183	1,025	74,363	*

Edgar Filing: Ardea Biosciences, Inc./DE - Form S-3

667 L.P.(4)	1,646,964	230,975	1,462,184	8.20%
Baker Brothers Life Sciences, L.P.(5)	3,193,943	736,461	2,604,774	14.60%
14159, L.P.(6)	70,036	20,116	53,943	*
Baker Bros. Investments, L.P.(7)	88,893		88,893	*
FBB Associates(8)	1,218		1,218	*
Jennison Health Sciences Fund(9)	860,495	471,375	483,395	2.71%
Pacific Select Fund, Health Sciences Portfolio(10)	110,698	60,122	62,600	*
Visium Balanced Fund, LP(11)	270,327	86,158	201,400	1.13%
Visium Balanced Offshore Fund, Ltd.(12)	656,805	221,550	479,565	2.69%
Visium Long Bias Offshore Ltd	220,534		220,534	1.24%
Visium Long Bias Fund, LP	72,630		72,630	*
RA Capital Healthcare Fund II, LP(13)	13,622	9,231	6,237	*
RA Capital Healthcare Fund, LP(14)	1,481,140	1,221,606	503,855	2.82%
Tang Capital Partners L.P.(15)	3,320,112	195,815	3,163,460	17.74%
Broadfin Healthcare Master Fund, LTD(16)	130,297	162,246	500	*
	18			

---

**Table of Contents**

- \* Indicates less than one percent ownership.
  
- (1) Does not include shares held by affiliates, except as otherwise indicated. Does not include shares issuable pursuant the warrants acquired in the Private Placement, as such warrants are not exercisable within 60 days of December 31, 2008.
  
- (2) Number of shares being offered includes 998 shares of common stock issuable upon the exercise of warrants acquired in the Private Placement. The sole general partner of Baker Tisch Investments, L.P. is Baker Tisch Capital, L.P. The sole general partner of Baker Tisch Capital, L.P. is Baker Tisch Capital (GP), LLC. Felix

Baker and Julian Baker are the managing members of Baker Tisch Capital (GP), LLC and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary interest therein.

- (3) Number of shares being offered includes 205 shares of common stock issuable upon the exercise of a warrant acquired in the Private Placement. The sole general partner of Baker Bros. Investments II, LP. is Baker Bros. Capital, L.P. The sole general partner of Baker Bros. Capital, L.P. is Baker Bros. Capital (GP), LLC. Felix Baker and Julian Baker are the managing members of Baker Bros. Capital (GP),

LLC.

Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary interest therein.

- (4) Number of shares being offered includes 46,195 shares of common stock issuable upon the exercise of a warrant acquired in the Private Placement. The sole general partner of 667, L.P is Baker Biotech Capital, L.P. The sole general partner of Baker Biotech Capital, L.P. is Baker Biotech Capital (GP), LLC . Felix Baker and Julian Baker are the managing members of Baker Biotech Capital (GP), LLC and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their

pecuniary  
interest therein.

- (5) Number of shares being offered includes 147,292 shares of common stock issuable upon the exercise of a warrant acquired in the Private Placement. The sole general partner of Baker Brothers Life Sciences, L.P. is Baker Brothers Life Sciences Capital, L.P.. The sole general partner of Baker Brothers Life Sciences Capital, L.P. is Baker Brothers Life Sciences Capital (GP), LLC. Felix Baker and Julian Baker are the managing members of Baker Brothers Life Sciences Capital (GP), LLC and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary

interest therein.

(6) Number of shares being offered includes 4,023 shares of common stock issuable upon the exercise of a warrant acquired in the Private Placement. The sole general partner of 14159, L.P. is 14159 Capital, L.P. The sole general partner of 14159 Capital, L.P. is 14159 Capital (GP), LLC. Felix Baker and Julian Baker are the managing members of 14159 Capital (GP), LLC and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary interest therein.

(7) The sole general partner of Baker Bros. Investments, L.P. is Baker Bros. Capital, L.P. The sole general partner

of Baker Bros. Capital, L.P. is Baker Bros. Capital (GP), LLC. Felix Baker and Julian Baker are the managing members of Baker Bros. Capital (GP), LLC and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary interest therein.

(8) Felix Baker and Julian Baker are the controlling members of FBB Associates and have voting and investment control over these shares. Messrs. Baker disclaim beneficial ownership of these securities, except to the extent of their pecuniary interest therein.

(9) Number of shares being offered includes 94,275 shares of common stock issuable upon

the exercise of a warrant acquired in the Private Placement. Jennison Associates LLC ( Jennison ) serves as sub-advisor with power to direct investments and/or power to vote the shares owned by Jennison Health Sciences Fund, a series of Jennison Sector Funds, Inc., and may be deemed to beneficially own the shares held by this entity. Jennison expressly disclaims ownership of such shares. Jennison is a wholly-owned subsidiary of Prudential Financial, Inc., which is a publicly-traded financial services firm. Jennison has represented to us that it has purchased the shares in the ordinary course of business and, at the time of purchase, with no arrangement or understanding, directly or

indirectly, with  
any persons  
regarding the  
distribution of  
such shares.

**Table of Contents**

(10) Number of shares being offered includes 12,024 shares of common stock issuable upon the exercise of a warrant acquired in the Private Placement. Jennison Associates LLC ( Jennison ) serves as sub-advisor with power to direct investments and/or power to vote the shares owned by Pacific Select Fund, Health Sciences Portfolio, and may be deemed to beneficially own the shares held by this entity. Jennison expressly disclaims ownership of such shares. Jennison is a wholly-owned subsidiary of Prudential Financial, Inc., which is a publicly-traded financial services firm. Jennison has represented to us that it has purchased the shares in the ordinary course

of business and,  
at the time of  
purchase, with  
no arrangement  
or  
understanding,  
directly or  
indirectly, with  
any persons  
regarding the  
distribution of  
such shares.

(11) Number of  
shares being  
offered includes  
17,231 shares of  
common stock  
issuable upon  
the exercise of a  
warrant  
acquired in the  
Private  
Placement.

(12) Number of  
shares being  
offered includes  
44,310 shares of  
common stock  
issuable upon  
the exercise of a  
warrant  
acquired in the  
Private  
Placement.

(13) Number of  
shares being  
offered includes  
1,846 shares of  
common stock  
issuable upon  
the exercise of a  
warrant  
acquired in the  
Private  
Placement.

(14) Number of  
shares being

offered includes  
244,321 shares  
of common  
stock issuable  
upon the  
exercise of a  
warrant  
acquired in the  
Private  
Placement.

- (15) Number of  
shares being  
offered includes  
39,163 shares of  
common stock  
issuable upon  
the exercise of a  
warrant  
acquired in the  
Private  
Placement.  
Kevin C. Tang  
is a director of  
the Company  
and the sole  
manager of  
Tang Capital  
Management,  
LLC, which is  
the general  
partner of Tang  
Capital Partners,  
LP. Mr. Tang  
disclaims  
beneficial  
ownership of  
the securities  
except to the  
extent of his  
pecuniary  
interest therein.

- (16) Number of  
shares being  
offered includes  
32,449 shares of  
common stock  
issuable upon  
the exercise of a  
warrant

acquired in the  
Private  
Placement.

#### **PLAN OF DISTRIBUTION**

We are registering the shares of common stock issued to the selling stockholders to permit the resale of these shares of common stock by the holders of the shares of common stock from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. The selling stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

**Table of Contents**

privately negotiated transactions;

settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;

the distribution of the shares by any selling stockholder to its partners, members or stockholders;

through one or more underwritten offerings on a firm commitment or best efforts basis;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with NASD Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with NASD IM-2440.

In connection with sales of the shares of common stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholders may also sell shares of common stock short and if such short sale shall take place after the date that this Registration Statement is declared effective by the Commission, the selling stockholders may deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the selling stockholders have been advised that they may not use shares registered on this registration statement to cover short sales of our common stock made prior to the date the registration statement, of which this prospectus forms a part, has been declared effective by the SEC.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the

shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealer or agents participating in the distribution of the shares of common stock may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling Stockholders who are underwriters within the meaning of Section 2(11) of the Securities Act will be subject to the applicable prospectus delivery requirements of the Securities Act, including Rule 172 thereunder, and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

**Table of Contents**

Each selling stockholder has informed the Company that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock. Upon the Company being notified in writing by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commissions and markups, which, in the aggregate, would exceed eight percent (8%). The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares of common stock against certain liabilities, including liabilities arising under the Securities Act.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any selling stockholder will sell any or all of the shares of common stock registered pursuant to the shelf registration statement, of which this prospectus forms a part.

Each selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the registration rights agreement, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or blue sky laws; *provided, however*, that each selling stockholder will pay all underwriting discounts and selling commissions, if any and any related legal expenses incurred by it. We will indemnify the selling stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the registration rights agreements, or the selling stockholders will be entitled to contribution. We may be indemnified by the selling stockholders against civil liabilities, including liabilities under the Securities Act, that may arise from any written information furnished to us by the selling stockholders specifically for use in this prospectus, in accordance with the related registration rights agreements, or we may be entitled to contribution.

**LEGAL MATTERS**

The validity of the issuance of the shares of our common stock offered by this prospectus will be passed upon for us by Cooley Godward Kronish LLP, San Diego, California.

**EXPERTS**

Stonefield Josephson, Inc., independent registered public accounting firm, has audited our consolidated financial statements as of and for the year ended December 31, 2007, as set forth in their report, which is included in our Annual Report on Form 10-K for the year ended December 31, 2007 and is incorporated by reference in this prospectus and elsewhere in the registration statement. These financial statements are incorporated by reference in reliance on Stonefield Josephson, Inc.'s report, given on their authority as experts in accounting and auditing.

**Table of Contents**

**WHERE YOU CAN FIND MORE INFORMATION**

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549 or at the SEC's other public reference facilities. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. Our SEC filings are available at the SEC's website at <http://www.sec.gov>.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's internet website.

**INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

We are allowed to incorporate by reference information contained in documents that we file with the SEC. This means that we can disclose important information to you by referring you to those documents and that the information in this prospectus is not complete. You should read the information incorporated by reference for more detail. We incorporate by reference in two ways. First, we list certain documents that we have already filed with the SEC. The information in these documents is considered part of this prospectus. Second, the information in documents that we file in the future will update and supersede the current information in, and incorporated by reference in, this prospectus.

We incorporate by reference the documents listed below and any filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date we filed the initial registration statement of which this prospectus is a part and before the effective date of the registration statement and any future filings we will make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act from the date of this prospectus, but prior to the termination of the offering (in each case, except for the information in any of the foregoing Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 therein):

Annual report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 24, 2008;

The description of our common stock set forth in our registration statement on Form 8-A12B (File No. 001-33734), filed under the Securities Exchange Act of 1934 on October 9, 2007, and any amendment or report filed for the purpose of updating that description;

Quarterly reports on Form 10-Q for the three month period ended March 31, 2008, filed with the SEC on May 9, 2008, the three and six month periods ended June 30, 2008, filed with the SEC on August 14, 2008, and the three and nine month periods ended September 30, 2008, filed with the SEC on November 13, 2008; and

Current reports on Form 8-K filed with the SEC on January 10, 2008, March 18, 2008, March 25, 2008, April 2, 2008, May 13, 2008, May 23, 2008, June 13, 2008, November 13, 2008, December 16, 2008, December 18, 2008 and December 22, 2008 (except for the information in such reports that shall not be deemed filed for purposes of Section 18 of the Exchange Act).

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request of such person, a copy of any and all of the documents that have been incorporated by reference in this prospectus (not including exhibits to such documents, unless such exhibits are specifically incorporated by reference in this prospectus or into such documents). Such request may be directed to:

Ardea Biosciences, Inc.  
4939 Directors Place  
San Diego, CA 92121  
Attn: Investor Relations

(858) 652-6500

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's internet website. You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of these documents.

**Table of Contents**

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. *Other Expenses of Issuance and Distribution.***

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

Registration Fee	\$ 1,615
Legal Fees and Expenses	\$ 5,000
Accounting Fees	\$ 8,500
Printer Fees	\$ 5,000
Total	\$20,115

**Item 15. *Indemnification of Directors and Officers.***

Section 145 of the Delaware General Corporation Law authorizes a court to award or a corporation's board of directors to grant indemnification to directors and officers on terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act.

Our Bylaws provide that we must indemnify our directors and officers to the fullest extent not prohibited by the Delaware General Corporation Law or any other applicable law. Our Bylaws also provide that we may indemnify our other employees and other agents as set forth in the Delaware General Corporation Law or any other applicable law.

In addition, our Amended and Restated Certificate of Incorporation provides that our directors shall not be liable for monetary damages to the fullest extent under Delaware Law. However, this provision in the Certificate of Incorporation does not eliminate the fiduciary duty of the directors, and in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware law. In addition, each director will continue to be subject to liability for breach of fiduciary duty as a director for (i) any breach of the director's duty of loyalty to us or our stockholders, (ii) acts or omissions not in good faith or involving intentional misconduct or a knowing violation of law, (iii) payment of dividends or approval of stock repurchases and redemptions that are unlawful under Delaware law and (iv) any transaction from which the director derived any improper personal benefit. The provision also does not affect a director's responsibilities under the federal securities laws.

We have entered into indemnification agreements with each of our directors and officers. These agreements, among other things, require us to indemnify each director and officer for certain expenses including attorneys' fees, judgments, fines and settlement amounts incurred by any such person in any action or proceeding, including any action by or in the right of us, arising out of the person's services as our director or officer, or as a director, officer or other fiduciary of an affiliate of ours to which the person provides services at our request.

**Table of Contents**

**Item 16. Exhibits.**

<b>Exhibit No.</b>	<b>Description</b>
2.1	Asset Purchase Agreement with Valeant Research & Development and Valeant Pharmaceuticals International dated December 21, 2006, incorporated by reference to our Form 8-K (File No. 000-29993) filed with the Securities and Exchange Commission on December 28, 2006.
4.1	Restated Certificate of Incorporation, incorporated by reference to our Form 10-Q (File No. 001-33734) filed with the Securities and Exchange Commission on November 13, 2008.
4.2	Amended and Restated Bylaws, incorporated by reference to our Form 8-K (File No. 000-29993) filed with the Securities and Exchange Commission on August 2, 2007.
4.3	Securities Purchase Agreement, dated as of December 17, 2008, by and among the Company and the Investors listed on the signature pages thereto, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 22, 2008.
4.4	Registration Rights Agreement, dated as of December 17, 2008, by and among the Company and the Investors listed on the signature pages thereto, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 22, 2008.
4.5	Form of Warrant to Purchase Common Stock issued by the Company pursuant to the Securities Purchase Agreement dated December 17, 2008, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 18, 2008.
5.1*	Opinion of Cooley Godward Kronish LLP.
23.1*	Consent of Stonefield Josephson, Inc.
23.3*	Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1).
24.1*	Power of attorney (included on the signature page to this registration statement).

\* Filed herewith.

We have applied for confidential treatment of certain provisions of this exhibit with the Securities and Exchange Commission. The confidential portions of this

exhibit are marked by an asterisk and have been omitted and filed separately with the Securities and Exchange Commission pursuant to our request for confidential treatment.

II-2

---

**Table of Contents**

**Item 17. Undertakings.**

A. The undersigned registrant hereby undertakes:

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

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

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

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; *provided, however*, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the registration statement is on Form S-3 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

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

(4) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

**Table of Contents**

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

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

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

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

**Table of Contents****SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of San Diego, State of California, on January 13, 2009.

**ARDEA BIOSCIENCES, INC.**

By: /s/ Barry D. Quart, Pharm.D.  
Barry D. Quart, Pharm.D.  
Chief Executive Officer

**POWER OF ATTORNEY**

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

**Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.**

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Barry D. Quart, Pharm.D.	Chief Executive Officer, Director <i>(Principal Executive Officer)</i>	
<b>Barry D. Quart, Pharm.D.</b>		January 13, 2009
/s/ John W. Beck, C.P.A	Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	
<b>John W. Beck, C.P.A</b>		January 13, 2009
/s/ Henry J. Fuchs, M.D.		
<b>Henry J. Fuchs, M.D.</b>	Director	January 13, 2009
/s/ Craig A. Johnson		
<b>Craig A. Johnson</b>	Director	January 13, 2009
/s/ John Poyhonen		
<b>John Poyhonen</b>	Director	January 13, 2009
/s/ Jack S. Remington, M.D.		
	Director	January 13, 2009

**Jack S. Remington, M.D.**

**/s/ Kevin C. Tang**

**Kevin C. Tang**

Director

January 13, 2009

II-5

---

**Table of Contents**

**EXHIBIT INDEX**

<b>Exhibit No.</b>	<b>Description</b>
2.1	Asset Purchase Agreement with Valeant Research & Development and Valeant Pharmaceuticals International dated December 21, 2006, incorporated by reference to our Form 8-K (File No. 000-29993) filed with the Securities and Exchange Commission on December 28, 2006.
4.1	Restated Certificate of Incorporation, incorporated by reference to our Form 10-Q (File No. 001-33734) filed with the Securities and Exchange Commission on November 13, 2008.
4.2	Amended and Restated Bylaws, incorporated by reference to our Form 8-K (File No. 000-29993) filed with the Securities and Exchange Commission on August 2, 2007.
4.3	Securities Purchase Agreement, dated as of December 17, 2008, by and among the Company and the Investors listed on the signature pages thereto, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 22, 2008.
4.4	Registration Rights Agreement, dated as of December 17, 2008, by and among the Company and the Investors listed on the signature pages thereto, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 22, 2008.
4.5	Form of Warrant to Purchase Common Stock issued by the Company pursuant to the Securities Purchase Agreement dated December 17, 2008, incorporated by reference to our Form 8-K (File No. 001-33734) filed with the Securities and Exchange Commission on December 18, 2008.
5.1*	Opinion of Cooley Godward Kronish LLP.
23.1*	Consent of Stonefield Josephson, Inc.
23.3*	Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1).
24.1*	Power of attorney (included on the signature page to this registration statement).

\* Filed herewith.

We have applied for confidential treatment of certain provisions of this exhibit with the Securities and Exchange Commission. The confidential portions of this

exhibit are marked by an asterisk and have been omitted and filed separately with the Securities and Exchange Commission pursuant to our request for confidential treatment.

II-6