

Ardea Biosciences, Inc./DE  
Form 424B5  
January 31, 2012  
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**The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.**

Filed Pursuant to Rule 424(b)(5)  
Registration Statement No. 333-178746

**SUBJECT TO COMPLETION, DATED JANUARY 31, 2012**

## **PRELIMINARY PROSPECTUS SUPPLEMENT**

(to Prospectus dated January 12, 2012)

# **Shares**

## **Common Stock**

We are offering \_\_\_\_\_ shares of our common stock. Our common stock is listed on The NASDAQ Global Select Market under the symbol RDEA . On January 30, 2012, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$18.13 per share.

Entities affiliated with two of our directors and principal stockholders have indicated interest in purchasing shares of our common stock in this offering at the public offering price. Because such indications of interest are not binding agreements or commitments to purchase, any or all of these entities may elect not to purchase any shares in this offering, or the underwriters may elect not to sell any shares in this offering to any or all of these entities.

**Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-7 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.**

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

|  | <b>PER SHARE</b> | <b>TOTAL</b> |
|--|------------------|--------------|
| Public Offering Price                  | \$               | \$           |
| Underwriting Discounts and Commissions | \$               | \$           |
| Proceeds to Ardea before expenses      | \$               | \$           |

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Delivery of the shares of common stock is expected to be made on or about February , 2012. We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares of our common stock solely to cover over-allotments. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ , and the total proceeds to us, before expenses, will be \$ .

*Sole Book-Running Manager*

**Jefferies**

*Co-Lead Managers*

**Cowen and Company**

**Lazard Capital Markets**

**Leerink Swann**

**Oppenheimer & Co.**

**Wells Fargo Securities**

*Co-Managers*

**JMP Securities**

**Mizuho Securities**

Prospectus Supplement dated February , 2012

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**You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled **Where You Can Find More Information** and **Incorporation of Certain Information by Reference**.**

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**About this Prospectus Supplement**

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated January 12, 2012, including the documents incorporated by reference therein, provides more general information about the securities we may offer from time to time, some of which may not apply to the offering described in this prospectus supplement. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement to Ardea, we, our or similar references mean Ardea Biosciences, Inc. and its wholly owned subsidiary.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference may include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

**Table of Contents****Prospectus Supplement Summary**

*This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the factors described under the heading *Risk Factors* in this prospectus supplement beginning on page S-7 and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.*

**Company Overview**

We are a biotechnology company focused on the development of small-molecule therapeutics for the treatment of serious diseases. The current status of our development programs is as follows:

**Product Portfolio**

| <b>PRODUCT CANDIDATE</b> | <b>TARGET INDICATION</b> | <b>DEVELOPMENT STATUS</b> |
|--------------------------|--------------------------|---------------------------|
| Lesinurad (RDEA594)      | Gout                     | Phase 3 ongoing           |
| RDEA3170                 | Gout                     | Phase 1 ongoing           |
| BAY 86-9766 (RDEA119)    | Cancer                   | Phase 2 ongoing           |

**GOUT**

Gout is a painful, debilitating and progressive disease caused by abnormally elevated levels of uric acid in the blood stream, a condition called hyperuricemia. While gout is a treatable condition, there are limited treatment options, and a number of adverse effects are associated with most current therapies.

Drugs currently used to treat the underlying cause of gout work by lowering blood or serum uric acid (sUA) levels and are referred to as urate-lowering therapies (ULTs). Approximately 90 percent of gout patients are considered to have a defect in their ability to excrete sufficient amounts of uric acid and are classified as *under-excretors* of uric acid, which leads to excessive levels of sUA.

*Lesinurad*

Lesinurad, our most advanced product candidate, previously called RDEA594, is an inhibitor of URAT1, a transporter in the kidney that regulates uric acid excretion from the body. Lesinurad has been shown to normalize the amount of uric acid excreted by gout patients. Since the majority of gout patients are *under-excretors*, normalizing uric acid excretion by moderating URAT1 transporter activity with lesinurad may provide the most physiologically appropriate means of reducing sUA levels. In addition, because increasing the excretion of sUA is additive to the effects of ULTs that decrease the production of uric acid, such as allopurinol and febuxostat (Uloric<sup>®</sup>, Takeda Pharmaceutical Company Limited), lesinurad in combination with such drugs has the potential to treat the significant portion of the gout patient population that is not adequately treated with existing therapies.

Approximately 3.1 million gout patients in the U.S. are prescribed ULTs annually. Allopurinol, the most commonly prescribed ULT in the U.S., currently accounts for more than 90 percent of U.S. unit sales of all ULTs. However, in recent controlled clinical studies, only about 30 to 40 percent of gout patients responded adequately to allopurinol, defined as achieving sUA levels of less than 6 mg/dL, the medically recommended target. Febuxostat, the most recently approved, orally-administered ULT in the U.S., has similar response rates in clinical practice according to a 2010 BioTrends Research Group, Inc. report. We are developing lesinurad to be used in combination with allopurinol to treat the large number of patients who do not reach target sUA levels taking allopurinol alone, and in combination with febuxostat in patients with tophaceous gout, a condition characterized by the presence of disfiguring deposits of uric acid crystals in and around the joints. We are also developing lesinurad to be used as a monotherapy for those patients who are intolerant to either allopurinol or febuxostat.



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Lesinurad has been evaluated in a comprehensive Phase 2 development program designed to demonstrate its clinical utility. Results from this program have shown the following:

- n Positive results from the main portion of a 28-day Phase 2b study (Study 203) in 208 allopurinol-refractory gout patients demonstrated that adding lesinurad to allopurinol produced highly statistically significant reductions in sUA of up to 30 percent at the highest lesinurad dose tested, compared to a 3 percent increase on allopurinol plus placebo. This resulted in a response rate of 79 percent for the 600 mg dose using the more rigorous intent-to-treat analysis, which considers all patients without efficacy results at week 4 as non-responders, including those who discontinue for any reason. Using a last observation carried forward analysis, which was the method utilized for the U.S. Food and Drug Administration, or FDA, approval of febuxostat, 87 percent of patients taking the combination reached the medically recommended target of reducing sUA to below 6 mg/dL at the highest dose tested. Response rates on this study increased in a dose-related manner and were highly clinically and statistically significant at all dose levels when compared to allopurinol alone.
  
- n Results from the ongoing extension period of Study 203 demonstrated consistent, sustained reductions in sUA levels, with 90 percent of patients on combination therapy at week 44 reaching the medically recommended target of 6 mg/dL and 81 percent reaching less than 5 mg/dL. In addition, at the lowest dose of 200 mg, patients experienced continued sUA reductions out to 16 weeks and a 27 percent decline in sUA at week 44. The combination of lesinurad and allopurinol was generally well tolerated in the main 28-day dosing period and has been generally well tolerated in the ongoing extension period. No significant safety concerns and no dose-related side effects have been observed with the combination.
  
- n In a 21-day, Phase 1b clinical pharmacology study evaluating the use of lesinurad in combination with febuxostat (Study 111) in 21 gout patients with hyperuricemia (sUA greater than or equal to 8 mg/dL), 100 percent of patients receiving the combination of lesinurad and febuxostat achieved sUA levels below the medically recommended target level of 6 mg/dL, compared to 67 percent and 56 percent for patients receiving 40 mg and 80 mg, respectively, of febuxostat alone. At the highest combination doses tested (600 mg lesinurad combined with 80 mg febuxostat), 100 percent of patients reached sUA levels below 4 mg/dL, with 58 percent achieving levels below 3 mg/dL. No patient achieved these reduced sUA levels on either dose of febuxostat alone. The combination of lesinurad and febuxostat was also generally well tolerated, with no serious adverse events or discontinuations due to adverse events and no clinically relevant drug interactions between lesinurad and febuxostat observed.
  
- n In a 20-patient, 21-day Phase 1b clinical pharmacology study evaluating the use of lesinurad in combination with 300 mg of allopurinol (Study 110) in gout patients with hyperuricemia (sUA greater than or equal to 8mg/dL), 100 percent of patients at all combination doses evaluated achieved sUA levels below the target of 6 mg/dL, compared to 20 percent of patients on allopurinol alone. The combination of lesinurad and allopurinol was generally well tolerated, with no serious adverse events or discontinuations that were considered possibly related to lesinurad or the combination.
  
- n When administered as a single agent in a 28-day, Phase 2b study (Study 202), lesinurad was generally well tolerated and produced significant reductions in uric acid in the blood. In this randomized, double-blind, placebo-controlled, dose-escalation study of 123 gout patients with hyperuricemia, uric acid levels decreased and response rates increased in a dose-related manner and were highly clinically and statistically significant at the two highest doses tested. At the highest dose, the response rate was 60 percent, compared to 0 percent for placebo ( $p < 0.0001$ ). Lesinurad was also generally well tolerated in this study, with no serious adverse events and only two discontinuations due to adverse events on lesinurad.



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- n Results from multiple studies have indicated that the activity of lesinurad is not diminished in patients with mild to moderate renal impairment. Lesinurad was generally well tolerated in these studies with a similar safety profile in subjects with normal or impaired renal function.
- n Results from a thorough QT study of 54 healthy subjects in which lesinurad was administered as a single therapeutic dose of 400 mg and as a single supratherapeutic dose of 1600 mg demonstrated no signal for lesinurad on any ECG interval, including cardiac repolarization.
- n Based on findings thus far, single doses of lesinurad from 5 mg to 1600 mg given alone, and multiple doses of lesinurad from 100 mg to 600 mg given either alone or in combination with allopurinol or febuxostat, appear to be generally well tolerated.

We have initiated a Phase 3 development program for lesinurad that includes the following main studies:

- n An open-label, Phase 4 interventional study of allopurinol in gout patients, called *LASSO*. Given the low response rate typically observed with allopurinol and its well-established side effect profile, we expect a significant number of patients from this study will be eligible to enroll directly into our Phase 3 studies.
- n A combination study in North America of lesinurad in allopurinol standard of care inadequate responders, called *CLEAR #1* a Phase 3, randomized, placebo-controlled trial of lesinurad added to allopurinol in patients not reaching target sUA levels with allopurinol alone. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after six months of dosing. Key secondary endpoints will include an assessment of gout flare rate and tophus resolution after 12 months of dosing.
- n An identical global combination study of lesinurad in allopurinol standard of care inadequate responders, called *CLEAR #2* a Phase 3, randomized, placebo-controlled trial of lesinurad added to allopurinol in patients not reaching target sUA levels with allopurinol alone. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after six months of dosing. Key secondary endpoints will include an assessment of gout flare rate and tophus resolution after 12 months of dosing.
- n A global monotherapy study of lesinurad in gout patients for whom allopurinol or febuxostat treatment is not advised, or contraindicated, called *LIGHT* a Phase 3, randomized, placebo-controlled trial of lesinurad as monotherapy in gout patients for whom febuxostat or allopurinol treatment is contraindicated due to factors such as intolerance, co-morbidities, or the risk of significant drug interactions. Patients will be dosed for a total of six months in this study and the primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after the end of the dosing period.
- n A global combination study of lesinurad and febuxostat in patients with tophaceous gout, called *CRYSTAL* a randomized, placebo-controlled study of lesinurad in combination with 80 mg febuxostat for the treatment of hyperuricemia in gout patients with tophi. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 5.0 mg/dL after six months of dosing. Key secondary endpoints will include the proportion of patients with resolution of tophi, an assessment of gout flare rate and quality of life measurements after 12 months of dosing.

We will need to successfully complete these pivotal Phase 3 clinical trials of lesinurad, as well as potential additional non-pivotal clinical trials, in order to be approved for marketing by the FDA and other regulatory authorities around the world.

*RDEA3170*

We are also developing RDEA3170, a next-generation inhibitor of the URAT1 transporter for the chronic treatment of gout. Based on preclinical results, RDEA3170 demonstrates many of the same positive attributes as lesinurad, but with greater potency against the URAT1 transporter. Initial results have shown sustained



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reductions in sUA of up to 60 percent after a single 40 mg dose of RDEA3170 was administered to healthy volunteers in a Phase 1 study.

### **CANCER**

Mitogen-activated ERK kinase (MEK) is believed to play an important role in cancer cell proliferation, programmed cell death and the spread of cancer from one organ or body part to another non-adjacent organ or body part. BAY 86-9766, formerly known as RDEA119, is a potent and highly selective inhibitor of MEK currently in Phase 2 development for the treatment of cancer.

Preclinical and clinical data suggest that BAY 86-9766 (RDEA119) has favorable properties, including once-daily oral dosing and excellent selectivity. In addition, BAY 86-9766 (RDEA119) has been shown to suppress tumor cell growth *in vitro* and *in vivo*. Preclinical *in vitro* and *in vivo* oncology studies of BAY 86-9766 (RDEA119) have demonstrated significant potential synergy across multiple tumor types when used in combination with other anti-cancer agents, including sorafenib (Nexavar<sup>®</sup>, Bayer HealthCare AG ( Bayer ) and Onyx Pharmaceuticals, Inc.).

We have completed a Phase 1 study of BAY 86-9766 (RDEA119) as a single agent in advanced cancer patients with different tumor types and we have identified the maximum tolerated dose (MTD) of BAY 86-9766 (RDEA119) in a Phase 1/2 study in combination with sorafenib. Dosing in the MTD expansion cohort of the Phase 1/2 study is ongoing.

Phase 1 results to date in refractory patients with advanced solid tumors have demonstrated that BAY 86-9766 (RDEA119) is generally well tolerated and a number of patients have achieved stable disease or partial response to treatment. A Phase 2 study of BAY 86-9766 (RDEA119) in combination with sorafenib as first-line therapy for primary liver cancer and a Phase 1/2 study of BAY 86-9766 (RDEA119) in combination with gemcitabine in patients with advanced pancreatic cancer are ongoing and are being conducted by our global development and commercialization licensee, Bayer. See Bayer Relationship below.

### **Market Opportunity**

We believe that there is a significant market opportunity for our product candidates, 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 as many chronic gout sufferers are unable to achieve target reductions in uric acid with current treatments.

There have been only two new products approved in the United States for the treatment of gout in the last 40 years. According to Decision Resources, an estimated 19.7 million adults in seven major markets (the United States, Japan, France, Germany, Italy, Spain and United Kingdom) suffer from gout. The prevalence of gout is increasing in the United States. According to the Annals of Rheumatic Diseases, there was a 288% increase in gout-related hospitalizations from 1988 to 2005 and over \$11.2 billion in gout-related hospital costs were incurred in 2005 in the United States.

We are developing products for the treatment of hyperuricemia and gout that inhibit URAT1. We believe there may also be opportunities to develop uric acid-lowering agents to treat diseases other than gout. Evidence suggests that hyperuricemia may also have systemic consequences, including an increased risk for kidney dysfunction, elevated C-reactive protein, hypertension and possibly other cardiovascular risk factors.

We believe that there is growing interest in targeted therapies, including kinase inhibitors, for the treatment of both cancer and inflammatory disease. Worldwide sales of products used in the treatment of cancer were \$52.4 billion in 2009, according to IMS Health Incorporated, fueled by strong acceptance of innovative and effective targeted therapies. In addition to cancer, MEK appears to play a role in inflammatory diseases, and we believe that BAY 86-9766 (RDEA119) and our next generation MEK inhibitors, if successfully developed, approved and commercialized, could help address these growing markets.

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### **Bayer Relationship**

In April 2009, we entered into the License Agreement with Bayer to develop and commercialize our small-molecule MEK inhibitors, including BAY 86-9766 (RDEA119), for all indications. Potential payments under the License Agreement could total up to \$407.5 million, including the \$35.0 million non-refundable license fee and the \$15.0 million development milestone for initiation of Phase 2 studies of BAY 86-9766 (RDEA119) that we have received to date. We will also be eligible to receive low double-digit royalties on worldwide sales of products under the License Agreement. Under the terms of the License Agreement, we were responsible for completion of the Phase 1 and Phase 1/2 studies that were underway when we entered into it. Bayer is responsible for reimbursing us for third-party development costs associated with these studies, as well as a portion of the personnel costs of employees involved in the development of BAY 86-9766 (RDEA119), up to a specified amount. Thereafter, Bayer is responsible for the further development and commercialization of BAY 86-9766 (RDEA119) and any of our other MEK inhibitors. BAY 86-9766 (RDEA119) is currently being evaluated in a Phase 2 study in combination with sorafenib in patients with hepatocellular carcinoma and a Phase 1/2 study in combination with gemcitabine in patients with advanced pancreatic cancer.

### **Valeant Relationship**

In December 2006, we acquired intellectual property and other assets from Valeant Research & Development, Inc., or Valeant, related to RDEA806, a non-nucleoside reverse transcriptase inhibitor (NNRTI) that had been developed for the treatment of human immunodeficiency virus, or HIV, and our next generation NNRTI program, as well as BAY 86-9766 (RDEA119) and our next generation MEK inhibitor program. In consideration for the assets purchased from Valeant, and subject to the satisfaction of certain conditions, Valeant received certain rights, including the right to receive from us development- and regulatory-based contingent event-based payments and sales-based royalty payments. There is one set of potential contingent event-based payments totaling up to \$25.0 million for RDEA806 and the next generation NNRTI program, and a separate set of potential contingent event-based payments totaling up to \$17.0 million for BAY 86-9766 (RDEA119) and the next generation MEK inhibitor program. As of December 31, 2010, the first, and only Phase 2 development-based contingent event-based payment related to BAY 86-9766 (RDEA119) had been achieved and the Company recorded \$1.0 million to research and development expense in the fourth quarter of 2010. The \$1.0 million payment to Valeant was subsequently made in January 2011, reducing the total of potential development- and regulatory-based contingent event-based payments related to BAY 86-9766 (RDEA119) and our next-generation MEK inhibitor program to \$16.0 million. The royalty rates on the products covered by our agreement with Valeant are in the mid-single digits.

### **Preliminary December 31, 2011 Cash, Cash Equivalents, and Short-Term Investments**

We estimate that our cash, cash equivalents and short-term investments, available-for-sale were approximately \$96.0 million as of December 31, 2011. This amount is preliminary, unaudited, subject to change upon completion of our year-end audit, and may differ from what will be reflected in our audited consolidated financial statements as of and for the year ended December 31, 2011. Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2011. Our audited consolidated financial statements will not be available until after this offering is complete, and consequently will not be available to you prior to investing in this offering.

### **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). The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

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**The Offering**

|  |  |
|--|--|
| Common stock offered by us                                     | shares   |
| Common stock to be outstanding immediately after this offering | shares   |
| Over-allotment option  | We have granted the underwriters an option to purchase up to additional shares of our common stock to cover over-allotments, if any. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.   |
| Use of proceeds  | We intend to use the net proceeds from this offering for general corporate purposes, which may include research and development expenses, including expenses related to Phase 3 clinical trials of lesinurad, capital expenditures, working capital, and general and administrative expenses. See Use of Proceeds on page S-9 of this prospectus supplement.   |
| NASDAQ Global Select Market listing                            | Our common stock is listed on The NASDAQ Global Select Market under the symbol RDEA.   |
| Risk factors   | Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-7 of this prospectus supplement.  |
| Insider Participation  | Entities affiliated with two of our directors and principal stockholders, Felix J. Baker and Kevin C. Tang, have indicated interest in purchasing shares of our common stock in this offering at the public offering price. Because such indications of interest are not binding agreements or commitments to purchase, any or all of these entities may elect not to purchase any shares in this offering, or the underwriters may elect not to sell any shares in this offering to any or all of these entities. |

**Outstanding Shares**

The number of shares of our common stock to be outstanding immediately after this offering is based on 26,913,223 shares outstanding as of December 31, 2011, and excludes as of that date:

- n 4,572,493 shares of common stock issuable upon the exercise of outstanding stock options under our equity incentive plans, with a weighted average exercise price of \$16.75 per share;
- n 910,721 shares of common stock available for future grants under our equity incentive plans;
- n 117,911 shares of common stock available for issuance under our employee stock purchase plan;

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- n 14,584 shares of common stock issuable upon vesting of outstanding restricted stock awards; and
  
- n 624,332 shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$11.14 per share.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their over-allotment option.

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**Risk Factors**

*Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing the risks described below, you should also refer to the information contained in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2011 and other documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, and other documents that we file from time to time with the SEC.*

**Risks Related to this Offering**

**Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.**

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates and cause the price of our common stock to decline.

**If you purchase the common stock sold in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.**

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution with respect to the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$            per share and our net tangible book value as of September 30, 2011, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$            per share with respect to the net tangible book value of the common stock. See the section entitled Dilution for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

In addition, we have a significant number of stock options and warrants outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders or result in downward pressure on the price of our common stock.

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**Forward-Looking Statements**

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated herein by reference and any free writing prospectus prepared by or on behalf of us or to which we have referred you contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry, and involve known and unknown risks, uncertainties and other factors that may cause our results, levels of activity, performance or achievement to be materially different from any future results, levels of activity, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- n the safety and efficacy of our product candidates;
- n the progress, timing and results of clinical trials and research and development efforts involving our product candidates;
- n the submission and timing of applications for regulatory approvals;
- n our ability to obtain and maintain regulatory approvals for our product candidates;
- n our expectations with regard to our intellectual property position and our ability to successfully protect our intellectual property;
- n our plans to conduct future clinical trials or research and development efforts;
- n estimates of the potential markets for our product candidates;
- n our operating and growth strategies, industry, planned products, and our expected future revenues, operations and expenditures and projected cash needs;
- n our expectations about partnering, acquisitions, licensing and marketing, including receipt of payments under any such arrangements;
- n our estimated cash and cash equivalents and short-term investments;
- n the use of proceeds from this offering; and
- n economic conditions, both generally and those specifically related to the biotechnology industry.

In some cases, you can identify forward-looking statements by terms such as anticipate, believe, could, estimate, expect, intend, may, potential, predict, project, should, will, would and similar expressions intended to identify forward-looking statements. While we believe we have a reasonable basis for each forward-looking statement, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. We discuss many of these risks, uncertainties and other factors in greater detail under the sections captioned **Risk Factors** contained in this prospectus supplement and in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2011. Given these risks, uncertainties and other factors, you should not place undue



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reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should read carefully both this prospectus supplement and the accompanying prospectus, together with the information incorporated herein and therein by reference as described under the heading **Incorporation of Certain Information by Reference** in this prospectus supplement, completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

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**Use of Proceeds**

We estimate that the net proceeds from the sale of the \_\_\_\_\_ shares of common stock that we are offering will be approximately \$ \_\_\_\_\_ million, or approximately \$ \_\_\_\_\_ million if the underwriters exercise in full their option to purchase up to \_\_\_\_\_ additional shares of common stock, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for general corporate purposes, which may include research and development expenses, including expenses related to Phase 3 clinical trials of lesinurad, capital expenditures, working capital, and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in complementary businesses, products and technologies. Although we currently have no specific agreements, commitments or understandings with respect to any acquisition or investment, we evaluate acquisition and investment opportunities and engage in related discussions with other companies from time to time.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering efforts, technological advances and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short term, interest-bearing instruments.

**Dividend Policy**

To date, we have paid no cash dividends to our stockholders, and we do not intend to pay cash dividends in the foreseeable future.

**Table of Contents****Dilution**

Our net tangible book value as of September 30, 2011 was approximately \$83.1 million, or \$3.09 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2011. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this public offering and the net tangible book value per share of our common stock immediately after this public offering.

After giving effect to the sale of \_\_\_\_\_ shares of our common stock in this offering at the public offering price of \$ \_\_\_\_\_ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2011 would have been approximately \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and immediate dilution in net tangible book value of \$ \_\_\_\_\_ per share to investors purchasing our common stock in this offering at the public offering price.

The following table illustrates this dilution on a per share basis:

|  |         |
|--|---------|
| Public offering price per share  | \$      |
| Net tangible book value per share as of September 30, 2011   | \$ 3.09 |
| Increase in net tangible book value per share attributable to new investors purchasing our common stock in this offering |         |

As adjusted net tangible book value per share on September 30, 2011, after giving effect to this offering

|  |    |
|--|----|
| Dilution per share to new investors purchasing our common stock in this offering | \$ |
|--|----|

If the underwriters exercise in full their option to purchase up to \_\_\_\_\_ additional shares of common stock at the public offering price of \$ \_\_\_\_\_ per share, the as adjusted net tangible book value as of September 30, 2011 after this offering would have been \$ \_\_\_\_\_ per share, representing an increase in net tangible book value of \$ \_\_\_\_\_ per share to existing stockholders and immediate dilution in net tangible book value of \$ \_\_\_\_\_ per share to investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 26,849,233 shares outstanding as of September 30, 2011, and excludes as of that date:

- n 3,850,044 shares of common stock issuable upon the exercise of outstanding stock options under our equity incentive plans, with a weighted average exercise price of \$16.23 per share;
- n 1,668,016 shares of common stock available for future grants under our equity incentive plans;
- n 147,055 shares of common stock available for issuance under our employee stock purchase plan;

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- n 16,146 shares of common stock issuable upon vesting of outstanding restricted stock awards; and
  
- n 624,332 shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$11.14 per share.

To the extent that outstanding options or warrants outstanding as of September 30, 2011 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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**Table of Contents****Underwriting**

Subject to the terms and conditions set forth in the underwriting agreement to be dated on or about \_\_\_\_\_, 2012, between us and the underwriters named below, we have agreed to sell to the underwriters and the underwriters have severally agreed to purchase from us the number of shares of common stock indicated in the table below:

| <b>UNDERWRITERS</b>         | <b>NUMBER OF SHARES<br/>OF COMMON STOCK</b> |
|-----------------------------|---|
| Jefferies & Company, Inc.   |   |
| Cowen and Company, LLC      |   |
| Lazard Capital Markets LLC  |   |
| Leerink Swann LLC           |   |
| Oppenheimer & Co. Inc.      |   |
| Wells Fargo Securities, LLC |   |
| JMP Securities LLC          |   |
| Mizuho Securities USA Inc.  |   |
| <b>Total</b>                |   |

Jefferies & Company, Inc. is acting as sole book-running manager of this offering and as representative of the underwriters named above.

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased, except as described below under Option to Purchase Additional Shares. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that they currently intend to make a market in the common stock. However, the underwriters are not obligated to do so and may discontinue any market-making activities at any time without notice. No assurance can be given as to the liquidity of the trading market for the common stock.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

**Commission and Expenses**

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ \_\_\_\_\_ per share of common stock. After the offering, the public offering price and concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The underwriters may sell shares of our common stock to entities affiliated with two of our directors and principal stockholders, Felix J. Baker and Kevin C. Tang, at the public offering price set forth on the cover page of this prospectus supplement. The underwriters will not receive any underwriting discount on the sale of such shares. The number of shares that will be sold to such investors in this offering will depend on market conditions. We cannot provide any assurance as to the exact number of shares of common stock that will be sold to such investors, if any. Any common stock not sold by the underwriters to such investors may be sold by the underwriters to other investors on the terms set forth in this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.



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|  | PER SHARE  |   | TOTAL  |   |
|--|--|---|--|---|
|  | WITHOUT<br>OPTION TO<br>PURCHASE<br>ADDITIONAL<br><br>SHARES | WITH<br>OPTION TO<br>PURCHASE<br>ADDITIONAL<br>SHARES | WITHOUT<br>OPTION TO<br>PURCHASE<br>ADDITIONAL<br>SHARES | WITH<br>OPTION TO<br>PURCHASE<br>ADDITIONAL<br>SHARES |
| Public offering price  | \$   | \$  | \$   | \$  |
| Underwriting discounts<br>and commissions paid<br>by us  | \$   | \$  | \$   | \$  |
| Proceeds to us, before<br>expenses   | \$   | \$  | \$   | \$  |
| We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$ . |  |   |  |   |

**Listing**

Our shares of common stock are listed on The NASDAQ Global Select Market under the trading symbol RDEA .

**Option to Purchase Additional Shares**

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to an aggregate of additional shares of common stock at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares of common stock proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares of common stock than the total number set forth on the cover page of this prospectus supplement.

**No Sales of Similar Securities**

We and each of our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- n sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Exchange Act, or
- n otherwise dispose of any common stock, options or warrants to acquire common stock, or securities exchangeable or exercisable for or convertible into common stock currently or hereafter owned either of record or beneficially, or
- n publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies & Company, Inc.

These restrictions terminate after the close of trading of the common stock on and including the 90 days after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

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during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

    n    prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period, then in either case the expiration of the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies & Company, Inc. waives, in writing, such an extension.

Jefferies & Company, Inc. may, in its sole discretion and at any time or from time to time before the termination of the 90-day period, without public notice, release all or any portion of the securities subject to lock-up agreements.

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There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

### **Stabilization**

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in transactions, including overallotment, stabilizing bids, syndicate covering transactions or the imposition of penalty bids, which may have the effect of stabilizing or maintaining the market price of our common stock at a level above that which might otherwise prevail in the open market. Overallotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares of common stock available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares of common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters makes any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on the NASDAQ Global Select Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

### **Electronic Distribution**

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of our common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site

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maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

**Affiliations**

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve our securities and/or instruments. The underwriters and certain of their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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**Notice to Investors**

**European Economic Area**

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (as defined below) (each, a Relevant Member State), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, an offer of our common stock to the public may not be made in that Relevant Member State prior to the publication of a prospectus in relation to our common stock which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive if they have been implemented in the Relevant Member State:

- a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;
- c) to fewer than 100 natural or legal persons per Relevant Member State (other than qualified investors as defined in the Prospectus Directive); or
- d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of our common stock to the public in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common stock to be offered so as to enable an investor to decide to purchase or subscribe for our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

**United Kingdom**

Shares of our common stock may not be offered or sold and will not be offered or sold to any persons in the United Kingdom other than to persons whose ordinary activities involve them acquiring, holding, managing or disposing of investments (as principal or as agent) for the purposes of their businesses or otherwise in circumstances which have not resulted or will not result in an offer to the public in the United Kingdom within the meaning of the Financial Services and Markets Act 2000, or the FSMA.

In addition, any invitation or inducement to engage in investment activity (within the meaning of section 21 of the FSMA) in connection with the issue or sale of shares of our common stock may only be communicated or caused to be communicated in circumstances in which Section 21(1) of the FSMA does not apply to us. Without limitation to the other restrictions referred to herein, this prospectus supplement and the accompanying prospectus are directed only at (1) persons outside the United Kingdom or (2) persons who:

- a) are qualified investors as defined in section 86(7) of FSMA, being persons falling within the meaning of article 2.1(e)(i), (ii) or (iii) of the Prospectus Directive; and
- b) are either persons who fall within article 19(1) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or Order, or are persons who fall within article 49(2)(a) to (d) ( high net worth companies, unincorporated associations, etc. ) of the Order; or

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c) to whom it may otherwise lawfully be communicated in circumstances in which Section 21(1) of the FSMA does not apply.

Without limitation to the other restrictions referred to herein, any investment or investment activity to which this prospectus supplement and the accompanying prospectus relate is available only to, and will be engaged in only with, such persons, and persons within the United Kingdom who receive this communication (other than persons who fall within (2) above) should not rely or act upon this communication.

**Italy**

This prospectus supplement and the accompanying prospectus have not been and will not be filed with or cleared by the Italian securities exchange commission (Commissione Nazionale per le società e la Borsa, or the CONSOB) pursuant to Legislative Decree No. 58 of 24 February 1998 (as amended, the Finance Law) and to CONSOB Regulation No. 11971 of 14 May 1999 (as amended, the Issuers Regulation). Accordingly, copies of this prospectus supplement and the accompanying prospectus or any other document relating to our common stock may not be distributed, made available or advertised in Italy, nor may our common stock be offered, purchased, sold, promoted, advertised or delivered, directly or indirectly, to the public other than (i) to Professional Investors (such being the persons and entities as defined pursuant to article 31(2) of CONSOB Regulation No. 11522 of 1 July 1998, as amended, the Intermediaries Regulation) pursuant to article 100 of the Finance Law; (ii) to prospective investors where the offer of our common stock relies on the exemption from the investment solicitation rules pursuant to, and in compliance with, the conditions set out by article 100 of the Finance Law and article 33 of the Issuers Regulation, or by any applicable exemption; provided that any such offer, sale, promotion, advertising or delivery of our common stock or distribution of this prospectus supplement and the accompanying prospectus, or any part thereof, or of any other document or material relating to our common stock in Italy is made: (a) by investment firms, banks or financial intermediaries authorized to carry out such activities in the Republic of Italy in accordance with the Finance Law, the Issuers Regulation, Legislative Decree No. 385 of 1 September 1993, as amended, the Intermediaries Regulation, and any other applicable laws and regulations; and (b) in compliance with any applicable notification requirement or duty which may, from time to time, be imposed by CONSOB, Bank of Italy or by any other competent authority.

**Germany**

Any offer or solicitation of securities within Germany must be in full compliance with the German Securities Prospectus Act (Wertpapierprospektgesetz, or the WpPG). The offer and solicitation of securities to the public in Germany requires the publication of a prospectus that has to be filed with and approved by the German Federal Financial Services Supervisory Authority (Bundesanstalt für Finanzdienstleistungsaufsicht, or the BaFin). This prospectus supplement and the accompanying prospectus have not been and will not be submitted for filing and approval to the BaFin and, consequently, will not be published. Therefore, this prospectus supplement and the accompanying prospectus do not constitute a public offer under the WpPG. This prospectus supplement, the accompanying prospectus and any other document relating to our common stock, as well as any information contained therein, must therefore not be supplied to the public in Germany or used in connection with any offer for subscription of our common stock to the public in Germany, any public marketing of our common stock or any public solicitation for offers to subscribe for or otherwise acquire our common stock. This prospectus supplement, the accompanying prospectus and other offering materials relating to the offer of our common stock are strictly confidential and may not be distributed to any person or entity other than the designated recipients hereof.

**France**

This prospectus supplement and the accompanying prospectus have not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers, or the AMF, and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. None of this

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prospectus supplement, the accompanying prospectus or any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

### **Sweden**

This is not a prospectus under, and has not been prepared in accordance with the prospectus requirements provided for in, the Swedish Financial Instruments Trading Act (lagen (1991:980) om handel med finansiella instrument) nor any other Swedish enactment. Neither the Swedish Financial Supervisory Authority nor any other Swedish public body has examined, approved, or registered this document.

### **Switzerland**

The shares of our common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares of our common stock or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Issuer, the shares of our common stock have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares of our common stock will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA and the offer of shares of our common stock has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares of our common stock.

### **Hong Kong**

No shares of our common stock have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus supplement has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

### **Singapore**

This prospectus supplement has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed,

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nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a) a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:
  - i) to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;
  - ii) where no consideration is given for the transfer; or
  - iii) where the transfer is by operation of law.

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### **Legal Matters**

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, San Diego, California. Latham & Watkins LLP, San Diego, California, is counsel for the underwriters in connection with this offering.

### **Experts**

Marcum LLP, an independent registered public accounting firm, has audited our consolidated financial statements as of and for the year ended December 31, 2010, and the effectiveness of our internal control over financial reporting as of December 31, 2010, as set forth in their reports, which are included in our Annual Report on Form 10-K for the year ended December 31, 2010 filed with the SEC on March 11, 2011 and incorporated by reference in this prospectus supplement and elsewhere in the related registration statement. These financial statements are incorporated by reference in reliance on such reports, given on their authority as experts in accounting and auditing.

Our consolidated financial statements as of December 31, 2009 and for the years ended December 31, 2009 and 2008 have been audited by Stonefield Josephson, Inc., an independent registered public accounting firm, as set forth in their report, which is included in our Annual Report on Form 10-K for the year ended December 31, 2010 filed with the SEC on March 11, 2011 and incorporated by reference in this prospectus supplement and elsewhere in the related registration statement. These financial statements are incorporated herein by reference in reliance on such report, given on their authority as experts in accounting and auditing.

### **Where You Can Find More Information**

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

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**Incorporation of Certain Information by Reference**

The SEC allows us to incorporate by reference information from other documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the prospectus supplement and before the sale of all the securities covered by this prospectus supplement:

- n our Annual Report on Form 10-K for the year ended December 31, 2010, filed with the SEC on March 11, 2011 (including information specifically incorporated by reference into our Form 10-K from our Proxy Statement for our 2011 Annual Meeting of Stockholders);
- n our Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, filed with the SEC on May 9, 2011, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2011, filed with the SEC on August 5, 2011, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2011, filed with the SEC on November 4, 2011;
- n our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on January 19, 2011, January 21, 2011, April 8, 2011, May 25, 2011 and December 22, 2011; and
- n the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on October 9, 2007, including any amendments or reports filed for the purposes of updating this description.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Ardea Biosciences, Inc.

Attn: Investor Relations

4939 Directors Place

San Diego, California 92121

(858) 652-6500

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.



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**PROSPECTUS**

**\$150,000,000**

**Ardea Biosciences, Inc.**

**Common Stock**

**Preferred Stock**

**Debt Securities**

**Warrants**

Our common stock is listed on The NASDAQ Global Select Market under the symbol RDEA. On January 11, 2012, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$15.44 per share.

We may, from time to time, offer to sell up to \$150,000,000 of any of our common stock, preferred stock, debt securities or warrants described in this prospectus, either individually or in combination, at prices and on terms described in one or more supplements to this prospectus. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants. We may also authorize one or more free writing prospectus to be provided to you in connection with these offerings.

This prospectus describes some of the general terms that may apply to an offering of our securities. The specific terms and any other information relating to a specific offering will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part, in a supplement to this prospectus, in a free writing prospectus or may be set forth in one or more documents incorporated by reference in this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus and any applicable prospectus supplement or free writing prospectus carefully before you invest.

**Investing in our securities involves a high degree of risk. See Risk Factors on page 7 of this prospectus and as updated in our future filings made with the Securities and Exchange Commission, or the SEC, which are incorporated by reference into this prospectus.**

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

The securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus and in the applicable prospectus supplement. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

**Neither the SEC 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 12, 2012.

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You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement or free writing prospectus. We have not authorized anyone to provide you with different information. We are not making an offer to sell or seeking an offer to buy securities under this prospectus or any applicable prospectus supplement or free writing prospectus in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, any applicable prospectus supplement or free writing prospectus and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus or any sale of a security.

**ABOUT THIS PROSPECTUS**

This prospectus is part of a registration statement that we filed with the SEC using a shelf registration process. Under this shelf registration statement, we may sell from time to time in one or more offerings up to a total dollar amount of \$150,000,000 of common stock, preferred stock, various series of debt securities and warrants to purchase any of such securities, either individually or in combination, as described in this prospectus. Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectus to be provided to you that may contain material information relating to these offerings. We may also add, update or change in a prospectus supplement or free writing prospectus any of the information contained in this prospectus or in documents we have incorporated by reference into this prospectus. This prospectus, together with any applicable prospectus supplement or free writing prospectus and the documents incorporated by reference into this prospectus or such prospectus supplement, include all material information relating to this offering. You should carefully read both this prospectus and any applicable prospectus supplement and any related free writing prospectus together with the additional information described under Where You Can Find More Information before buying securities in this offering.

**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 securities being sold in this offering, you should read carefully the entire prospectus, the prospectus supplement and the other documents to which we may refer you, including Risk Factors 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 subsidiary, unless the context requires otherwise.*

**ARDEA BIOSCIENCES, INC.****Overview and Business Strategy**

Ardea Biosciences, Inc., of San Diego, California, is a biotechnology company focused on the development of small-molecule therapeutics for the treatment of serious diseases. The current status of our development programs is as follows:

**Product Portfolio**

| <b>Product Candidate</b> | <b>Target Indication</b> | <b>Development Status</b> |
|--------------------------|--------------------------|---------------------------|
| Lesinurad (RDEA594)      | Gout                     | Phase 3 ongoing           |
| RDEA3170                 | Gout                     | Phase 1 ongoing           |
| BAY 86-9766 (RDEA119)    | Cancer                   | Phase 2 ongoing           |

**GOUT**

Gout is a painful, debilitating and progressive disease caused by abnormally elevated levels of uric acid in the blood stream, a condition called hyperuricemia. While gout is a treatable condition, there are limited treatment options, and a number of adverse effects are associated with most current therapies.

Drugs currently used to treat the underlying cause of gout work by lowering blood or serum uric acid (sUA) levels and are referred to as urate-lowering therapies (ULTs). Approximately 90 percent of gout patients are considered to have a defect in their ability to excrete sufficient amounts of uric acid and are classified as under-excretors of uric acid, which leads to excessive levels of sUA.

**Lesinurad**

Lesinurad, our most advanced product candidate, previously called RDEA594, is an inhibitor of URAT1, a transporter in the kidney that regulates uric acid excretion from the body. Lesinurad normalizes the amount of uric acid excreted by gout patients. Since the majority of gout patients are under-excretors, normalizing uric acid excretion by moderating URAT1 transporter activity with lesinurad may provide the most physiologically appropriate means of reducing sUA levels. In addition, because increasing the excretion of sUA is additive to the effects of ULTs that decrease the production of uric acid, such as allopurinol and febuxostat (Uloric®, Takeda Pharmaceutical Company Limited), lesinurad in combination with such drugs has the potential to treat the significant portion of the gout patient population that is not adequately treated with existing therapies.

Approximately 2.6 million gout patients in the U.S. are prescribed ULTs annually. Allopurinol, the most commonly prescribed ULT in the U.S., currently accounts for more than 90 percent of U.S. unit sales of all ULTs. However, in recent controlled clinical studies, only 30-40 percent of gout patients responded adequately to allopurinol, defined as achieving sUA levels of less than 6 mg/dL, the medically recommended target. Febuxostat, the most recently approved, orally-administered ULT in the U.S., has similar response rates in clinical practice according to a 2010 BioTrends Research Group, Inc. report. We are developing lesinurad to be used in combination with allopurinol to treat the large number of patients who do not reach target sUA levels

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while on this agent or as a monotherapy for those patients who are intolerant to allopurinol. We are also developing lesinurad to be used in combination with febuxostat in patients with tophaceous gout, a condition characterized by the presence of disfiguring deposits of uric acid crystals in and around the joints.

Lesinurad has been evaluated in a comprehensive Phase 2 development program designed to demonstrate its clinical utility. Results from this program have shown the following:

Positive results from the main portion of a 28-day Phase 2b study (Study 203) in 208 allopurinol-refractory gout patients demonstrated that adding lesinurad to allopurinol produced highly statistically significant reductions in sUA of up to 30 percent at the highest lesinurad dose tested, compared to a 3 percent increase on allopurinol plus placebo. This resulted in a response rate of 79 percent for the 600 mg dose using the more rigorous intent-to-treat (ITT) analysis, which considers all patients without efficacy results at week 4 as non-responders, including those who discontinue for any reason. Using a last observation carried forward (LOCF) analysis, which was the method utilized for the U.S. approval of febuxostat, 87 percent of patients taking the combination reached the medically recommended target of reducing sUA to below 6 mg/dL at the highest dose tested. Response rates on this study increased in a dose-related manner and were highly clinically and statistically significant at all dose levels when compared to allopurinol alone.

Results from the ongoing, extension portion of Study 203 demonstrated that of those patients who had reached week 28 of the extension period, 91 percent of those patients receiving lesinurad in combination with allopurinol achieved sUA levels below the medically recommended target of 6 mg/dL. Importantly, continued reductions in sUA were observed beyond the initial 28 days of dosing with a majority of the responding patients remaining on a 200 mg dose of lesinurad. The combination of lesinurad and allopurinol was generally well tolerated in the main 28-day dosing period and has been well tolerated in the ongoing extension period. Adverse events were infrequent, not dose related and comparable between the groups receiving lesinurad and placebo.

In a 21-day, Phase 1b clinical pharmacology study evaluating the use of lesinurad in combination with febuxostat (Study 111) in 21 gout patients with hyperuricemia (sUA greater than or equal to 8 mg/dL), 100 percent of patients receiving the combination of lesinurad and febuxostat achieved sUA levels below the medically recommended target level of 6 mg/dL, compared to 67 percent and 56 percent for patients receiving 40 mg and 80 mg, respectively, of febuxostat alone. At the highest combination doses tested (600 mg lesinurad combined with 80 mg febuxostat), 100 percent of patients reached sUA levels below 4 mg/dL, with 58 percent achieving levels below 3 mg/dL. No patient achieved these reduced sUA levels on either dose of febuxostat alone. The combination of lesinurad and febuxostat was also generally well tolerated, with no serious adverse events or discontinuations due to adverse events and no clinically relevant drug interactions between lesinurad and febuxostat observed.

In a 20-patient, 21-day Phase 1b clinical pharmacology study evaluating the use of lesinurad in combination with 300 mg of allopurinol (Study 110) in gout patients with hyperuricemia (sUA greater than or equal to 8mg/dL), 100 percent of patients at all combination doses evaluated achieved sUA levels below the target of 6 mg/dL, compared to 20 percent of patients on allopurinol alone. The combination of lesinurad and allopurinol was generally well tolerated, with no serious adverse events or discontinuations that were considered possibly related to lesinurad or the combination.

When administered as a single agent in a 28-day, Phase 2b study (Study 202), lesinurad was generally well tolerated and produced significant reductions in uric acid in the blood. In this randomized, double-blind, placebo-controlled, dose-escalation study of 123 gout patients with hyperuricemia, uric acid levels decreased and response rates increased in a dose-related manner and were highly clinically and statistically significant at the two highest doses tested. At the highest dose, the response rate was 60 percent, compared to 0 percent for placebo ( $p < 0.0001$ ). Lesinurad was also generally well tolerated in this study, with no serious adverse events and only two discontinuations due to adverse events on lesinurad.

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Results from multiple studies have indicated that the activity of lesinurad is not diminished in patients with mild to moderate renal impairment. Lesinurad was generally safe and well tolerated in these studies with a similar safety profile in subjects with normal or impaired renal function.

Based on findings thus far, single and multiple doses of lesinurad from 5 mg to 600 mg appear to be generally well tolerated, both alone and in combination with allopurinol or febuxostat.

We have initiated our Phase 3 development program which includes the following main studies:

An open-label, Phase 4 interventional study of allopurinol in gout patients, called **LASSO**. This study is currently underway. Given the low response rate typically observed with allopurinol and its well-established side effect profile, we expect a substantial number of patients from this study will be eligible to enroll directly into our Phase 3 studies.

A combination study in North America of lesinurad in allopurinol standard of care inadequate responders, called **CLEAR #1** a Phase 3, randomized, placebo-controlled trial of lesinurad added to allopurinol in patients not reaching target sUA levels with allopurinol alone. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after six months of dosing. Key secondary endpoints will include an assessment of gout flare rate, tophi resolution and quality of life measurements after 12 months of dosing.

A global combination study of lesinurad in allopurinol standard of care inadequate responders, called **CLEAR #2** a Phase 3, randomized, placebo-controlled trial of lesinurad added to allopurinol in patients not reaching target sUA levels with allopurinol alone. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after six months of dosing. Key secondary endpoints will include an assessment of gout flare rate, tophi resolution and quality of life measurements after 12 months of dosing.

A global monotherapy study of lesinurad in gout patients for whom allopurinol or febuxostat treatment is not advised, or contraindicated, called **LIGHT** a Phase 3, randomized, placebo-controlled trial of lesinurad as monotherapy in gout patients for whom febuxostat or allopurinol treatment is contraindicated due to factors such as intolerance, co-morbidities, or the risk of significant drug interactions. Patients will be dosed for a total of six months in this study and the primary endpoint will be the proportion of subjects with sUA levels below 6.0 mg/dL after the end of the dosing period.

A global combination study of lesinurad and febuxostat in patients with tophaceous gout, called **CRYSTAL** a randomized, placebo-controlled study of lesinurad in combination with febuxostat for the treatment of hyperuricemia in gout patients with tophi. Patients will be dosed for a total of 12 months in this study. The primary endpoint will be the proportion of subjects with sUA levels below 5.0 mg/dL after six months of dosing. Key secondary endpoints will include the proportion of patients with resolution of tophi, an assessment of gout flare rate and quality of life measurements after 12 months of dosing.

Lesinurad will need to successfully complete these pivotal Phase 3 clinical trials, as well as potential additional non-pivotal clinical trials, in order to be approved for marketing by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities around the world.

### **RDEA3170**

We are also developing RDEA3170, a next-generation inhibitor of the URAT1 transporter for the chronic treatment of gout. Based on preclinical results, RDEA3170 demonstrates many of the same positive attributes as lesinurad, but with greater potency against the URAT1 transporter. A Phase 1 clinical trial of RDEA3170 is ongoing.

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### **CANCER**

Mitogen-activated ERK kinase ( MEK ) is believed to play an important role in cancer cell proliferation, programmed cell death and the spread of cancer from one organ or body part to another non-adjacent organ or body part. BAY 86-9766, formerly known as RDEA119, is a potent and highly selective inhibitor of MEK currently in Phase 2 development for the treatment of cancer.

Preclinical and clinical data suggest that BAY 86-9766 (RDEA119) has favorable properties, including once-daily oral dosing and excellent selectivity. In addition, BAY 86-9766 (RDEA119) has been shown to suppress tumor cell growth *in vitro* and *in vivo*. Preclinical *in vitro* and *in vivo* oncology studies of BAY 86-9766 (RDEA119) have demonstrated significant potential synergy across multiple tumor types when used in combination with other anti-cancer agents, including sorafenib (Nexavar<sup>®</sup>, Bayer HealthCare AG ( Bayer ) and Onyx Pharmaceuticals, Inc.).

We have completed a Phase 1 study of BAY 86-9766 (RDEA119) as a single agent in advanced cancer patients with different tumor types and we have identified the maximum tolerated dose (MTD) of BAY 86-9766 (RDEA119) in a Phase 1/2 study in combination with sorafenib. Dosing in the MTD expansion cohort of the Phase 1/2 study is ongoing.

Phase 1 results to date in refractory patients with advanced solid tumors have demonstrated that BAY 86-9766 (RDEA119) is generally well tolerated and a number of patients have achieved stable disease or partial response to treatment. Based on the promising preclinical and Phase 1 and Phase 1/2 results, a Phase 2 study of BAY 86-9766 (RDEA119) in combination with sorafenib as first-line therapy for primary liver cancer and a Phase 1/2 study of BAY 86-9766 (RDEA119) in combination with gemcitabine in patients with advanced pancreatic cancer was recently initiated by our global development and commercialization licensee, Bayer.

### **Bayer Relationship**

In April 2009, we entered into the License Agreement with Bayer to develop and commercialize our small-molecule MEK inhibitors, including BAY 86-9766 (RDEA119), for all indications. Potential payments under the License Agreement could total up to \$407.5 million, including the \$35.0 million non-refundable license fee and the \$15.0 million development milestone for initiation of Phase 2 studies of BAY 86-9766 (RDEA119) that we have received to date. We will also be eligible to receive low double-digit royalties on worldwide sales of products under the License Agreement. Under the terms of the License Agreement, we are responsible for completion of the Phase 1 and Phase 1/2 studies that were underway when we entered into it. Bayer is responsible for reimbursing us for third-party development costs associated with these studies, as well as a portion of the personnel costs of employees involved in the development of BAY 86-9766 (RDEA119), up to a specified amount. Thereafter, Bayer will be responsible for the further development and commercialization of BAY 86-9766 (RDEA119) and any of our other MEK inhibitors. BAY 86-9766 (RDEA119) is currently being evaluated in a Phase 2 study in combination with sorafenib in patients with hepatocellular carcinoma and a Phase 1/2 study in combination with gemcitabine in patients with advance pancreatic cancer.

### **Valeant Relationship**

In December 2006, we acquired intellectual property and other assets from Valeant Research & Development, Inc., or Valeant, related to RDEA806, a non-nucleoside reverse transcriptase inhibitor (NNRTI) that had been developed for the treatment of human immunodeficiency virus, or HIV, and our next generation NNRTI program, as well as BAY 86-9766 (RDEA119) and our next generation MEK inhibitor program. In consideration for the assets purchased from Valeant, and subject to the satisfaction of certain conditions, Valeant received certain rights, including the right to receive from us development- and regulatory-based contingent event-based payments and sales-based royalty payments. There is one set of potential contingent event-based payments totaling up to \$25.0 million for RDEA806 and the next generation NNRTI program, and a separate set of potential contingent event-based payments totaling up to \$17.0 million for BAY 86-9766 (RDEA119) and the

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next generation MEK inhibitor program. As of December 31, 2010, the first, and only Phase 2 development-based contingent event-based payment related to BAY 86-9766 (RDEA119) had been achieved and the Company recorded \$1.0 million to research and development expense in the fourth quarter of 2010. The \$1.0 million payment to Valeant was subsequently made in January 2011, reducing the total of potential development- and regulatory-based contingent event-based payments related to BAY 86-9766 (RDEA119) and our next-generation MEK inhibitor program to \$16.0 million. The royalty rates on the products covered by our agreement with Valeant are in the mid-single digits.

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.

### **THE SECURITIES WE MAY OFFER**

We may offer shares of our common stock or preferred stock, various series of debt securities or warrants to purchase any of such securities, either individually or in combination, with a total value of up to \$150,000,000 from time to time under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity;

original issue discount;

rates and times of payment of interest or dividends;

redemption, conversion, exercise, exchange or sinking fund terms;

ranking;

restrictive covenants;

voting or other rights;

conversion or exchange prices or rates and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange; and



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a discussion of material United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

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

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We and our agents, underwriters and dealers reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents, underwriters or dealers, we will include in the applicable prospectus supplement:

the names of those agents, underwriters or dealers;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

**Common Stock.** We may issue shares of our common stock from time to time. Common stockholders are entitled to one vote per share for the election of directors and on all other matters that require common stockholder approval.

Subject to any preferential rights of any outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any outstanding preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

**Preferred Stock.** We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

**Debt Securities.** We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the

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terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

**Warrants.** We may issue warrants for the purchase of common stock, preferred stock or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, any forms of warrant agreements and forms of warrant certificates containing the terms of the warrants being offered, and any supplemental warrant agreements and forms of warrant certificates containing the terms of the warrants being offered.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

## **RISK FACTORS**

*An investment in our securities involves a high degree of risk. Before you make a decision to invest in our securities, you should consider carefully the risks described in the section entitled Risk Factors contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010, as filed with the SEC on March 11, 2011, and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2011, June 30, 2011 and September 30, 2011, as filed with the SEC on May 9, 2011, August 5, 2011 and November 4, 2011, respectively, each of which is incorporated herein by reference in its entirety, as well as any amendment or update thereto reflected in subsequent filings with the SEC and any information in this prospectus or any accompanying prospectus supplement. If any of these risks actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock, or if applicable, other securities, to decline and you may lose part or all of your investment. Moreover, the risks described are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, operating results, prospects or financial condition.*

## **FORWARD-LOOKING STATEMENTS**

This prospectus, the documents that we incorporate by reference herein and the applicable prospectus supplement or free writing prospectus 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 of 1934, as amended, or the Exchange Act. 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, goal, 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.

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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 or free writing prospectus, 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.

Further, any forward-looking statement speaks only as of the date on which it is made. Except as required by law, we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. 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.

**RATIO OF EARNINGS TO FIXED CHARGES**

The following table sets forth our ratio of earnings to fixed charges for the periods indicated:

|                                    | Year Ended December 31, |      |      |      |      | Nine Months<br>Ended<br>September 30, |
|------------------------------------|-------------------------|------|------|------|------|---------------------------------------|
|                                    | 2006                    | 2007 | 2008 | 2009 | 2010 | 2011                                  |
| Ratio of earnings to fixed charges |                         |      |      |      |      |                                       |

For the purpose of this table, earnings consist of loss from continuing operations before income taxes, extraordinary items, cumulative effect of accounting changes, equity in net losses of affiliates and fixed charges, and fixed charges consist of interest expense and the portion of operating lease expense that we estimate represents interest. For the fiscal years ended December 31, 2006, 2007, 2008, 2009 and 2010, and the nine months ended September 30, 2011, we had no earnings. Our earnings for those periods were insufficient to cover fixed charges by \$2.7 million, \$27.6 million, \$56.7 million, \$31.3 million, \$42.0 million and \$56.1 million, respectively.

**USE OF PROCEEDS**

Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of the securities offered hereby to fund the costs of clinical trial and other research and development activities and for general corporate purposes, including working capital. We may also use a portion of the net proceeds to in-license, invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

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**DESCRIPTION OF CAPITAL STOCK**

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 70,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, \$0.001 par value per share. As of December 22, 2011, 26,908,223 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary describes the material terms of our capital stock and is qualified by reference to our certificate of incorporation and our bylaws, which are incorporated by reference as exhibits into the registration statement of which this prospectus is a part.

**Common Stock**

*Voting.* Common stockholders are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval. Under our certificate of incorporation and bylaws, directors are elected by a plurality vote, and our stockholders do not have cumulative voting rights. Accordingly, the holders of a majority of our outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. In all other matters, an action by our common stockholders requires the affirmative vote of the holders of a majority of our outstanding shares of common stock entitled to vote.

*Dividends and Other Distributions.* Subject to the rights of any outstanding shares of preferred stock, holders of our common stock are entitled to share in an equal amount per share in any dividends declared by our board of directors on the common stock and paid out of legally available assets. Any dividends on our common stock will be non-cumulative.

*Distribution on Liquidation or Dissolution.* In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets legally available for distribution to our stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any outstanding shares of our preferred stock.

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

**Preferred Stock**

Under our certificate of incorporation, our board of directors has the authority, without further action by stockholders, to designate up to 5,000,000 shares of preferred stock in one or more series and to fix or alter, from time to time, the designations, powers and rights of each series of preferred stock and the qualifications, limitations or restrictions of any series of preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and the liquidation preference of any wholly unissued series of preferred stock, any or all of which may be greater than the rights of the common stock, and to establish the number of shares constituting any such series.

Our board of directors will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and any applicable prospectus supplements in the certificate of designation relating to each such series. We will incorporate by reference as an exhibit to the registration statement of which this prospectus is a part or as an exhibit to one or more current reports on Form 8-K, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

the title and stated value;

the number of shares we are offering;

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the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing;

the provisions for a sinking fund;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable for debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights of the preferred stock;

preemptive rights;

restrictions on transfer, sale or other assignment;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

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any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable.

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

### **Anti-Takeover Provisions**

*Delaware Law.* We are governed by the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless (i) before the date that the person became an interested stockholder, our board of directors approved either the business combination or the transaction which makes the person an interested stockholder, (ii) the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers

and (b) shares owned by employee stock plans in which employee participants do not have the right to determine

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confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer, or (iii) after the date that the person became an interested stockholder, the business combination is approved by our board of directors and the vote of at least 66 2/3% of our outstanding voting stock that is not owned by the interested stockholder. Generally, a business combination includes (A) any merger or consolidation involving the corporation and the interested stockholder, (B) any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation; (C) subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; (D) any transaction involving the corporation that has the effect of increasing the proportionate share of its stock owned by the interested stockholder; or (E) the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation. An interested stockholder is a person who either owns 15% or more of our outstanding voting stock or, together with affiliates and associates, owns or, within three prior years, did own, 15% or more of our outstanding voting stock. The statute could have the effect of delaying, deferring or preventing a change in our control.

*Bylaws and Certificate of Incorporation Provisions.* Our certificate of incorporation and bylaws include a number of provisions that may have the effect of deterring hostile takeovers or delaying or preventing changes in our control or our managements, including, but not limited to the following:

Our board of directors can issue up to 5,000,000 shares of preferred stock with any rights or preferences, including the right to approve or not approve an acquisition or change in our control.

Our certificate of incorporation and bylaws provide that all stockholder actions must be effected at a duly called meeting of holders and not by written consent.

Our bylaws provide that special meetings of our stockholders may be called only by the Chairman of our board of directors, our Chief Executive Officer, or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

Our bylaws provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide timely notice in writing and also specify requirements as to the form and content of a stockholder's notice. These provisions may delay or preclude stockholders from bringing matters before a meeting of our stockholders or from making nominations for directors at a meeting of stockholders, which could delay or deter takeover attempts or changes in our management.

Our certificate of incorporation and bylaws provide that, subject to the rights of the holders of any outstanding series of preferred stock, all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office. Our certificate of incorporation provides that the authorized number of directors must be set within a range of five to eleven pursuant to a resolution adopted by a majority of the directors then in office.

Our certificate of incorporation does not include a provision for cumulative voting for directors. Under cumulative voting, a minority stockholder holding a sufficient percentage of a class of shares could be able to ensure the election of one or more directors.

### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is ComputerShare Trust Company, N.A.

### **Listing on The NASDAQ Global Select Market**

Our common stock is listed on The NASDAQ Global Select Market under the symbol RDEA.





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**DESCRIPTION OF DEBT SECURITIES**

We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indentures, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

If we issue debt securities under this prospectus, we will issue the senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture, and we will issue the subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. The indentures will be qualified under the Trust Indenture Act of 1939. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable. We have filed forms of indentures to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any free writing prospectuses that we may authorize to be provided to you in connection with the debt securities that we may offer under this prospectus, as well as the complete indentures that contain the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

**General**

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including, to the extent applicable:

the title;

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

whether or not we will issue the series of debt securities in global form, the terms and who the depository will be;

the maturity date;

whether and under what circumstances we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

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restrictions on transfer, sale or other assignment;

our right to defer payment of interest and the maximum length of any such deferral period;

the date after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends and make distributions in respect of our capital stock and the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders and affiliates;

issue or sell stock of our subsidiaries; or

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effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of material United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

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### **Conversion or Exchange Rights**

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities, if applicable. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

### **Consolidation, Merger or Sale**

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

### **Events of Default Under the Indenture**

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the debenture trustee or holders of at least a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the debenture trustee or the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the debenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each series of debt securities then outstanding shall be due and payable without any notice or other action on the part of the debenture trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of



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the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act of 1939, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

the holder has given written notice to the debenture trustee of a continuing event of default with respect to that series;

the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the debenture trustee regarding our compliance with specified covenants in the indentures.

## **Modification of Indenture; Waiver**

We and the debenture trustee may change an indenture without the consent of any holders with respect to specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under **Description of Debt Securities Consolidation, Merger or Sale** ;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act of 1939;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under **Description of Debt Securities General**, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;



to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

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In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the debenture trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

## **Discharge**

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities. Notwithstanding the foregoing, we cannot be discharged from certain specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the debenture trustee;

compensate and indemnify the debenture trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the debenture trustee money or government obligations sufficient to pay all of the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

## **Form, Exchange and Transfer**

We will issue each series of debt securities only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in a prospectus supplement with respect to that series. See [Legal Ownership of Securities](#) for a further description of the terms relating to any book-entry securities.

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At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

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We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

### **Information Concerning the Debenture Trustee**

The debenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

### **Payment and Paying Agents**

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

### **Governing Law**

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

### **Subordination of Subordinated Debt Securities**

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue, nor does it limit us from issuing any other secured or unsecured debt.

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**DESCRIPTION OF WARRANTS**

We may issue warrants for the purchase of common stock, preferred stock or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from these securities. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all of the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any free writing prospectuses that we may authorize to be provided to you in connection with the warrants, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

**General**

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including, to the extent applicable:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

the date on and after which the warrants and the related securities will be separately transferable;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of material United States federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

### **Exercise of Warrants**

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant or warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent, if applicable, in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of any warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to any warrant agent.

Upon receipt of the required payment and any warrant certificate properly completed and duly executed at the corporate trust office of any warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by a warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

### **Governing Law**

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

### **Enforceability of Rights by Holders of Warrants**

Any warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one series of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of any related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

## **LEGAL OWNERSHIP OF SECURITIES**

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

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### **Book-Entry Holders**

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

### **Street Name Holders**

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

### **Legal Holders**

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.



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### **Special Considerations For Indirect Holders**

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

### **Global Securities**

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

### **Special Considerations For Global Securities**

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank, broker or other financial institution for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

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an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;

we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your bank, broker or other financial institution may require you to do so as well; and

financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

### **Special Situations When a Global Security Will Be Terminated**

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks, brokers or other financial institutions to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived. The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

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**PLAN OF DISTRIBUTION**

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

to or through underwriters or dealers;

directly to one or more purchasers; or

through agents.

We may distribute the securities:

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

at market prices prevailing at the time of sale;

at prices related to the prevailing market prices; or

at negotiated prices.

Each time we offer and sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms of the offering, including:

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

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

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

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

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

the public offering price of the securities;

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

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

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

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

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment. We may authorize underwriters, dealers or

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agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

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

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

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

Any underwriters who are qualified market makers on the Nasdaq Global Select Market may engage in passive market making transactions in our common stock, preferred stock, warrants and debt securities, as applicable, on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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

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

### **LEGAL MATTERS**

The validity of the securities offered by this prospectus will be passed upon for us by Cooley LLP, San Diego, California.

### **EXPERTS**

Marcum LLP, an independent registered public accounting firm, has audited our consolidated financial statements as of and for the year ended December 31, 2010, and the effectiveness of our internal control over financial reporting as of December 31, 2010, as set forth in their reports, which are included in our Annual Report on Form 10-K for the year ended December 31, 2010 and incorporated by reference in this prospectus and elsewhere in the related registration statement. These financial statements are incorporated by reference in reliance on such reports, given on their authority as experts in accounting and auditing.

Our consolidated financial statements as of December 31, 2009 and for the years ended December 31, 2009 and 2008 have been audited by Stonefield Josephson, Inc., an independent registered public accounting firm, as set forth in their report, which is included in our Annual Report on Form 10-K for the year ended December 31, 2010 and incorporated by reference in this prospectus and elsewhere in the related registration statement. These financial statements are incorporated herein by reference in reliance on such report, given on their authority as experts in accounting and auditing.

### **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. Our SEC filings are also 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.

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We incorporate by reference the documents listed below of this prospectus 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 and Form 8-K/A furnished under Item 2.02 or Item 7.01 therein):

Annual report on Form 10-K for the year ended December 31, 2010, filed with the SEC on March 11, 2011 (including information specifically incorporated by reference into our Form 10-K from our Proxy Statement for our 2011 Annual Meeting of Stockholders);

Quarterly report on Form 10-Q for the quarter ended March 31, 2011, filed with the SEC on May 9, 2011;

Quarterly report on Form 10-Q for the quarter ended June 30, 2011, filed with the SEC on August 5, 2011;

Quarterly report on Form 10-Q for the quarter ended September 30, 2011, filed with the SEC on November 4, 2011;

Current reports on Form 8-K filed with the SEC on January 19, 2011, January 21, 2011, April 8, 2011, May 25, 2011, September 7, 2011, November 7, 2011, December 19, 2011, December 22, 2011 and January 9, 2012, (except for the information in such reports that shall not be deemed filed for purposes of Section 18 of the Exchange Act); and

The description of our common stock set forth in our registration statement on Form 8-A12B (File No. 001-33734), filed under the Exchange on October 9, 2007.

You may request a copy of these filings at no cost, by writing or telephoning us at the following address or telephone number:

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.



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**Leerink Swann**

**Oppenheimer & Co.**

**Wells Fargo Securities**

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**JMP Securities**

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February , 2012

