

Ardea Biosciences, Inc./DE
Form 424B5
January 19, 2011

Table of Contents

The information contained in this prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-170105**

Subject to Completion
Preliminary Prospectus Supplement dated January 19, 2011

PROSPECTUS SUPPLEMENT

(to Prospectus dated November 15, 2010)

2,500,000 Shares

Common Stock

We are selling 2,500,000 shares of our common stock.

Our shares trade on The NASDAQ Global Select Market under the symbol RDEA. On January 18, 2011, the last sale price of the shares as reported on The NASDAQ Global Select Market was \$27.58 per share.

Entities affiliated with two of our directors and principal stockholders have indicated an interest in purchasing an aggregate of approximately 545,000 shares of the common stock offered in this offering at the price offered to the public. Because these 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 the common stock involves risks that are described in the Risk Factors section on page S-7 of this prospectus supplement.

	Price to Public	Underwriting Discount(1)	Proceeds, Before Expenses, to Us(1)
Per share	\$	\$	\$
Total	\$	\$	\$

==

- (1) The underwriters will not receive any underwriting discount on the sale of approximately 545,000 shares of our common stock to entities affiliated with two of our directors and principal stockholders.

The underwriters may also exercise their option to purchase up to an additional 375,000 shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus supplement to cover overallotments, if any.

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.

The shares will be ready for delivery on or about January , 2011.

Joint Book-Running Managers

BofA Merrill Lynch

Jefferies

The date of this prospectus supplement is January , 2011.

Table of Contents

Prospectus Supplement

<u>About this Prospectus Supplement</u>	S-ii
<u>Summary</u>	S-1
<u>Risk Factors</u>	S-7
<u>Forward-Looking Statements</u>	S-8
<u>Use of Proceeds</u>	S-9
<u>Dilution</u>	S-10
<u>Underwriting</u>	S-12
<u>Legal Matters</u>	S-18
<u>Experts</u>	S-18
<u>Where You Can Find More Information</u>	S-18
<u>Information Incorporated by Reference</u>	S-18

Prospectus

<u>About this Prospectus</u>	i
<u>Summary</u>	1
<u>Risk Factors</u>	5
<u>Forward-Looking Statements</u>	5
<u>Description of Capital Stock</u>	6
<u>Description of Warrants</u>	7
<u>Description of Units</u>	9
<u>Use of Proceeds</u>	10
<u>Plan of Distribution</u>	10
<u>Legal Matters</u>	11
<u>Experts</u>	11
<u>Where You Can Find More Information</u>	12
<u>Incorporation of Certain Information by Reference</u>	12

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us 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. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. 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 prepared by or on behalf of us 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 prepared by or on behalf of us 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 we have referred you to in the sections of this prospectus supplement entitled **Where You Can Find More Information and **Information Incorporated by Reference**.**

S-i

Table of Contents

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 November 15, 2010, including the documents incorporated by reference therein, provides more general information. 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.

All references in this prospectus supplement and the accompanying prospectus to Ardea, RDEA, the Company, we, us, our, or similar references refer to Ardea Biosciences, Inc., and its whollyowned subsidiary, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference 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**SUMMARY**

*This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, you should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering. If you invest in our common stock, you are assuming a high degree of risk. See *Risk Factors* in this prospectus supplement beginning on page S-7 and in the documents incorporated by reference into this prospectus supplement.*

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

Product Candidate	Target Indication	Development Status
RDEA594	Gout	Phase 2 completed
Next-generation URAT1 inhibitors BAY 86-9766 (formerly known as RDEA119)	Gout	Preclinical development ongoing
	Cancer	Phase 2 ongoing

Gout

Gout is a painful, debilitating and progressive disease. While gout is a treatable condition, there are limited treatment options, and a number of adverse effects are associated with most current therapies.

Gout is caused by abnormally elevated levels of uric acid in the blood stream. Drugs currently used to treat the underlying cause of gout work by lowering blood or serum uric acid (sUA) levels. 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-excreters of uric acid, which leads to excessive levels of uric acid in the blood stream. Our most advanced product candidate, RDEA594, is an inhibitor of URAT1, a transporter in the kidney that regulates uric acid excretion from the body. RDEA594 normalizes the amount of uric acid excreted by gout patients. Since the majority of gout patients are under-excreters, normalizing uric acid excretion by moderating URAT1 transporter activity with RDEA594 may provide the most physiologically appropriate and effective means of reducing blood or sUA levels. In addition, because RDEA594 works by increasing the excretion of uric acid rather than reducing the body's production of uric acid, it can be used in combination with sUA lowering agents that reduce the production of uric acid such as allopurinol or febuxostat (Uloric®, Takeda Pharmaceutical Company Limited).

Allopurinol is the most commonly prescribed sUA lowering drug in the United States, currently accounting for greater than 90 percent of U.S. unit sales of sUA lowering drugs. However, in recent controlled clinical studies, only 30-40 percent of gout patients achieved an adequate response to allopurinol as defined by the achievement of sUA

levels of less than 6 mg/dL, a commonly used medical target. We are developing RDEA594, both as monotherapy and to be used in combination with drugs like allopurinol, in order to treat patients not adequately responding to their current therapy.

S-1

Table of Contents

To date, results from our RDEA594 Phase 2 development program have indicated RDEA594's clinical utility, as follows:

In a Phase 2b study (Study 203) in 208 allopurinol refractory gout patients, adding RDEA594 to allopurinol produced highly statistically significant reductions in sUA of up to 30 percent with up to 89 percent of patients taking the combination reaching the medically recommended target of reducing sUA to below 6 mg/dL at the highest dose tested. The combination of RDEA594 and allopurinol was also well tolerated, with no serious adverse events and only two discontinuations due to adverse events on RDEA594. Patients admitted to the study had sUA levels greater than or equal to 6 mg/dL despite being on a stable dose of allopurinol. In this 28-day, randomized, double-blind, placebo-controlled study, each patient received once daily doses of 200 mg of RDEA594, 400 mg of RDEA594, 600 mg of RDEA594 or placebo while remaining on the stable dose of allopurinol such patient was receiving when he or she entered the study. Mean reductions in sUA after 4 weeks on 200 mg, 400 mg and 600 mg of RDEA594 plus a standard dose of allopurinol were 16 percent, 22 percent and 30 percent, respectively, compared to an increase in sUA of 3 percent on placebo. 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. Using a last observation carried forward (LOCF) analysis, which was the method utilized for the U.S. approval of Uloric[®], the response rates for the 200 mg, 400 mg and 600 mg plus a standard dose of allopurinol were 71 percent, 76 percent and 89 percent, respectively, compared to 29 percent on allopurinol alone.

In a Phase 1b clinical pharmacology study evaluating the use of RDEA594 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 RDEA594 and febuxostat achieved sUA levels below the clinically important 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 RDEA594 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 RDEA594 and febuxostat was also well tolerated, with no serious adverse events or discontinuations due to adverse events and no clinically relevant drug interactions observed between RDEA594 and febuxostat.

In a 20-patient Phase 1b clinical pharmacology study evaluating the use of RDEA594 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. Of patients receiving RDEA594 600 mg alone, 67 percent achieved sUA levels below 6 mg/dL, which was significantly higher than the percent reaching target on allopurinol alone ($p < 0.05$). At the highest combination doses tested (600 mg of RDEA594 combined with 300 mg of allopurinol), 90 percent of patients reached sUA levels below 5 mg/dL, and 50 percent reached levels below 4 mg/dL. The combination of RDEA594 and allopurinol was well tolerated, with no serious adverse events or discontinuations that were considered possibly related to RDEA594 or the combination. No clinically relevant drug interactions were observed between RDEA594 and allopurinol in this study; however, plasma levels of oxypurinol, an active metabolite of allopurinol, were decreased approximately 25-35 percent.

When administered as a single agent in a Phase 2b study (Study 202), RDEA594 was 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 (sUA levels greater

than or equal to 8 mg/dL) the primary endpoint was a significant increase in the proportion of patients who achieved a response, defined as a reduction of uric acid in the

S-2

Table of Contents

blood to < 6 mg/dL after four weeks of treatment, compared to placebo. The primary endpoint was achieved, uric acid 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 ($p < 0.0001$). RDEA594 was also well tolerated in this study, with no serious adverse events and only two discontinuations due to adverse events on RDEA594.

Results from multiple studies have indicated that the activity of RDEA594 is not diminished in patients with mild renal impairment. A smaller dataset from Study 202 indicate that after 4 weeks of monotherapy with RDEA594, patients with moderate renal impairment had similar reductions in sUA as compared to patients with no renal impairment.

We are also developing next-generation inhibitors of the URAT1 transporter for the treatment of gout patients with hyperuricemia. Based on preclinical results, our next-generation inhibitors demonstrate many of the same positive attributes as RDEA594, but with greater potency against the URAT1 transporter. Preclinical development activities with respect to these next-generation product candidates are ongoing.

Cancer

Mitogen-activated ERK kinase (MEK) is believed to play an important role in cancer cell proliferation, apoptosis and metastasis. BAY 86-9766 (formerly known as RDEA119) is a potent and selective inhibitor of MEK in development for the treatment of cancer. *In vivo* preclinical tests have shown BAY 86-9766 to have potent anti-tumor activity. In addition, preclinical *in vitro* and *in vivo* studies of BAY 86-9766 have demonstrated synergistic activity across multiple tumor types when BAY 86-9766 is used in combination with other anti-cancer agents, including sorafenib (Nexavar®, Bayer HealthCare AG (Bayer) and Onyx Pharmaceuticals, Inc.).

In April 2009, we entered into a global license agreement with Bayer to develop and commercialize MEK inhibitors for the treatment of cancer. Under the license agreement, we are responsible for the completion of the Phase 1 and Phase 1/2 studies. Thereafter, Bayer will be responsible for the further development and commercialization of BAY 86-9766 and any of our other MEK inhibitors.

We have completed our Phase 1 study of BAY 86-9766 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 in our 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 is well tolerated with a number of patients achieving stable disease or partial response to treatment. Based on the preclinical and Phase 1/2 results, Bayer recently initiated a Phase 2 study of BAY 86-9766 in combination with sorafenib as first-line therapy for primary liver cancer.

Market Opportunity

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

We believe that there is a significant need for new products for the treatment and prevention of gout. There have been only two new products approved in the United States for the treatment of gout in the last 40 years. According to the Decision Resources, an estimated 19.7 million adults in the seven major markets (the United States, Japan, France, Germany, Italy, Spain and United Kingdom) suffer from gout. The incidence and severity of gout is increasing in the

United States. According to the Annals of Rheumatic Diseases, there

S-3

Table of Contents

was a 288% increase in gout-related hospitalizations from 1988-2005 and over \$11.2 billion in gout-related hospital costs were incurred in 2005 in the United States. Many chronic gout sufferers are unable to achieve target reductions in uric acid with current treatments. Scientists have recently discovered defects in multiple transporters in the kidney that play important roles in uric acid transport and are genetically linked to a higher risk of gout. URAT1 has been identified as the most important transporter for uric acid. We are developing products for the treatment of hyperuricemia and gout that inhibit URAT1, thereby increasing the excretion of uric acid and lowering serum uric acid levels. In addition, we believe there may be opportunities to develop uric acid-lowering agents to treat diseases other than gout. Evidence suggests that the chronic elevation of uric acid associated with gout, known as hyperuricemia, may also have systemic consequences, including an increased risk for kidney dysfunction, elevated C-reactive protein, hypertension and possibly other cardiovascular risk factors.

We also believe that there is growing interest in the potential for targeted therapies, including kinase inhibitors, for the treatment of both cancer and inflammatory disease. Sales of products used in the treatment of cancer were \$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 and our next generation MEK inhibitors, if successfully developed, approved and commercialized, could participate in these growing markets.

Bayer Relationship

Under the terms of our license agreement with Bayer, we granted to Bayer a worldwide, exclusive license to develop and commercialize our MEK inhibitors for all indications. In June 2009, Bayer paid us a non-refundable, upfront cash payment of \$35 million in partial consideration for the exclusive right to develop and commercialize our MEK inhibitors. In January 2011, we received a \$15 million milestone payment from Bayer triggered by the initiation of a Phase 2 study evaluating BAY 86-9766 in combination with sorafenib for the treatment of hepatocellular carcinoma or primary liver cancer. Potential payments under the license agreement with Bayer could total up to \$407 million, not including royalties. This amount includes the upfront cash payment and the \$15 million milestone payment we received in January 2011, as well as additional cash payments upon achievement of certain development, regulatory and sales-based milestones. We are also eligible to receive low double-digit royalties on sales of products under the license agreement.

Valeant Relationship

In December 2006, we acquired intellectual property and other assets from Valeant Research & Development, Inc. (Valeant) related to RDEA806 and our next generation non-nucleoside reverse transcriptase inhibitor (NNRTI) program, as well as BAY 86-9766 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-based milestone payments and sales-based royalty payments. There is one set of potential milestones totaling up to \$25 million for RDEA806 and the next generation NNRTI program, and a separate set of potential milestones totaling up to \$17 million for BAY 86-9766 and the next generation MEK inhibitor program. The first milestone payment of \$2 million in the NNRTI program would be due after the first patient is dosed in the first Phase 2b study. The first milestone payment of \$1 million in the MEK inhibitor program was paid to Valeant in January 2011 in connection with the initiation of a Phase 2 study relating to BAY 86-9766. The royalty rates on all products under our agreement with Valeant are in the mid-single digits.

Table of Contents

Financial Update

We estimate that the total amount of our cash, cash equivalents and short-term investments, available-for-sale as of December 31, 2010 was approximately \$80.6 million. This amount is preliminary, has not been audited and is subject to change upon completion of our ongoing audit. Moreover, this amount does not reflect the \$15 million milestone payment we received in January 2011 described above. Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2010.

Corporate Information

We were incorporated in the State of Delaware in January 1994. Our principal executive 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. 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.

S-5

Table of Contents

THE OFFERING

Common stock offered by us	2,500,000 shares
Common stock to be outstanding immediately after this offering	25,866,979 shares
Overallotment option	The underwriters have an option to purchase up to 375,000 additional shares of our common stock to cover overallotments, if any. The underwriters may exercise this option at any time within 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, including clinical trial expenses, research and development expenses and general and administrative expenses, including working capital. See the sections entitled Use of Proceeds and Underwriting in this prospectus supplement.
Nasdaq Global Select Market symbol	RDEA
Risk factors	An investment in our common stock involves a high degree of risk. See the section entitled Risk Factors in this prospectus supplement.
Insider participation	Entities affiliated with two of our directors and principal stockholders, Felix J. Baker and Kevin C. Tang, have indicated an interest in purchasing an aggregate of approximately 545,000 shares of the common stock offered in this offering at the public offering price. Because these 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.

The number of shares of our common stock to be outstanding immediately after this offering is based on 23,366,979 shares outstanding as of December 31, 2010 and excludes:

3,538,191 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2010, having a weighted-average exercise price of approximately \$14.46 per share;

684,332 shares of our common stock subject to warrants outstanding as of December 31, 2010, having an exercise price of \$11.14 per share; and

an aggregate of 1,247,390 shares of common stock reserved for future issuance under our 2002 Non-Officer Equity Incentive Plan, as amended, 2000 Employee Stock Purchase Plan, and Amended and Restated 2004 Stock Incentive Plan as of December 31, 2010.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriters of their overallotment option. Furthermore, except as otherwise indicated, all information in this prospectus supplement assumes 545,000 of the offered shares will be sold to entities affiliated with two of our directors and principal stockholders as described above and in the section entitled Underwriting.

Table of Contents

RISK FACTORS

*An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned **Risk Factors** contained in our **Quarterly Report on Form 10-Q** for the quarterly period ended September 30, 2010, which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with the other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and in any free writing prospectus prepared by or on behalf of us that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flows could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.*

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.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

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 in the net tangible book value of the common stock you purchase in this offering. Based on an assumed public offering price of \$27.58 per share (the closing price of our common stock on January 18, 2011), and our net tangible book value per share as of September 30, 2010, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$22.23 per share in the net tangible book value of the common stock. See the section entitled **Dilution** below for a more detailed discussion of the dilution you would incur if you purchase common stock in this offering.

You may experience future dilution as a result of future equity offerings or other equity issuances.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering. As of December 31, 2010, an aggregate of 1,247,390 shares of common stock were reserved and available for future grant under our 2002 Non-Officer Equity Incentive Plan, as amended, 2000 Employee Stock Purchase Plan, and Amended and Restated 2004 Stock Incentive Plan. Also as of such date, options to purchase 3,538,191 shares of our common stock and warrants to purchase 684,332 shares of our common stock were outstanding. You will incur dilution upon the grant of any shares pursuant to any of such plans, upon vesting of any stock awards under any of such plans, or upon exercise of any such outstanding options or warrants.

Table of Contents

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, or Securities Act, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or 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:

- the safety and efficacy of our product candidates;
- the progress, timing and results of clinical trials and research and development efforts involving our product candidates;
- the submission and timing of applications for regulatory approvals;
- our ability to obtain and maintain regulatory approvals for our product candidates;
- our expectations with regard to our intellectual property position and our ability to successfully protect our intellectual property;
- our plans to conduct future clinical trials or research and development efforts;
- estimates of the potential markets for our product candidates;
- our operating and growth strategies, industry, planned products, and our expected future revenues, operations and expenditures and projected cash needs;
- our expectations about partnering, acquisitions, licensing and marketing;
- our estimated cash and cash equivalents and short-term investments;
- the use of proceeds from this offering; and
- 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, plan, potential, predict, project, should, will, would and similar expressions in forward-looking statements. While we believe that 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, 2010. Given these risks, uncertainties and other factors, you should not place undue 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 by reference as described under the heading "Information Incorporated 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.

S-8

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 2,500,000 shares of common stock that we are offering will be approximately \$65.4 million, or approximately \$75.1 million if the underwriters exercise in full their option to purchase 326,250 additional shares of common stock, based on the assumed public offering price of \$27.58 per share (the closing price of our common stock on January 18, 2011) and after deducting the estimated underwriting discount and estimated offering expenses payable by us. Each \$1.00 increase (decrease) in the assumed public offering price of \$27.58 per share would increase (decrease) the net proceeds to us from this offering by approximately \$2.4 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$26.3 million, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our uses of proceeds from this offering, although it may impact the amount of time prior to which we will need to seek additional capital. For more details, see the section entitled "Underwriting" in this prospectus supplement.

We intend to use the net proceeds from this offering for general corporate purposes, including clinical trial expenses, research and development expenses and general and administrative expenses, including working capital. We may also use a portion of the net proceeds from this offering to in-license, invest in or acquire businesses, technologies, product candidates or other intellectual property that we believe are complementary to our own, although we have no current plans, commitments or agreements to do so as of the date of this prospectus supplement. The amounts and timing of these expenditures will depend on a number of factors, such as the timing, scope, progress and results of our research and development efforts, the timing and progress of any partnering efforts, 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 of the net proceeds to us from this offering. Accordingly, we will retain broad discretion over the use of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the net proceeds in interest-bearing, investment-grade securities.

Table of Contents**DILUTION**

Our net tangible book value as of September 30, 2010 was approximately \$73.0 million, or \$3.17 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, 2010. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 2,500,000 shares of our common stock in this offering at an assumed public offering price of \$27.58 per share (the closing price of our common stock on January 18, 2011) and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2010 would have been approximately \$138.5 million, or \$5.35 per share. This represents an immediate increase in net tangible book value of \$2.18 per share to existing stockholders and immediate dilution in net tangible book value of \$22.23 per share to new investors purchasing our common stock in this offering at the assumed public offering price. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		\$ 27.58
Net tangible book value per share as of September 30, 2010	\$ 3.17	
Increase per share attributable to investors purchasing our common stock in this offering	2.18	
As adjusted net tangible book value per share after this offering		5.35
Dilution per share to investors purchasing our common stock in this offering		\$ 22.23

Each \$1.00 increase (decrease) in the assumed public offering price of \$27.58 per share would increase (decrease) our as adjusted net tangible book value after this offering by approximately \$2.4 million, or approximately \$0.10 per share, and the dilution per share to new investors by approximately \$22.13 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 1,000,000 shares in the number of shares offered by us would increase our as adjusted net tangible book value after this offering by approximately \$26.3 million, or \$0.78 per share, and the dilution per share to new investors would be \$21.45 per share, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discount and estimated offering expenses payable by us. Similarly, a decrease of 1,000,000 shares in the number of shares offered by us would decrease our as adjusted net tangible book value after this offering by approximately \$26.3 million, or \$0.84 per share, and the dilution per share to new investors would be \$23.07 per share, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discount and estimated offering expenses payable by us. The information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

If the underwriters exercise in full their option to purchase 375,000 additional shares of common stock at the assumed public offering price of \$27.58 per share, the as adjusted net tangible book value after this offering would be \$5.65 per share, representing an increase in net tangible book value of \$2.48 per share to existing stockholders and immediate dilution in net tangible book value of \$21.93 per share to new investors purchasing our common stock in this offering at the assumed public offering price.

Table of Contents

The number of shares of our common stock to be outstanding immediately after this offering is based on 23,076,321 shares outstanding as of September 30, 2010 and excludes:

3,200,217 shares of our common stock issuable upon the exercise of options outstanding as of September 30, 2010, having a weighted-average exercise price of approximately \$12.23 per share;

684,332 shares of our common stock subject to warrants outstanding as of September 30, 2010, having an exercise price of \$11.14 per share; and

an aggregate of 1,876,022 shares of common stock reserved for future issuance under our 2002 Non-Officer Equity Incentive Plan, as amended, 2000 Employee Stock Purchase Plan, and Amended and Restated 2004 Stock Incentive Plan as of September 30, 2010.

To the extent that outstanding options or warrants are exercised, you will 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.

Table of Contents**UNDERWRITING**

Merrill Lynch, Pierce, Fenner & Smith Incorporated and Jefferies & Company, Inc. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated Jefferies & Company, Inc.	
Total	2,500,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. 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 against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The underwriters may sell an aggregate of approximately 545,000 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 common shares that will be sold to such investors, if any. Any common shares 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.

Table of Contents

The following table shows the per share and total underwriting discount (other than in connection with the sale of 545,000 shares of our common stock to entities affiliated with two of our directors and principal stockholders). The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Without Option	With Option
Per share	\$	\$
Total	\$	\$

The expenses of the offering, not including the underwriting discount, are estimated at \$300,000 and are payable by us. However, the underwriters have agreed to reimburse us for certain of our expenses incurred in connection with this offering.

Overallotment Option

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 375,000 additional shares at the public offering price, less the underwriting discount. The underwriters may exercise this option solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and certain of our principal stockholders have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for common stock, for 90 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

offer, pledge, transfer, sell or contract or grant any option to sell (including without limitation any short sale) any shares of common stock;

establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Exchange Act of shares of common stock; or

otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. In the event that either (x) during the last 17 days of the lock-up period referred to above, we issue an earnings release or material news or a material event relating to the Company occurs or (y) prior to the expiration of the lock-up period, we announce that we will release earnings results or become aware that material news or a material event will occur during the 16-day period beginning on the last day of the lock-up period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

Table of Contents

Nasdaq Global Select Market Listing

The shares are listed on the Nasdaq Global Select Market under the symbol RDEA.

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters overallotment option described above. The underwriters may close out any covered short position by either exercising their overallotment option or purchasing shares 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 available for purchase in the open market as compared to the price at which they may purchase shares through the overallotment option. Naked short sales are sales in excess of the overallotment option. The underwriters must close out any naked short position by purchasing shares 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 our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of 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. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make 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. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in the common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock 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. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Table of Contents

Electronic Offer, Sale and Distribution of Shares

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail. In addition, certain of the underwriters may facilitate Internet distribution for this offering to certain of their Internet subscription customers. Certain of the underwriters may allocate a limited number of shares for sale to their online brokerage customers. An electronic prospectus is available on the Internet web sites maintained by certain of the underwriters. Other than the prospectus in electronic format, the information under such underwriter's web sites is not part of this prospectus.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and 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. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the EEA

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any securities which are the subject of the offering contemplated by this prospectus supplement (the Shares) may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised 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) by the Managers to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the underwriters for any such offer; or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Shares shall result in a requirement for the publication by us or any Manager of a prospectus pursuant to Article 3 of the Prospectus Directive.

Any person making or intending to make any offer of securities within the EEA should only do so in circumstances in which no obligation arises for us or any of the underwriters to produce a prospectus for such

Table of Contents

offer. Neither we nor the underwriters have authorized, nor do they authorize, the making of any offer of securities through any financial intermediary, other than offers made by the underwriters which constitute the final offering of securities contemplated in this prospectus.

For the purposes of this provision, the expression an offer to the public in relation to any Shares 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 any Shares to be offered so as to enable an investor to decide to purchase any Shares, 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.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any securities under, the offer of securities contemplated by this prospectus will be deemed to have represented, warranted and agreed to and with us and each underwriter that:

- (A) it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and
- (B) in the case of any securities acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the securities acquired by it in the offering have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors (as defined in the Prospectus Directive), or in circumstances in which the prior consent of the representatives has been given to the offer or resale; or (ii) where securities have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those securities to it is not treated under the Prospectus Directive as having been made to such persons.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The Shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (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 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 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 will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of Shares has not been and will not be authorized

S-16

Table of Contents

under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of Shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This offering memorandum relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (DFSA). This offering memorandum is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this offering memorandum nor taken steps to verify the information set forth herein and has no responsibility for the offering memorandum. The securities to which this offering memorandum relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this offering memorandum you should consult an authorized financial advisor.

S-17

Table of Contents

LEGAL MATTERS

The validity of the shares of 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

Stonefield Josephson, Inc., independent registered public accounting firm, has audited our consolidated financial statements as of and for the year ended December 31, 2009 and the effectiveness of our internal control over financial reporting as of December 31, 2009, as set forth in their reports, each of which are included in our Annual Report on Form 10-K for the year ended December 31, 2009 as filed with the SEC on March 12, 2010, and are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. These financial statements are incorporated by reference in reliance on Stonefield Josephson, Inc.'s reports, 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 Securities Exchange Act of 1934, as amended, 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.

INFORMATION INCORPORATED BY REFERENCE

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

We incorporate by reference the documents listed below and any filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act of 1934, as amended, after the date we filed the initial registration statement of which this prospectus is a part and before the effective date of the registration statement and any future filings we will make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act of 1934, as amended, 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):

our Annual Report on Form 10-K for the year ended December 31, 2009, filed with the SEC on March 12, 2010 (including information specifically incorporated by reference into our Form 10-K from our Proxy Statement for our 2010 Annual Meeting of Stockholders);

S-18

Table of Contents

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed with the SEC on May 7, 2010;

our Quarterly Report on Form 10-Q for the quarter ended June 30, 2010, filed with the SEC on August 6, 2010;

our Quarterly Report on Form 10-Q for the quarter ended September 30, 2010, filed with the SEC on November 9, 2010;

our Current Reports on Form 8-K filed with the SEC on February 9, 2010, March 8, 2010, April 5, 2010, April 9, 2010, May 27, 2010, September 17, 2010, October 7, 2010 (as amended by Amendment No. 1 to Current Report on Form 8-K/A, filed with the SEC on October 22, 2010) and December 21, 2010; 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 Act on October 9, 2007, and any amendment or report filed for the purpose of updating that description.

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

Table of Contents

PROSPECTUS

\$100,000,000

Ardea Biosciences, Inc.

**Common Stock
Warrants
Units**

Our common stock is listed on The NASDAQ Global Market under the symbol RDEA. On November 15, 2010, the last reported sale price of our common stock on The NASDAQ Global Market was \$22.29 per share.

We may, from time to time, offer to sell up to \$100,000,000 of any combination of the securities described in this prospectus, either individually or in units, at prices and on terms described in one or more supplements to this prospectus. We may also offer common stock upon the exercise of warrants.

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 or in a supplement to this 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 prospectus supplement carefully before you invest.

Investing in our securities involves a high degree of risk. See Risk Factors on page 5 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 in 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. 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 November 15, 2010.

TABLE OF CONTENTS

<u>About This Prospectus</u>	i
<u>Summary</u>	1
<u>The Securities We May Offer</u>	4
<u>Risk Factors</u>	5
<u>Forward-Looking Statements</u>	5
<u>Description of Capital Stock</u>	6
<u>Description of Warrants</u>	7
<u>Description of Units</u>	9
<u>Use of Proceeds</u>	10
<u>Plan of Distribution</u>	10
<u>Legal Matters</u>	11
<u>Experts</u>	11
<u>Where You Can Find More Information</u>	12
<u>Incorporation of Certain Information by Reference</u>	12

You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. 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 in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, any applicable prospectus supplement and the documents incorporated by reference herein and therein are accurate only as of their respective dates, regardless of the time of delivery of this prospectus or any sale of a security.

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 \$100 million of common stock and warrants to purchase common stock, either individually or in units, 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 add, update or change in a prospectus supplement 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 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 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

Product Candidate	Target Indication	Development Status
RDEA594	Gout	Phase 2b ongoing
Next-generation	Gout	Preclinical development ongoing
BAY 86-9766 (formerly known as RDEA119)	Cancer	Phase 1 completed and Phase 1/2 ongoing
Multiple candidates	HIV	Further development will be dependent upon our ability to partner this program

GOUT

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

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 uric acid in the blood. Our most advanced product candidate, RDEA594, is a selective inhibitor of URAT1, a transporter in the kidney that regulates uric acid excretion from the body. RDEA594 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 RDEA594 may provide the most physiologically appropriate and effective means of reducing blood or serum uric acid (sUA) levels when used alone or in combination with other sUA lowering agents, such as allopurinol or febuxostat (Uloric®, Takeda Pharmaceutical Company Limited; Adenuric®, Ipsen and Menarini), which act by reducing the production of uric acid in the body.

To date, results from our Phase 2 development program have indicated RDEA594's clinical utility, as follows:

When administered as a single agent in a Phase 2b study (Study 202), RDEA594 was 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 (sUA levels greater than or equal to 8 mg/dL) the primary endpoint was a significant increase in the proportion of patients who achieved a response, defined as a reduction of uric acid in the blood to < 6 mg/dL after four weeks of treatment, compared to placebo. The primary endpoint was achieved, uric acid 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 ($p < 0.0001$). RDEA594 was also well tolerated in this study.

The combination of RDEA594 and allopurinol in a Phase 2a study (Study 201) in gout patients was well tolerated and reduced sUA levels an additional 24 percent compared to allopurinol alone. Interim results from an ongoing Phase 1b clinical pharmacology study (Study 110) of RDEA594 in combination with allopurinol demonstrated that the combination

Table of Contents

was well tolerated and produced 100 percent response rates in gout patients receiving two different doses of RDEA594 in combination with allopurinol.

The combination of RDEA594 and febuxostat in a Phase 1 study (Study 105) in healthy volunteers was well tolerated and resulted in sUA reductions of approximately 70 to 80 percent from baseline.

Results from multiple studies have indicated that the activity of RDEA594 is not diminished in patients with mild to moderate renal impairment.

Additional results from our Phase 2 development program will include data from a Phase 2b study (Study 203) evaluating 200 mg, 400 mg and 600 mg of RDEA594 as an add-on to allopurinol in patients on a stable dose of allopurinol that do not respond adequately to allopurinol alone, additional data from a Phase 1b clinical pharmacology study (Study 110) evaluating the combination of RDEA594 and allopurinol in gout patients and results from a Phase 1b dose-ranging study (Study 111) of RDEA594 in combination with febuxostat in gout patients.

Based on preclinical results, our next-generation inhibitors of the URAT1 transporter for the treatment of gout patients with hyperuricemia demonstrate many of the same positive attributes as RDEA594, but with greater potency against the URAT1 transporter. Preclinical development activities with respect to these next-generation product candidates are ongoing.

CANCER

Mitogen-activated ERK kinase (MEK) is believed to play an important role in cancer cell proliferation, apoptosis and metastasis. BAY 86-9766 (formerly known as RDEA119) is a potent and selective inhibitor of MEK in development for the treatment of cancer. *In vivo* preclinical tests have shown BAY 86-9766 to have potent anti-tumor activity. In addition, preclinical *in vitro* and *in vivo* studies of BAY 86-9766 have demonstrated synergistic activity across multiple tumor types when BAY 86-9766 is used in combination with other anti-cancer agents, including sorafenib (Nexavar®, Bayer HealthCare AG (Bayer) and Onyx Pharmaceuticals, Inc.).

In April 2009, we entered into a global license agreement with Bayer to develop and commercialize MEK inhibitors for the treatment of cancer. Under the license agreement, we are responsible for the completion of the ongoing Phase 1 and Phase 1/2 studies. Thereafter, Bayer will be responsible for the further development and commercialization of BAY 86-9766 and any of our other MEK inhibitors.

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

HIV

We have developed multiple product candidates from our HIV program including RDEA806, a non-nucleoside reverse transcriptase inhibitor, or NNRTI, for the treatment of HIV, which has successfully completed Phase 1 and Phase 2a studies and has been evaluated in over 250 subjects. Results from a Phase 2a monotherapy proof-of-concept study of RDEA806 demonstrated placebo-adjusted plasma viral load reductions of up to 2.0 log₁₀ on day 8 with once-daily dosing of RDEA806. All dosing regimens tested were well tolerated in this study.

We have also developed RDEA427, a next generation NNRTI, that is from a chemical class that is distinct from the RDEA806 chemical class. Based on preclinical results, RDEA427 demonstrates many of the same positive attributes as RDEA806, but is more potent, has superior pharmacokinetic properties, and has even greater activity against a wide

range of drug-resistant viral isolates, than RDEA806. We have evaluated RDEA427 in a human micro-dose pharmacokinetic study.

Further development of RDEA806 and RDEA427 will be dependent upon our ability to partner this program.

Market Opportunity

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

We believe that there is a significant need for new products for the treatment and prevention of gout. There have been only two new products approved in the United States for the treatment of gout in the last 40 years. According to the Decision Resources, an

Table of Contents

estimated 19.7 million adults in the seven major markets (the United States, Japan, France, Germany, Italy, Spain and United Kingdom) suffer from gout. The incidence and severity of gout is increasing in the United States. According to the Annals of Rheumatic Diseases there was a 288% increase in gout-related hospitalizations from 1988-2005 and over \$11.2 billion in gout-related hospital costs were incurred in 2005 in the United States. Many chronic gout sufferers are unable to achieve target reductions in uric acid with current treatments. Scientists have recently discovered defects in multiple transporters in the kidney that play important roles in uric acid transport and are genetically linked to a higher risk of gout. URAT1 has been identified as the most important transporter for uric acid. We are developing products for the treatment of hyperuricemia and gout that inhibit URAT1, thereby increasing the excretion of uric acid and lowering serum uric acid levels. In addition, we believe there may be opportunities to develop uric acid-lowering agents to treat diseases other than gout. Evidence suggests that the chronic elevation of uric acid associated with gout, known as hyperuricemia, may also have systemic consequences, including an increased risk for kidney dysfunction, elevated CRP, hypertension and possibly other cardiovascular risk factors.

We also believe that there is growing interest in the potential for targeted therapies, including kinase inhibitors, for the treatment of both cancer and inflammatory disease. Sales of products used in the treatment of cancer were \$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 and our next generation MEK inhibitors, if successfully developed, approved and commercialized, could participate in these growing markets.

In 2009, global sales of HIV antivirals were approximately \$13.8 billion. While the treatment of HIV has improved dramatically over the past decade, we believe that there remains a significant need for new treatments that are effective against drug-resistant virus, safer for women and African-Americans, well tolerated and convenient to take. According to the Centers for Disease Control and Prevention (CDC), 56,300 people were newly infected with HIV in 2006, 40% more than estimated previously. African-Americans accounted for more than 45% of the new infections. Women account for 27% of the new infections. We have developed products for the treatment of HIV that are highly active against resistant strains, have a high genetic barrier to resistance, have a better safety profile than current drugs in African-Americans and women, can be taken once a day, and are easy to formulate in a combination pill with current drugs. The further development of these drugs will depend on our ability to partner the HIV program.

Bayer Relationship

Under the terms of our license agreement with Bayer, we granted to Bayer a worldwide, exclusive license to develop and commercialize our MEK inhibitors for all indications. In June 2009, Bayer paid us a non-refundable, upfront cash payment of \$35 million in partial consideration for the exclusive right to develop and commercialize our MEK inhibitors. Potential payments under the license agreement with Bayer could total up to \$407 million, not including royalties. This amount includes the upfront cash payment, as well as additional cash payments upon achievement of certain development, regulatory and sales-based milestones. We are also eligible to receive low double-digit royalties on sales of products under the license agreement. We are responsible for the completion of the Phase 1 and Phase 1/2 studies currently being conducted for BAY 86-9766.

Valeant Relationship

In December 2006, we acquired intellectual property and other assets from Valeant Research & Development, Inc. (Valeant) related to RDEA806 and our next generation non-nucleoside reverse transcriptase inhibitor (NNRTI) program, and BAY 86-9766 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-based milestone payments and sales-based royalty payments. There is one

set of potential milestones totaling up to \$25 million for RDEA806 and the next generation NNRTI program, and a separate set of potential milestones totaling up to \$17 million for BAY 86-9766 and the next generation MEK inhibitor program. The first milestone payments of \$2 million and \$1 million in the NNRTI program and the MEK inhibitor program, respectively, would be due after the first patient is dosed in the first Phase 2b study. The royalty rates on all products are in the mid-single digits.

Under the asset purchase agreement, Valeant retains a one-time option to repurchase commercialization rights in territories outside the United States and Canada for our first NNRTI product derived from the acquired intellectual property to advance to a Phase 2b HIV clinical trial. If Valeant exercises this option, which it can do following the completion of a Phase 2b clinical trial, but prior to the initiation of a Phase 3 clinical trial, Valeant would pay us a \$10 million option fee, up to \$21 million in milestone payments based on regulatory approvals, and a mid-single-digit royalty on product sales in the Valeant Territories.

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

Table of Contents

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 warrants to purchase shares of our common stock, either individually or in units, with a total value of up to \$100,000,000 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:

aggregate offering price;

redemption, exercise or exchange terms;

restrictive covenants;

voting or other rights;

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

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.

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.

Warrants. We may issue warrants for the purchase of common stock in one or more series. We may issue warrants independently or together with common stock and the warrants may be attached to or separate from such common stock. 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.

Table of Contents

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.

Units. We may issue, in one or more series, units consisting of common stock and warrants for the purchase of common stock. In this prospectus, we have summarized certain general features of the units. 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 units being offered, as well as any unit agreement that contains the terms of the units. 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 form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

Any units issued under this prospectus may be evidenced by unit certificates. Units also may be issued under an applicable unit agreement that we enter into with a unit agent. We will indicate the name and address of the unit agent, if applicable, in the prospectus supplement relating to the particular series of units 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, 2009, as filed with the SEC on March 12, 2010, and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2010 and June 30, 2010, as filed with the SEC on May 7, 2010 and August 6, 2010, 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 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.

Because the factors discussed in this prospectus, incorporated by reference herein or discussed in the applicable prospectus supplement, and even factors of which we are not yet aware, could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by or on behalf of us, you should not

place undue reliance on any such forward-looking statements. These statements are subject to risks and uncertainties, known and unknown, which could cause actual results and developments to differ materially from those expressed or implied in such statements. We have included important factors in the cautionary statements included in this prospectus, in the applicable prospectus supplement, particularly under the heading RISK FACTORS, and in our SEC filings that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. These and other risks are also detailed in our reports filed from time to time under the Securities Act and/or the Exchange Act. You are encouraged to read these filings as they are made.

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

Table of Contents

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 October 21, 2010, 23,178,099 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.

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 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 merger, asset sale or other transaction resulting in a

Table of Contents

financial benefit to the stockholder. 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 Market

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

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock in one or more series. We may issue warrants independently or together with common stock and the warrants may be attached to or separate from such common stock. 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 the form of the warrant agreement and the form of the warrant certificate 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 agreement 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

Table of Contents

prospectuses that we may authorize to be provided to you in connection with the warrants, and the complete warrant agreement and warrant certificate 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 date on and after which the warrants and the related securities will be separately transferable;

the number of shares of common stock 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 shares of common stock 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 agreement and warrants may be modified;

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

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

Before exercising their warrants, holders of warrants will not have any of the rights of holders of common stock purchasable upon such exercise, including 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 shares of our common stock 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 shares of common stock 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 agreement will be governed by and construed in accordance with the laws of the State of New York.

Table of Contents

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.

DESCRIPTION OF UNITS

We may issue, in one more series, units consisting of common stock and warrants for the purchase of common stock. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

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 form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all of the provisions of any unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units 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 units and any unit agreement and any supplemental agreements that contain the terms of the units.

General

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. Any unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

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

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under **Description of Capital Stock** and **Description of Warrants** will apply to each unit and to any common stock or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in such number of distinct series as we determine.

Enforceability of Rights by Holders of Units

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

Table of Contents

Title

We and any unit agent and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary.

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.

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.

Table of Contents

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 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.

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.

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

Stonefield Josephson, Inc., independent registered public accounting firm, has audited our consolidated financial statements as of and for the year ended December 31, 2009 and the effectiveness of Ardea Biosciences, Inc.'s internal control over financial reporting as of December 31, 2009, as set forth in their reports, each of which are included in our Annual Report on Form 10-K for the year ended December 31, 2009 as filed with the SEC on March 12, 2010, and are incorporated by reference in this prospectus and

Table of Contents

elsewhere in the registration statement. These financial statements are incorporated by reference in reliance on Stonefield Josephson, Inc.'s reports, 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.

We incorporate by reference the documents listed below and any filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date we filed the initial registration statement of which this prospectus is a part and before the effective date of the registration statement and any future filings we will make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act from the date of this prospectus but prior to the termination of the offering (in each case, except for the information in any of the foregoing Current Reports on Form 8-K 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, 2009, filed with the SEC on March 12, 2010 (including information specifically incorporated by reference into our Form 10-K from our Proxy Statement for our 2010 Annual Meeting of Stockholders);

Quarterly report on Form 10-Q for the quarter ended March 31, 2010, filed with the SEC on May 7, 2010;

Quarterly report on Form 10-Q for the quarter ended June 30, 2010, filed with the SEC on August 6, 2010;

Current reports on Form 8-K filed with the SEC on February 9, 2010, March 8, 2010, April 5, 2010, April 9, 2010, May 27, 2010, September 17, 2010 and October 7, 2010 (except for the information in such reports that shall not be deemed filed for purposes of Section 18 of the Exchange Act); and

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.

Table of Contents

2,500,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

BofA Merrill Lynch

Jefferies

January , 2011