RIGEL PHARMACEUTICALS INC
Form 424B5
October 03, 2012

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-179979

PROSPECTUS SUPPLEMENT
(to Prospectus dated March 22, 2012)

13,685,000 Shares

Common Stock

We are offering 13,685,000 shares of our common stock. Our common stock is listed on The NASDAQ Global Select Market under the symbol "RIGL." On October 2, 2012, the last reported sales price of our common stock on The NASDAQ Global Select Market was $10.35 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-7 of this prospectus supplement.

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

	PER SHARE	TOTAL
Public Offering Price	$ 9.50	$ 130,007,500
Underwriting Discounts and Commissions	0.57	7,800,450
Proceeds to Rigel Pharmaceuticals, Inc. before expenses	8.93	122,207,050

Delivery of the shares of common stock is expected to be made on or about October 9, 2012. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 2,052,750 shares of our common stock solely to cover overallotments. If the underwriters exercise the option in full, the underwriting discounts and commissions payable by us will be $8,970,518, and the proceeds to us, before expenses, will be $140,538,107.

Joint Book-Running Managers

Jefferies **J.P. Morgan**

Lead Manager

Citigroup

Co-Managers

BMO Capital Markets **Piper Jaffray** **Wells Fargo Securities**

Prospectus Supplement dated October 3, 2012

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not, and the underwriters 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 or to which we have referred you. We 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 or to which we have referred you, is accurate only as of the date of those respective documents, regardless of the time of delivery 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 or to which we have referred you, 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."

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About this Prospectus Supplement

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated March 22, 2012, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. In this prospectus supplement, as permitted by law, we "incorporate by reference" information from other documents that we file with the Securities and Exchange Commission, or the SEC. This means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus and should be read with the same care. When we update the information contained in documents that have been incorporated by reference by making future filings with the SEC, the information included or incorporated by reference in this prospectus supplement is considered to be automatically updated and superseded. In other words, in case of a conflict or inconsistency between information contained in this prospectus supplement and information in the accompanying prospectus or incorporated by reference into this prospectus supplement, you should rely on the information contained in the document that was filed later.

Unless otherwise indicated or the context requires otherwise, references in this prospectus supplement and the accompanying prospectus to "Rigel," "the company," "we," "us" and "our" refer to Rigel Pharmaceuticals, Inc. The name Rigel Pharmaceuticals and our logo are our trademarks. All other trademarks, trade names or service marks included or incorporated by reference in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

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Prospectus Supplement 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 prepared by or on behalf of us or to which we have referred you. If you invest in our common stock, you are assuming a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement.

Company Overview

We are a clinical-stage drug development company that discovers and develops novel, small-molecule drugs for the treatment of inflammatory and autoimmune diseases, as well as muscle disorders. Our pioneering research focuses on intracellular signaling pathways and related targets that are critical to disease mechanisms. Our productivity has resulted in strategic collaborations with large pharmaceutical partners to develop and market our product candidates. Current product development programs include fostamatinib, an oral spleen tyrosine kinase, or SYK, inhibitor that is in Phase 3 clinical trials for rheumatoid arthritis, or RA, with our partner AstraZeneca AB, or AZ; R343, an inhaled SYK inhibitor that has completed Phase 1 clinical trials for asthma; R333, a topical janus kinase /SYK inhibitor for discoid lupus; and R548, an oral janus kinase 3, or JAK3, inhibitor for the treatment of transplant rejection and other immune disorders.

Product Development Programs

Our product development portfolio features multiple novel, small-molecule drug candidates whose specialized mechanisms of action are intended to provide therapeutic benefit for a range of inflammatory and autoimmune diseases, as well as muscle disorders.

Partnered Clinical Programs

Fostamatinib Rheumatoid Arthritis

Disease background. RA is a systemic autoimmune inflammatory disease that causes damage to the joints and other organs, affecting approximately 1 in 100 people in the United States. It is a major cause of disability and is also associated with reduced life expectancy, especially if it is not adequately treated. Despite current treatment options, many patients still experience significant disease activity, including continued joint destruction leading to pain and disability; therefore, new treatment options are needed.

The current treatment options for RA have significant potential side effects and other shortfalls, including gastrointestinal complications and kidney damage. RA patients may receive multiple drugs, depending on the extent and aggressiveness of their disease. Most RA patients eventually require some form of disease modifying anti-rheumatic drugs, or DMARDs. This category of drugs includes methotrexate, or MTX, and a variety of intravenously-delivered immunomodulatory agents (tumor necrosis factor, or TNF, inhibitors and co-stimulation inhibitors).

Orally-available SYK inhibitor program. Fostamatinib is an orally bio-available SYK inhibitor. It has a novel mechanism of action for the treatment of RA in which it reversibly blocks signaling in multiple cell types involved in inflammation and tissue degradation (*e.g.* macrophages, osteoclasts, mast cells and B cells). RA is an autoimmune disease characterized by chronic inflammation that affects multiple tissues, but typically produces its most pronounced symptoms in the joints.

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OSKIRA

The Oral SYK Inhibition in Rheumatoid Arthritis (OSKIRA) Phase 3 clinical trial program is designed to investigate fostamatinib as a treatment for RA in patients with an inadequate response to DMARDs, including MTX. AZ announced that the OSKIRA clinical trial program included three pivotal Phase 3 studies assessing the efficacy and tolerability of fostamatinib: two 12-month studies examining the effect of fostamatinib on patients responding inadequately to DMARDs (including MTX), and a six-month study assessing the effect of fostamatinib on patients who have previously responded inadequately to anti-TNF therapy. The fostamatinib clinical trial program is also expected to include long-term safety extension studies involving more than 2,000 of the patients recruited during the course of the Phase 2 and 3 clinical trial programs. AZ also announced that in the first quarter of 2011 they had commenced a Phase 2b clinical trial (OSKIRA-4) that explores fostamatinib as a monotherapy in RA. This trial will provide information on the profile of fostamatinib without concomitant treatment with a DMARD. Recently, AZ indicated that the Phase 3 clinical studies in RA are continuing as planned. OSKIRA-1 completed enrollment in the fourth quarter of 2011 and OSKIRA-2 completed enrollment in the second quarter of 2012. AZ expects to report Phase 3 results from OSKIRA-1, OSKIRA-2, and OSKIRA-3 in the first half of 2013. AZ also expects to report data from OSKIRA-4 by late 2012. AZ has stated that they expect to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for fostamatinib, and a European equivalent, in the second half of 2013.

TASKi2

In July 2009, we announced that fostamatinib produced significant clinical improvement in RA patients in the *TASKi2* Phase 2b clinical trial, which evaluated 457 RA patients for up to six months. *TASKi2* was a multi-center, randomized, double-blind, placebo-controlled, parallel-dose clinical trial involving RA patients in the United States, Latin America and Europe who had failed to respond to MTX alone. Patients received either 100 mg of fostamatinib b.i.d. (twice a day), 150 mg q.d. (once a day) or placebo. The groups treated with 100 mg of fostamatinib b.i.d. and 150 mg q.d. reported higher response rates than the placebo group in all criteria levels. The efficacy results for the two dosing groups were comparable, although the response rates for the 100 mg b.i.d. group were uniformly greater. Consistent with the previous Phase 2a clinical trial *(TASKi1)*, the onset effect of fostamatinib occurred within one week after the initiation of therapy and was maintained. The most frequent adverse events were expected based on results from *TASKi1* and appeared to be manageable. The most common, clinically-meaningful, drug-related adverse events noted in *TASKi2* were diarrhea and hypertension. Dose reduction options were pre-specified in the trial protocol and, in cases where doses were reduced, patients generally completed the clinical trial with minimal safety issues. The most common adverse events in the clinical trial overall were related to infections, though these were generally evenly distributed among the fostamatinib and placebo groups.

TASKi3

In July 2009, we also announced results for the *TASKi3* Phase 2b clinical trial involving 219 RA patients who had failed to respond to at least one biologic treatment. In the *TASKi3* clinical trial, patients received either 100 mg of fostamatinib b.i.d. or placebo b.i.d. for up to three months. The group treated with fostamatinib did not report significantly higher American College of Rheumatology, or ACR, 20, ACR 50, ACR 70 and Disease Activity Score, or DAS, 28 response rates than the placebo group at three months, and therefore, the trial failed to meet its efficacy endpoints. The objective components (C-Reactive Protein and Erythrocyte Sedimentation Rate) of these ACR scores did show a statistically significant difference; however, the subjective reported response rate components did not show a statistically significant difference as compared to placebo.

TASKi3 was the first clinical trial for fostamatinib in which anatomical changes in the patients' wrists and hands were evaluated using Magnetic Resonance Imaging and scored using the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring, or RAMRIS, system. Those results showed improvements in the

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treated group versus the placebo group in the Synovitis and Osteitis scores, while the Erosion scores, known to be the slowest to change, showed no significant effect at three months. Similar to *TASKi2*, the most common, clinically-meaningful, drug-related adverse events noted in *TASKi3* were diarrhea and hypertension. Dose reduction options were pre-specified in the trial protocol and, in cases where doses were reduced, patients generally completed the clinical trial with minimal safety issues. The most common adverse events in the clinical trial overall were related to infections, though these were generally evenly distributed among the fostamatinib and placebo groups.

Fostamatinib Other Indications

In addition to RA, fostamatinib has been studied in patients with other immune disorders and some cancers. Our collaboration with AZ gives AZ sole responsibility for all development decisions for all indications. AZ commenced Phase 2 clinical trials to investigate the effect of fostamatinib on hematological malignancies in the first quarter of 2012.

Clinical Stage Programs

R343 Asthma

Disease background. Allergic asthma is a chronic inflammatory disorder of the airways. Asthma affects the lower respiratory tract and is marked by episodic flare-ups, or attacks, that can be life threatening. In some patients, allergens, such as pollen, trigger the production of immunoglobulin E, or IgE, antibodies, which then bind to mast cells and cause an intracellular signal that results in the release of various chemical mediators. When this process occurs repeatedly over time, it creates persistent inflammation of the airway passages, resulting in the chronic congestion and airway obstruction associated with allergic rhinitis and asthma, respectively.

Inhaled SYK inhibitor program. R343 is a potent SYK inhibitor that blocks IgE receptor signaling. Mast cells play important roles in both early and late phase allergic reactions, and SYK inhibitors could potentially prevent both phases. Based on its mechanism of action, this inhaled SYK inhibitor may provide a new treatment paradigm for the largest group of patients with allergic asthma whose symptoms range from acute to chronic phases of the disease.

In 2005, we announced a collaborative research and license agreement with Pfizer, Inc., or Pfizer, for the development of inhaled products for the treatment of allergic asthma. The collaboration was focused on our preclinical small-molecule compounds, which inhibit SYK. R343 was the oral SYK inhibitor small molecule at the center of this collaboration. Pfizer completed the Phase 1a clinical trial of an inhaled formulation of R343, which commenced in December 2007 and resulted in a payment of $5.0 million to us. Pfizer also completed an initial Phase 1b allergen challenge clinical trial. In 2011, we assumed development of R343 after Pfizer returned full rights to the R343 program to us as a result of its decision to exit research and development in the allergy and respiratory therapeutic area, and the collaborative research and license agreement was terminated.

SITAR. In September 2012, we initiated a Phase 2 clinical study designed to investigate R343 for the treatment of allergic asthma. The Phase 2 clinical study, called SITAR (SYK Inhibition for Treatment of Asthma with R343), is designed to randomize approximately 270 adults with allergic asthma into the three arms of the study for eight weeks of treatment with either of two different doses of the study agent or placebo. R343 will be delivered directly into the lungs via a dry inhalation device. We expect to complete this study in 2013.

R333 Discoid Lupus Erythematosus (DLE)

Disease background. DLE is an autoimmune disease of the skin characterized by disc-shaped sores with inflammation, swelling, scaling, scarring, pigment discoloration and even hair loss. The lesions most

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commonly appear in sun exposed areas, predominantly on the face, chest and scalp. This disease has an acute phase, which research has connected to SYK signaling within the immune cascade. There is also a chronic phase of the disease due to the abundance of JAK signaling. Current treatments for DLE have either poor efficacy or significant toxicities.

Topical JAK/SYK inhibitor program. R333 is a topical (ointment) JAK/SYK inhibitor, which may be useful in treating both the acute and chronic phases of DLE. We initiated Phase 1 clinical studies of its topical agent in the fourth quarter of 2011 to test its application in treating acute and chronic phases of DLE.

SKINDLE. In September 2012, we initiated a Phase 2 clinical study designed to investigate R333 for the treatment of DLE. In this Phase 2 clinical study, called SKINDLE (SYK Kinase Inhibition for DLE), more than 50 patients with active discoid skin lesions from DLE or Systemic Lupus Erythematosus, or SLE, will be randomized into two groups. One group will receive R333 in a topical ointment and the other a placebo ointment to be administered on the lesions twice daily for four weeks. We expect to complete this study in 2013.

R548 Transplant Rejection and Other Immune Disorders

Disease background. Transplant rejection is an area of tremendous medical need. While 90% of patients survive the first year after receiving the transplanted organ, chronic organ rejection rates rise to 50% within the 5 to 10 years following transplant surgery. Currently available therapeutics are not sufficient to achieve lasting recovery and limit the range of transplant options for certain organs. Furthermore, transplants of certain organs are rarely done because of the inadequacies of these therapies.

Oral JAK3 inhibitor program. R548 is an oral JAK3 inhibitor that is expected to moderate the immune system's response to the allograft and improve patient outcomes. R548 may also have application in treating other immune system disorders.

In January 2012, we announced that we initiated Phase 1 clinical studies in normal healthy volunteers in the fourth quarter of 2011 of R548 with a focus to treat transplant rejection and other immune system disorders.

Preclinical Programs

In the area of inflammation/immunology, we expect to initiate clinical trials with one new molecule in late 2012. We have a lead candidate, R348, which is a soluble JAK/SYK inhibitor for topical ophthalmic use which may be useful to treat Sjogren's syndrome, an autoimmune disorder that affects the lacrimal glands of the eye (tear ducts).

In the area of muscle atrophy and muscle endurance, we are focusing on several signaling pathways that are important for muscle homeostasis. Patients with chronic illnesses such as chronic heart failure, chronic obstructive pulmonary disease, or COPD, or diabetes, often experience a decrease in strength and increase in fatigue due to muscle myopathy. We are conducting preclinical studies of an oral activator of adenosine monophosphate (AMP)-activated protein kinase, or AMPK, to examine whether it can improve the body's energy utilization and restore muscle endurance in chronically ill subjects. Our focus for this program is to evaluate its potential treatment in patients with congestive heart failure, or CHF, COPD or peripheral vascular disease who exhibit exercise intolerance.

We also have an active small molecule discovery program in muscle wasting. Excessive loss of muscle in the context of illness can contribute significantly to both morbidity and mortality rates. Many conditions that have been associated with muscle atrophy, or the loss of muscle mass, including cancer, chronic heart failure, chronic kidney disease, mechanical ventilation and aging (sarcopenia), have significant patient populations that may benefit from therapeutics that counter such muscle loss. We are developing a program for intravenous inhibition of growth/differentiation factor 8, or GDF8, signaling for muscle strength. This

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preclinical program is focused on inhibiting the GDF8 signaling cascade which leads to loss of muscle in a variety of chronic disease states, but particularly in regard to loss of diaphragm muscle mass and strength (atrophy) associated with respiratory ventilator use. Preclinical studies have shown that inhibiting GDF8 signaling may be therapeutically useful to prevent muscle loss and improve muscle function. We may enter the clinic in 2013 with one of our muscle programs discussed above.

Research Programs

We are conducting proprietary research in the broad disease areas of inflammation/immunology and muscle wasting/muscle endurance. Within each disease area, our researchers are investigating mechanisms of action as well as screening compounds against potential novel targets and optimizing those leads that appear to have the greatest potential.

Corporate Collaborations

We conduct research and development programs independently and in connection with our corporate collaborators. We currently have a significant active collaboration with AZ, relating to fostamatinib for the treatment of RA and other indications. Our collaboration with AZ does not provide us with regular reimbursement of research expenses. If certain conditions are met, we are entitled to receive future payments and royalties. We cannot guarantee that these conditions will be met or that research and development efforts will be successful. As a result, we may not receive any further payments or royalties under the agreement with AZ.

Corporate Information

We were incorporated in Delaware in June 1996. Our principal executive office is located at 1180 Veterans Boulevard, South San Francisco, California 94080. Our telephone number is (650) 624-1100. Our website address is *www.rigel.com*. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

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The Offering

Common stock offered by us	**13,685,000 shares**
Common stock to be outstanding immediately after this offering	**85,280,137 shares**
Overallotment Option	

We have granted the underwriters an option to purchase up to 2,052,750 additional shares of our common stock to cover overallotments, if any. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds from this offering for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we currently are not planning or negotiating any such transactions. See "Use of Proceeds" on page S-24 of this prospectus supplement.

NASDAQ Global Select Market Listing

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

Risk Factors

An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement.

Outstanding Shares

The number of shares of our common stock to be outstanding immediately after this offering is based on 71,595,137 shares outstanding as of June 30, 2012 and excludes:

- 13,799,287 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2012, having a weighted-average exercise price of approximately $11.49 per share;
- 200,000 shares of our common stock issuable upon the exercise of a warrant outstanding as of June 30, 2012, having an exercise price of $6.61 per share; and
- an aggregate of 3,779,168 shares of our common stock available for issuance or future grant as of June 30, 2012 under our 2000 Equity Incentive Plan, or the 2000 Plan, our 2000 Employee Stock Purchase Plan, or the ESPP, our 2000 Non-Employee Directors' Stock Option Plan, or the Directors' Plan, and our 2011 Equity Incentive Plan, or the 2011 Plan.

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

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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, 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 or to which we have referred you. 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 Our Business

If our corporate collaborations or license agreements are unsuccessful, our research and development efforts could be delayed.

Our strategy depends upon the formation and sustainability of multiple collaborative arrangements and license agreements with third parties now and in the future. We rely on these arrangements for not only financial resources, but also for expertise we need now and in the future relating to clinical trials, manufacturing, sales and marketing, and for licenses to technology rights. To date, we have entered into several such arrangements with corporate collaborators; however, we do not know if these collaborations or additional third parties with which we may collaborate, if any, will dedicate sufficient resources or if any development or commercialization efforts by third parties will be successful. In addition, our corporate collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate or development program. Should a collaborative partner fail to develop or commercialize a compound or product to which it has rights from us for any reason, including corporate restructuring, such failure might delay our ongoing research and development efforts, because we might not receive any future payments, and we would not receive any royalties associated with such compound or product. In addition, the continuation of some of our partnered drug discovery and development programs may be dependent on the periodic renewal of our corporate collaborations.

In February 2010, we entered into an exclusive worldwide license agreement with AZ for the global development and commercialization of our oral SYK inhibitors for the treatment of human diseases other than those primarily involving respiratory or pulmonary dysfunction. The agreement includes a license of rights to fostamatinib, our late-stage investigational product candidate for the treatment of RA and other indications. AZ started its Phase 3 clinical trial program in patients in RA in September 2010. Our collaboration agreement with AZ does not include a research phase. The research phase of our collaboration agreement with Daiichi ended in 2005. Each of our collaborations could be terminated by the other party at any time, and we may not be able to renew these collaborations on acceptable terms, if at all, or negotiate additional corporate collaborations on acceptable terms, if at all. If these collaborations terminate or are not renewed, any resultant loss of revenues from these collaborations or loss of the resources and expertise of our collaborative partners could adversely affect our business.

Conflicts also might arise with collaborative partners concerning proprietary rights to particular compounds. While our existing collaborative agreements typically provide that we retain milestone payments and royalty rights with respect to drugs developed from certain derivative compounds, any such payments or royalty rights may be at reduced rates, and disputes may arise over the application of derivative payment provisions to such drugs, and we may not be successful in such disputes.

We are also a party to various license agreements that give us rights to use specified technologies in our research and development processes. The agreements pursuant to which we have in-licensed technology permit our licensors to terminate the agreements under certain circumstances. If we are not able to continue to license these and future technologies on commercially reasonable terms, our product development and research may be delayed or otherwise adversely affected.

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If conflicts arise between our collaborators or advisors and us, any of them may act in their self-interest, which may be adverse to our stockholders' interests.

If conflicts arise between us and our corporate collaborators or scientific advisors, the other party may act in its self-interest and not in the interest of our stockholders. Some of our corporate collaborators are conducting multiple product development efforts within each disease area that is the subject of the collaboration with us or may be acquired or merged with a company having a competing program. In some of our collaborations, we have agreed not to conduct, independently or with any third party, any research that is competitive with the research conducted under our collaborations. Our collaborators, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by our collaborators or to which our collaborators have rights, may result in their withdrawal of support for our product candidates.

If any of our corporate collaborators were to breach or terminate its agreement with us or otherwise fail to conduct the collaborative activities successfully and in a timely manner, the preclinical or clinical development or commercialization of the affected product candidates or research programs could be delayed or terminated. We generally do not control the amount and timing of resources that our corporate collaborators devote to our programs or potential products. We do not know whether current or future collaborative partners, if any, might pursue alternative technologies or develop alternative products either on their own or in collaboration with others, including our competitors, as a means for developing treatments for the diseases targeted by collaborative arrangements with us.

If we are unable to obtain regulatory approval to market products in the United States and foreign jurisdictions, we will not be permitted to commercialize products from our research and development.

We cannot predict whether regulatory clearance will be obtained for any product that we, or our collaborative partners, hope to develop. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Of particular significance to us are the requirements relating to research and development and testing.

Before commencing clinical trials in humans in the United States, we, or our collaborative partners, will need to submit and receive approval from the FDA of an investigational new drug application, or IND. Clinical trials are subject to oversight by institutional review boards and the FDA and:

- must be conducted in conformance with the FDA's good clinical practices and other applicable regulations;
- must meet requirements for institutional review board oversight;
- must meet requirements for informed consent;
- are subject to continuing FDA and regulatory oversight;
- may require large numbers of test subjects; and
- may be suspended by us, our collaborators or the FDA at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA finds deficiencies in the IND or the conduct of these trials.

While we have stated that we intend to file additional INDs for future product candidates, this is only a statement of intent, and we may not be able to do so because we may not be able to identify potential product candidates. In addition, the FDA may not approve any IND in a timely manner, or at all.

Before receiving FDA approval to market a product, we must demonstrate with substantial clinical evidence that the product is safe and effective in the patient population and the indication that will be treated. Data obtained from preclinical and clinical activities are susceptible to varying

interpretations that could delay,

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limit or prevent regulatory approvals. In addition, delays or rejections may be encountered based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, adverse publicity, as well as other regulatory action against our potential products or us. Additionally, we have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval.

If regulatory approval of a product is granted, this approval will be limited to those indications or disease states and conditions for which the product is demonstrated through clinical trials to be safe and efficacious. We cannot ensure that any compound developed by us, alone or with others, will prove to be safe and efficacious in clinical trials and will meet all of the applicable regulatory requirements needed to receive marketing approval.

Outside the United States, our ability, or that of our collaborative partners, to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. This foreign regulatory approval process typically includes all of the risks and costs associated with FDA approval described above and may also include additional risks and costs, such as the risk that such foreign regulatory authorities, which often have different regulatory and clinical study requirements, interpretations and guidance from the FDA, may require additional clinical trials or results for approval of a product candidate, any of which could result in delays, significant additional costs or failure to obtain such regulatory approval. For example, there can be no assurance that we or our collaborative partners, including AZ, will not have to provide additional information or analysis, or conduct additional studies, before receiving approval to market product candidates, such as fostamatinib in Europe, or other countries.

We might not be able to commercialize our product candidates successfully if problems arise in the clinical testing and approval process.

Commercialization of our product candidates depends upon successful completion of extensive preclinical studies and clinical trials to demonstrate their safety and efficacy for humans. Preclinical testing and clinical development are long, expensive and uncertain processes.

In connection with clinical trials of our product candidates, we face the risks that:

- the product candidate may not prove to be effective;
- the product candidate may cause harmful side effects;
- the clinical results may not replicate the results of earlier, smaller trials;
- we or the FDA or similar foreign regulatory authorities may terminate or suspend the trials;
- the results may not be statistically significant;
- patient recruitment and enrollment may be slower than expected;
- patients may drop out of the trials; and
- regulatory and clinical study requirements, interpretations or guidance may change.

We do not know whether we, or any of our collaborative partners, will be permitted to undertake clinical trials of potential products beyond the trials already concluded and the trials currently in process. It will take us, or our collaborative partners several years to complete any such

testing, and failure can occur at any stage of testing. Interim results of trials do not necessarily predict final results, and acceptable results in early trials may not be repeated in later trials. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier trials. Moreover, we or our collaborative partners or regulators may decide to discontinue development of any or all of these projects at any time for commercial, scientific or other reasons.

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There is a high risk that drug discovery and development efforts might not successfully generate good product candidates.

At the present time, the majority of our operations are in various stages of drug identification and development. We currently have four product compounds in the clinical testing stage: one with indication for RA subject to a collaboration agreement with AZ; one that has completed an initial Phase 1b allergen challenge trial for allergic asthma for which we initiated a Phase 2 clinical trial in September 2012; one with indication for DLE currently in a Phase 1 clinical trial for which we initiated a Phase 2 clinical trial in September 2012; and one with indication for transplant rejection currently in a Phase 1 clinical trial. In our industry, it is statistically unlikely that the limited number of compounds that we have identified as potential product candidates will actually lead to successful product development efforts, and we do not expect any drugs resulting from our research to be commercially available for several years, if at all.

Our compounds in clinical trials and our future leads for potential drug compounds are subject to the risks and failures inherent in the development of pharmaceutical products. These risks include, but are not limited to, the inherent difficulty in selecting the right drug and drug target and avoiding unwanted side effects, as well as unanticipated problems relating to product development, testing, obtaining regulatory approvals, maintaining regulatory compliance, manufacturing, competition and costs and expenses that may exceed current estimates. For example, in our two Phase 2b clinical trials for fostamatinib in RA, TASKi2 and TASKi3, the most common, clinically-meaningful, drug-related adverse events noted were diarrhea and hypertension. In both our TASKi2 and TASKi3 Phase 2b clinical trials, a meaningfully higher percentage of patients in the fostamatinib treatment groups had blood pressure medication adjusted or initiated during the course of the clinical trials as compared to the placebo group. In larger future clinical trials, we or our partners may discover additional side effects and/or higher frequency of side effects than those observed in completed clinical trials. If approved by the FDA, the side effect profile of fostamatinib may also result in a narrowly approved indication for use of the product, especially in light of other drugs currently available to treat RA, dependent on the safety profile of fostamatinib relative to those drugs.

The results of preliminary and mid-stage studies do not necessarily predict clinical or commercial success, and larger later-stage clinical trials may fail to confirm the results observed in the previous studies. Similarly, a clinical trial may show that a product candidate is safe and effective for certain patient populations in a particular indication, but other clinical trials may fail to confirm those results in a subset of that population or in a different patient population, which may limit the potential market for that product candidate. For example, fostamatinib produced significant clinical improvement in RA patients who had failed to respond to MTX alone in our TASKi2 Phase 2b clinical trial, but our TASKi3 Phase 2b clinical trial failed to meet its efficacy endpoints in RA patients who had failed to respond to at least one biologic treatment. In addition, if we were to repeat either of the TASKi2 and TASKi3 Phase 2b clinical trials, any such additional trials may not confirm the results observed in the original trials. The Phase 3 clinical program evaluating fostamatinib in RA patients, initiated by our partner, AZ, may not show fostamatinib to be safe and effective for the treatment of RA patients. With respect to our own compounds in development, we have established anticipated timelines with respect to the initiation of clinical studies based on existing knowledge of the compounds. However, we cannot provide assurance that we will meet any of these timelines for clinical development. Additionally, the initial results of the completed Phase 1b allergen challenge trial conducted by Pfizer for our asthma program does not necessarily predict final results and the results may not be repeated in our Phase 2 and later clinical trials.

Because of the uncertainty of whether the accumulated preclinical evidence (pharmacokinetic, pharmacodynamic, safety and/or other factors) or early clinical results will be observed in later clinical trials, we can make no assurances regarding the likely results from our future clinical trials or the impact of those results on our business.

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Our success is dependent on intellectual property rights held by us and third parties, and our interest in such rights is complex and uncertain.

Our success will depend to a large part on our own, our licensees' and our licensors' ability to obtain and defend patents for each party's respective technologies and the compounds and other products, if any, resulting from the application of such technologies. We have about 93 pending patent applications and about 220 issued patents in the United States, as well as corresponding pending foreign patent applications and issued foreign patents. In the future, our patent position might be highly uncertain and involve complex legal and factual questions. For example, we may be involved in interferences before the United States Patent and Trademark Office. Interferences are complex and expensive legal proceedings and there is no assurance we will be successful in any such proceedings. An interference could result in our losing our patent rights and/or our freedom to operate and/or require us to pay significant royalties. Additional uncertainty may result because no consistent policy regarding the breadth of legal claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims allowed in our or other companies' patents.

Because the degree of future protection for our proprietary rights is uncertain, we cannot ensure that:

- we were the first to make the inventions covered by each of our pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any of our pending patent applications will result in issued patents;
- any patents issued to us or our collaborators will provide a basis for commercially-viable products or will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies that are patentable; or
- the patents of others will not have a negative effect on our ability to do business.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable; however, trade secrets are difficult to protect. While we require employees, collaborators and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information.

We are a party to certain in-license agreements that are important to our business, and we generally do not control the prosecution of in-licensed technology. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we exercise over our internally-developed technology. Moreover, some of our academic institution licensors, research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, our ability to receive patent protection or protect our proprietary information may otherwise be impaired. In addition, some of the technology we have licensed relies on patented inventions developed using U.S. government resources. The U.S. government retains certain rights, as defined by law, in such patents, and may choose to exercise such rights. Certain of our in-licenses may be terminated if we fail to meet specified obligations. If we fail to meet such obligations and any of our licensors exercise their termination rights, we could lose our rights under those agreements. If we lose any of our rights, it may adversely affect the way we conduct our business. In addition, because certain of our licenses are sublicenses, the actions of our licensors may affect our rights under those licenses.

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If a dispute arises regarding the infringement or misappropriation of the proprietary rights of others, such dispute could be costly and result in delays in our research and development activities and partnering.

Our success will depend, in part, on our ability to operate without infringing or misappropriating the proprietary rights of others. There are many issued patents and patent applications filed by third parties relating to products or processes that are similar or identical to our licensors or ours, and others may be filed in the future. There can be no assurance that our activities, or those of our licensors, will not infringe patents owned by others. We believe that there may be significant litigation in the industry regarding patent and other intellectual property rights, and we do not know if our collaborators or we would be successful in any such litigation. Any legal action against our collaborators or us claiming damages or seeking to enjoin commercial activities relating to the affected products, our methods or processes could:

- require our collaborators or us to obtain a license to continue to use, manufacture or market the affected products, methods or processes, which may not be available on commercially reasonable terms, if at all;
- prevent us from using the subject matter claimed in the patents held by others;
- subject us to potential liability for damages;
- consume a substantial portion of our managerial and financial resources; and
- result in litigation or administrative proceedings that may be costly, whether we win or lose.

We will continue to need additional capital following this offering to sufficiently fund our operations and research.

We have consumed substantial amounts of capital to date as we continue our research and development activities, including preclinical studies and clinical trials. In February 2010, we entered into an exclusive worldwide license agreement with AZ for the global development and commercialization of our oral SYK inhibitors for the treatment of human diseases other than those primarily involving respiratory or pulmonary dysfunction. The agreement includes a license of rights to fostamatinib, our late-stage investigational product candidate for the treatment of RA and other indications. The agreement became effective on March 26, 2010 and, in connection with the effectiveness of the agreement, we received an upfront payment of $100.0 million in April 2010 from AZ. In October 2010, we received $25.0 million from AZ for completing the transfer of the fostamatinib long-term open label extension study to AZ and for the initiation of Phase 3 clinical trials in the fostamatinib program by AZ. AZ is required to pay us up to an additional $320.0 million if specified development, regulatory and launch events are achieved for fostamatinib, of which up to $25.0 million relate to the achievement of development events, up to $100.0 million relate to the achievement of regulatory events and up to $195.0 million relate to the achievement of product launch events. We are also eligible to receive up to an additional $800.0 million if specified sales levels are achieved for fostamatinib, as well as significant stepped double-digit royalties on net worldwide sales, if any. In June 2011, we completed an underwritten public offering in which we sold 18,745,000 shares of our common stock pursuant to an effective registration statement at a price to the public of $8.00 per share. We received net proceeds of approximately $140.5 million after deducting underwriting discounts and commissions and offering expenses. We will continue to need additional capital following this offering and the amount of future capital needed will depend largely on the success of our internally developed programs as they proceed in later and more expensive clinical trials. Unless and until we are able to generate a sufficient amount of product, royalty or milestone revenue, which may never occur, we expect to finance future cash needs through public and/or private offerings of equity securities, debt financings or collaboration and licensing arrangements, as well as through interest income earned on the investment of our cash balances and short-term investments. With the exception of contingent and royalty payments that we may receive under our existing collaborations, we do not currently have any commitments for future funding. We do not know whether additional financing will be available when needed, or that, if available, we will obtain financing on reasonable terms.

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To the extent we raise additional capital by issuing equity securities in the future, you could at that time experience substantial dilution. Any debt financing that we are able to obtain may involve operating covenants that restrict our business. To the extent that we raise additional funds through any new collaboration and licensing arrangements, we may be required to relinquish some rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

Our future funding requirements will depend on many uncertain factors.

Our future funding requirements will depend upon many factors, including, but not limited to:

- the achievement of the events identified in our collaborative agreements that trigger payments to us from our collaboration partners, most of which are out of our control and rely entirely on the efforts of our partners;
- the progress and success of clinical trials and preclinical activities (including studies and manufacture of materials) of our product candidates conducted by our collaborative partners or licensees or us;
- the progress of research programs carried out by us;
- any changes in the breadth of our research and development programs;
- the progress of the research and development efforts of our collaborative partners;
- our ability to acquire or license other technologies or compounds that we seek to pursue;
- competing technological and market developments;
- the costs and timing of obtaining, enforcing and defending our patent and intellectual property rights;
- the costs and timing of regulatory approvals and filings by us and our collaborators;
- our ability to manage our growth; and
- expenses associated with the pending and potential additional related purported securities class action lawsuits, as well as any unforeseen litigation.

Insufficient funds may require us to delay, scale back or eliminate some or all of our research and development programs, to lose rights under existing licenses or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose or may adversely affect our ability to operate as a going concern.

Our success as a company is uncertain due to our history of operating losses and the uncertainty of any future profitability.

Although we generated operating income of approximately $35.3 million for the year ended December 31, 2010, this resulted from the one-time upfront payment from AZ received in April 2010, as well as payment for completing the transfer of the fostamatinib long-term open label extension study to AZ and for the initiation of Phase 3 clinical trials in the fostamatinib program by AZ. We incurred a loss from operations of

approximately $48.2 million for six months ended June 30, 2012. Other than for 2010, we have historically operated at a loss each year since we were incorporated in June 1996, due in large part to the significant research and development expenditures required to identify and validate new product candidates and pursue our development efforts. We expect to continue to incur net operating losses for at least the next two years and there can be no assurance that we will generate operating income in the future. Currently, our only potential sources of revenues are upfront payments, research and development contingent payments and royalty payments pursuant to our collaboration arrangements. If our drug candidates fail or do not gain regulatory approval, or if our drugs do not achieve market acceptance, we may not be profitable. As of June 30, 2012, we had an accumulated deficit of approximately $709.3 million. The extent of our future losses or profitability, if any, is highly uncertain.

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Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses to offset future taxable income. Our existing net operating losses and credits may be subject to limitations arising from previous and future ownership changes under Section 382 of the Internal Revenue Code. To the extent we cannot completely utilize net operating loss carryforwards or tax credits in our financial statements to offset future taxable income, our tax expense may increase in future periods.

Because we expect to be dependent upon collaborative and license agreements, we might not meet our strategic objectives.

Our ability to generate revenue in the near term depends on the timing of recognition of certain upfront payments, achievement of certain payment triggering events with our existing collaboration agreements and our ability to enter into additional collaborative agreements with third parties. Our ability to enter into new collaborations and the revenue, if any, that may be recognized under these collaborations is highly uncertain. If we are unable to enter into one or more new collaborations, our business prospects could be harmed, which could have an immediate adverse effect on our ability to continue to develop our compounds and on the trading price of our stock. Our ability to enter into a collaboration may be dependent on many factors, such as the results of our clinical trials, competitive factors and the fit of one of our programs with another company's risk tolerance, including toward regulatory issues, patent portfolio, clinical pipeline, the stage of the available data, particularly if it is early, overall corporate goals and financial position.

To date, a portion of our revenues have been related to the research or transition phase of each of our collaborative agreements. Such revenues are for specified periods, and the impact of such revenues on our results of operations is at least partially offset by corresponding research costs. Following the completion of the research or transition phase of each collaborative agreement, additional revenues may come only from payments triggered by milestones and/or the achievement of other contingent events, and royalties, which may not be paid, if at all, until certain conditions are met. This risk is heightened due to the fact that unsuccessful research efforts may preclude us from receiving any contingent payments under these agreements. Our receipt of revenues from collaborative arrangements is also significantly affected by the timing of efforts expended by us and our collaborators and the timing of lead compound identification. We have received payments from our collaborations with Janssen Pharmaceutica N.V., a division of Johnson & Johnson, Novartis, Daiichi, Merck & Co., Inc., Merck Serono and Pfizer. Under many agreements, future payments may not be earned until the collaborator has advanced product candidates into clinical testing, which may never occur or may not occur until some time well into the future. If we are not able to generate revenue under our collaborations when and in accordance with our expectations or the expectations of industry analysts, this failure could harm our business and have an immediate adverse effect on the trading price of our common stock.

Our business requires us to generate meaningful revenue from royalties and licensing agreements. To date, we have not received any revenue from royalties for the commercial sale of drugs, and we do not know when we will receive any such revenue, if at all.

Delays in clinical testing could result in increased costs to us.

Significant delays in clinical testing could materially impact our product development costs and timing. We do not know whether planned clinical trials will begin on time, will need to be halted or redesigned or will be completed on schedule, or at all. In addition, clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a study, delays from scaling up of a study, delays in reaching agreement on acceptable clinical study agreement terms with prospective clinical sites, delays in obtaining institutional review board approval to conduct a study at a prospective clinical site or delays in recruiting subjects to participate in a study.

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In addition, we typically rely on third-party clinical investigators to conduct our clinical trials and other third-party organizations to oversee the operations of such trials and to perform data collection and analysis. The clinical investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. Failure of the third-party organizations to meet their obligations could adversely affect clinical development of our products. As a result, we may face additional delaying factors outside our control if these parties do not perform their obligations in a timely fashion. While we have not yet experienced delays that have materially impacted our clinical trials or product development costs, delays of this sort could occur for the reasons identified above or other reasons. If we have delays in testing or obtaining regulatory approvals, our product development costs will increase. For example, we may need to make additional payments to third-party investigators and organizations to retain their services or we may need to pay recruitment incentives. If the delays are significant, our financial results and the commercial prospects for our product candidates will be harmed, and our ability to become profitable will be delayed. Moreover, these third-party investigators and organizations may also have relationships with other commercial entities, some of which may compete with us. If these third-party investigators and organizations assist our competitors at our expense, it could harm our competitive position.

We have been named a defendant in a purported securities class action lawsuit. This, and potential similar or related litigation, could result in substantial damages and may divert management's time and attention from our business.

On February 6, 2009, a purported securities class action lawsuit was commenced in the United States District Court for the Northern District of California, naming as defendants us and certain of our officers, directors and underwriters for our February 2008 public offering of common stock, or the Stock Offering. An additional purported securities class action lawsuit containing similar allegations was subsequently filed in the United States District Court for the Northern District of California on February 20, 2009. By order of the Court dated March 19, 2009, the two lawsuits were consolidated into a single action. On June 9, 2009, the Court issued an order naming the Inter-Local Pension Fund GCC/IBT as lead plaintiff and Robbins Geller Rudman & Dowd LLP (formerly Coughlin Stoia) as lead counsel. The lead plaintiff filed a consolidated complaint on July 24, 2009. We filed a motion to dismiss on September 8, 2009. On December 21, 2009, the Court granted our motion and dismissed the consolidated complaint with leave to amend. Plaintiff filed its consolidated amended complaint on January 27, 2010. The lawsuit alleged violations of the Securities Act and the Exchange Act in connection with allegedly false and misleading statements made by us related to the results of the Phase 2a clinical trial of our product candidate fostamatinib (then known as R788). The plaintiff sought damages, including rescission or rescissory damages for purchasers in the Stock Offering, an award of their costs and injunctive and/or equitable relief for purchasers of our common stock during the period between December 13, 2007 and February 9, 2009, including purchasers in the Stock Offering. We filed a motion to dismiss the consolidated amended complaint on February 16, 2010. On August 24, 2010, the Court issued an order granting our motion and dismissed the consolidated complaint with leave to amend. On September 22, 2010, plaintiff filed a notice informing the Court that it will not amend its complaint and requested that the Court enter a final judgment. On October 28, 2010, the plaintiff submitted a proposed judgment requesting entry of such judgment in favor of the defendants. On November 1, 2010, judgment was entered dismissing the action. The plaintiff filed a notice of appeal on November 15, 2010 to the Ninth Circuit Court of Appeals, or the Circuit Court, appealing the district court's order granting our motion to dismiss the consolidated amended complaint. The plaintiff filed its opening brief on February 23, 2011. We filed our opposition brief on April 8, 2011. On May 9, 2011, the plaintiff filed its reply brief. On February 17, 2012, the Circuit Court heard oral arguments on plaintiff's appeal. On September 6, 2012, the Ninth Circuit affirmed the district court's dismissal of the complaint. On September 27, 2012, the plaintiff filed a petition for rehearing and rehearing en banc.

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We believe that we have meritorious defenses and intend to defend the lawsuit vigorously. This lawsuit and any other related lawsuits are subject to inherent uncertainties, and the actual costs to be incurred relating to the lawsuit will depend upon many unknown factors. The outcome of the litigation is necessarily uncertain, and we could be forced to expend significant resources in the defense of this suit, and we may not prevail. Monitoring and defending against legal actions is time-consuming for our management and detracts from our ability to fully focus our internal resources on our business activities. In addition, we may incur substantial legal fees and costs in connection with the litigation. We are not currently able to estimate the possible cost to us from this matter, and we cannot be certain how long it may take to resolve this matter or the possible amount of any damages that we may be required to pay. We have not established any reserves for any potential liability relating to this lawsuit. It is possible that we could, in the future, incur judgments or enter into settlements of claims for monetary damages. A decision adverse to our interests on this action could result in the payment of substantial damages, or possibly fines, and could have a material adverse effect on our cash flow, results of operations and financial position. In addition, the uncertainty of the currently pending litigation could lead to increased volatility in our stock price.

We lack the capability to manufacture compounds for development and rely on third parties to manufacture our product candidates, and we may be unable to obtain required material in a timely manner, at an acceptable cost or at a quality level required to receive regulatory approval.

We currently do not have the manufacturing capabilities or experience necessary to produce our product candidates for clinical trials, including R343 for our asthma program, R333 for DLE and R548 for transplant rejection. For each clinical trial of our unpartnered product candidates, we rely on third-party manufacturers for the active pharmaceutical ingredients, as well as various manufacturers to manufacture starting components, excipients and formulated drug products. We rely on manufacturers to produce and deliver all of the materials required for our clinical trials, and many of our preclinical efforts, on a timely basis and to comply with applicable regulatory requirements, including the FDA's current Good Manufacturing Practices (cGMP). In addition, we rely on our suppliers to deliver sufficient quantities of materials produced under cGMP conditions to enable us to conduct planned preclinical studies and clinical trials.

Our current and anticipated future dependence upon these third-party manufacturers may adversely affect our ability to develop and commercialize product candidates on a timely and competitive basis. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements and may also experience a shortage in qualified personnel. We may not be able to maintain or renew our existing third-party manufacturing arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third party manufacturers could terminate or decline to renew our manufacturing arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our planned clinical trials may be significantly delayed. Manufacturing delays could postpone the filing of our IND applications and/or the initiation or completion of clinical trials that we have currently planned or may plan in the future.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration, and other federal and state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards and they may not be able to comply. Switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly on acceptable terms, or at all. Additionally, if we are required to enter into new supply arrangements, we may not be able to obtain approval from the FDA of any alternate supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of any related product candidates. Failure of our

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third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, civil penalties, delays in or failure to grant marketing approval of our product candidates, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

If our competitors develop technologies that are more effective than ours, our commercial opportunity will be reduced or eliminated.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Many of the drugs that we are attempting to discover will be competing with existing therapies. In addition, a number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. For example, there are existing therapies and drug candidates in development for the treatment of RA that may be alternative therapies to fostamatinib, if it is ultimately approved for commercialization. Although fostamatinib has a novel mechanism of action for the treatment of RA, our partners may experience difficulties in convincing patients and healthcare providers to use fostamatinib, if approved, over other available treatments for RA. We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as from academic and research institutions and government agencies, both in the United States and abroad. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions as our research programs. Our major competitors include fully integrated pharmaceutical companies that have extensive drug discovery efforts and are developing novel small-molecule pharmaceuticals. We also face significant competition from organizations that are pursuing the same or similar technologies, including the discovery of targets that are useful in compound screening, as the technologies used by us in our drug discovery efforts.

Competition may also arise from:

- new or better methods of target identification or validation;
- other drug development technologies and methods of preventing or reducing the incidence of disease;
- new small molecules; or
- other classes of therapeutic agents.

Our competitors or their collaborative partners may utilize discovery technologies and techniques or partner with collaborators in order to develop products more rapidly or successfully than we or our collaborators are able to do. Many of our competitors, particularly large pharmaceutical companies, have substantially greater financial, technical and human resources and larger research and development staffs than we do. In addition, academic institutions, government agencies and other public and private organizations conducting research may