RIGEL PHARMACEUTICALS INC
Form 10-K
March 04, 2014

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

ý **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2013

or

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 0-29889

RIGEL PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3248524**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
1180 Veterans Blvd. South San Francisco, California	**94080**
(Address of principal executive offices)	(Zip Code)

(650) 624-1100
(Registrant's telephone number, including area code)

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

Title of each class:	**Name of each exchange on which registered:**
Common Stock, par value $.001 per share	The Nasdaq Global Market

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

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

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

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

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

The approximate aggregate market value of the Common Stock held by non-affiliates of the registrant, based upon the closing price of the registrant's Common Stock as reported on the Nasdaq Global Market on June 28, 2013, the last business day of the registrant's most recently completed second fiscal quarter, was $290,854,625. Shares of the registrant's outstanding Common Stock held by each executive officer, director and affiliates of the registrant's outstanding Common Stock have been excluded. The determination of affiliate status for the purposes of this calculation is not necessarily a conclusive determination for other purposes.

As of February 26, 2014, there were 87,524,349 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K incorporate information by reference from the definitive proxy statement for the registrant's 2014 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains statements indicating expectations about future performance and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act), and the Private Securities Litigation Reform Act of 1995, that involve risks and uncertainties. We usually use words such as "may," "will," "should," "could," "expect," "plan," ""anticipate," "might," "believe," "estimate," "predict," "intend" or the negative of these terms or similar expressions to identify these forward-looking statements. These statements appear throughout this Annual Report on Form 10-K and are statements regarding our current intent, belief or expectation, primarily with respect to our operations and related industry developments. Examples of these statements include, but are not limited to, statements regarding the following: our business and scientific strategies; the progress of our product development programs, including clinical testing, and the timing of commencement and results thereof; our corporate collaborations, and revenues that may be received from collaborations and the timing of those potential payments; our drug discovery technologies; our research and development expenses; protection of our intellectual property; and sufficiency of our cash resources and need for additional capital. You should not place undue reliance on these forward-looking statements. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including as a result of the risks and uncertainties discussed under the heading "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. A forward- looking statement speaks only as of the date on which it is made, and, except as required by law, we undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the 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.

PART I

Item 1. Business

Overview

Rigel Pharmaceuticals, Inc. was incorporated in Delaware in June 1996, and is based in South San Francisco, California. 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. We currently have five product candidates in development: fostamatinib, an oral spleen tyrosine kinase (SYK) inhibitor expected to enter Phase 3 clinical trials for immune thrombocytopenic purpura (ITP) and a Phase 2 clinical trial for immunoglobulin A nephropathy (IgAN) in the first half of 2014; R348, a topical JAK/SYK inhibitor currently in Phase 2 clinical trials for dry eye; R118, an adenosine monophosphate (AMP)-activated protein kinase (AMPK) activator entering Phase 1 in the first half of 2014; and two oncology product candidates in Phase 1 development with partners BerGenBio AS (BerGenBio) and Daiichi Sankyo (Daiichi), respectively.

Since the beginning of 2013, we have experienced the following business events:

In January 2014, we announced that we earned a payment of $5.8 million from AstraZeneca AB (AZ) resulting from AZ's continued development of R256 in asthma during December 2013.

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In October 2013, our representatives met with the U.S. Food and Drug Administration (FDA) for an end-of-Phase 2 meeting for fostamatinib, an oral SYK inhibitor in development for patients with ITP. We expect to enter a pivotal Phase 3 clinical study in the first half of 2014.

In October 2013, we announced that R333, which was being evaluated as a potential therapeutic for active skin lesions in patients with discoid lupus erythematosus (DLE), did not meet the primary endpoint in the completed Phase 2 clinical study. In light of the overall findings, we have decided not to pursue this indication further with R333.

In September 2013, we announced that we reduced our workforce by 18%, resulting in the elimination of 30 positions, mostly from the drug discovery area as a consequence of prioritizing projects and efforts to conserve our cash resources.

In August 2013, we announced that R343, an inhaled SYK inhibitor being evaluated as a potential therapeutic for patients with allergic asthma, did not meet the primary or secondary endpoints in the completed Phase 2 clinical study. In light of the overall findings, we have decided not to pursue this indication further with R343.

In July 2013, we initiated a Phase 2 study, called DROPS (Dry Eye Rigel Ophthalmic Phase 2 Study). This multi-center, randomized, double-masked study evaluates two doses of R348 versus placebo administered twice a day over a three-month period in approximately 210 patients with dry eye disease. Results of this Phase 2 study are expected in the second half of 2014.

In April 2013, AZ announced top-line results of OSKIRA-1, a Phase 3 study to assess the efficacy and safety of fostamatinib, the first oral SYK inhibitor in development for rheumatoid arthritis (RA). In June 2013, AZ announced the topline results from OSKIRA-2 and OSKIRA-3, two pivotal Phase 3 clinical trials in patients with RA. Based on the totality of the results of the OSKIRA Phase 3 program in patients with RA, in June 2013, AZ informed us that it would not proceed with regulatory filings and, instead would return the rights to the compound to us. In September 2013, we announced that we would not continue further development of fostamatinib for the treatment of RA or lymphoma due to insufficient efficacy findings from recent clinical trials and the competitive landscape in those indications.

Strategy

Our research team is focused on creating a portfolio of product candidates that may be developed as small-molecule therapeutics for our own proprietary programs or for development by potential collaborative partners. We recognize that the product development process is subject to both high costs and a high risk of failure. We believe that identifying a variety of product candidates and working in conjunction with other pharmaceutical partners may minimize the risk of failure, fill the product pipeline gap at major pharmaceutical companies, and ultimately increase the likelihood of advancing clinical development and potential commercialization of the product candidates.

The key elements to our business and scientific strategy are to:

develop a diverse portfolio of drug candidates that address a variety of therapeutic indications or that represent significant market opportunities;

utilize our robust discovery engine to rapidly discover and validate new product candidates in a broad range of therapeutic indications;

develop drug candidates through at least the proof of concept stage and establish strategic collaborations with pharmaceutical and biotechnology companies to further develop and market our product candidates; and

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develop and commercialize selected drug candidates on our own in markets where we believe a company our size can successfully compete.

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.

Pipeline	Current Stage	Status
Fostamatinib Oral SYK Inhibitor		
Immune Thrombocytopenic Purpura (ITP)	Phase 3	In October 2013, our representatives met with the FDA for an end-of-Phase 2 meeting for fostamatinib in development for patients with ITP. We expect to initiate a Phase 3 clinical program with two pivotal studies, one commencing in the first half of 2014 and one commencing in the third quarter of 2014, with top-line data for both studies expected by the second half of 2015.
IgA Nephropathy (IgAN)	Phase 2	We expect to initiate a Phase 2 clinical study to investigate fostamatinib for the treatment of IgAN in the summer of 2014.
R348 Topical Ophthalmic JAK/SYK Inhibitor		
Keratoconjunctivitis Sicca	Phase 2	In July 2013, we initiated a Phase 2 clinical study to investigate R348 for the treatment of keratoconjunctivitis sicca or chronic dry eye. Results of this Phase 2 study are expected in the second half of 2014.
Dry Eye in Patients with Ocular Graft-Versus-Host Disease	Phase 2	We expect to initiate a Phase 2 clinical study to investigate R348 for the treatment of dry eye in patients with ocular graft-versus-host disease (GvHD) in the second quarter of 2014.
R118 AMPK Activator		
Intermittent Claudication (IC)	Phase 1	We plan to initiate a Phase 1clinical trial of R118 in patients with IC in the first half of 2014.

Clinical Stage Programs

Fostamatinib Immune Thrombocytopenic Purpura

Disease background. Chronic ITP affects approximately 100,000 people, with the majority of these cases being in women. ITP is a blood disorder in which the immune system attacks and destroys the body's own blood platelets, which have an important role in the clotting and healing process. ITP

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patients can suffer bruising, bleeding and fatigue as a result of their low blood platelet counts. Currently marketed therapies aim to raise blood platelet counts, but do not address the underlying cause of the disorder.

Orally-available SYK inhibitor program. Platelet destruction from ITP is mediated by immunoglobulin G (IgG) signaling, and fostamatinib is a potent inhibitor of IgG signaling. The results of our Phase 2 study of fostamatinib to evaluate its safety and initial efficacy in chronic ITP patients, published in *Blood (2009, volume 113, number 14)*, showed that fostamatinib may be effective in treating this rare autoimmune disorder. In this clinical trial, fostamatinib was orally administered in varying doses for 30 or more days and demonstrated that it can improve platelet counts in highly refractory patients.

In October 2013, we met with the FDA for an end-of-Phase 2 meeting for fostamatinib in ITP. We expect to initiate a Phase 3 clinical program with two pivotal studies, one commencing in the first half of 2014 and one commencing in the third quarter of 2014. Each of these trials is expected to enroll approximately 75 patients who would be treated for six months and have the option to enroll in an extension study. These trials will be randomized, placebo-controlled and will enroll verified ITP patients with platelet counts below 30,000 platelets per microliter of blood. The goal of the trials will be to achieve a durable platelet count increase to over 50,000 platelets per microliter of blood. We expect top-line data from these studies in the second half of 2015.

Fostamatinib IgA Nephropathy

Disease background. IgAN is an autoimmune disease that severely affects the functioning of the kidneys. An estimated 12,000 Americans are diagnosed with this type of glomerulonephritis each year, with 25% of its victims eventually requiring dialysis and/or kidney transplantation over time. IgAN is characterized by the deposition of IgA immune complexes in the glomeruli of the kidneys leading to an inflammatory response and subsequent tissue damage that ultimately disrupts the normal filtering function of the kidneys. By inhibiting SYK in kidney cells, fostamatinib may block the signaling of IgA immune complex receptors and arrest or slow destruction of the glomeruli. We expect to enter a Phase 2 study of fostamatinib in patients with IgAN in the summer of 2014.

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.

In September 2013, we announced that we would not continue further development of fostamatinib for the treatment of RA or lymphoma due to insufficient efficacy findings from recent clinical trials and the competitive landscape in those indications.

OSKIRA

The OSKIRA (Oral SYK Inhibition in Rheumatoid Arthritis) program was designed to investigate fostamatinib as a potential new oral treatment option for RA and an alternative to injectable therapies for patients with an inadequate response to conventional disease modifying anti-rheumatic drugs (DMARDs). OSKIRA-1 was a 12-month study with approximately 900 patients, examining the effect of fostamatinib compared with placebo over a 24 week period, in patients responding inadequately to MTX. OSKIRA-1 had co-primary endpoints of American College of Rheumatology (ACR)20 scores and mTSS (x-ray endpoint assessing structural progression) at 24 weeks. OSKIRA-2 was a 12-month study with approximately 900 patients, examining the effect of fostamatinib compared with placebo over a 24 week period, in patients responding inadequately to DMARDs. OSKIRA-2 had a primary

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endpoint of ACR20 at 24 weeks. OSKIRA-3 was a six-month study of approximately 320 patients assessing the effect of fostamatinib compared with placebo in patients responding inadequately to TNF-α antagonist therapy. The primary endpoint of OSKIRA-3 was ACR20 at 24 weeks.

In June 2013, AZ announced the topline results from OSKIRA-2 and OSKIRA-3, two pivotal Phase 3 clinical trials investigating fostamatinib, the first oral SYK inhibitor in development for RA. In the OSKIRA-2 study of patients inadequately responding to DMARDs, fostamatinib in combination with DMARDs showed statistically significant improvements in ACR20 response rates at 24 weeks compared to placebo. In the OSKIRA-3 study of patients inadequately responding to MTX and a single TNF-alpha antagonist, fostamatinib in combination with MTX showed statistically significant improvements in ACR20 response rates at 24 weeks in the 100mg twice daily group but not in the group given 100mg twice daily for four weeks followed by 150mg once daily compared to placebo. The safety and tolerability findings for fostamatinib observed in the OSKIRA Phase 3 program were generally consistent with those previously reported in earlier studies. The most commonly reported adverse events in the OSKIRA program include hypertension, diarrhea, nausea, headache and nasopharyngitis (common cold).

Based on the totality of the results of the OSKIRA Phase 3 program in patients with RA, in June 2013, AZ informed us that it would not proceed with regulatory filings and, instead would return the rights to the compound to us. AZ was solely responsible for all costs and expenses incurred by both parties in connection with the transfer of responsibilities up to the effective termination of the agreement on December 4, 2013.

In April 2013, AZ announced top-line results of OSKIRA-1, a Phase 3 study to assess the efficacy and safety of fostamatinib. OSKIRA-1 had two primary endpoints: assessing signs and symptoms of RA as measured by ACR20 response rates, and an X-ray endpoint known as mTSS (modified Total Sharp Score). In the OSKIRA-1 study, fostamatinib achieved a statistically significant improvement in ACR 20 response rate at 24 weeks compared to placebo. Fostamatinib did not demonstrate a statistically significant difference in mTSS compared to placebo at 24 weeks. The safety and tolerability findings for fostamatinib observed in the OSKIRA-1 study were generally consistent with those previously reported for the *TASKi* Phase 2 program. The most commonly reported adverse events were typical of those seen in earlier studies, including hypertension, diarrhea, nausea, headache and nasopharyngitis (common cold).

Fostamatinib Other Indications

In addition to RA, fostamatinib had been studied in patients with other immune disorders and some cancers. AZ commenced Phase 2 clinical trials to investigate the effect of fostamatinib on hematological malignancies in the first quarter of 2012. The randomized double-blind Phase 2 clinical trial was designed to evaluate the effectiveness of two doses of fostamatinib (100mg twice daily and 200mg twice daily) in patients with worsening or unmanageable diffuse large B-cell lymphoma. As discussed above, we have decided not to continue further development of fostamatinib for the treatment of lymphoma.

R348 Keratoconjunctivitis Sicca

Disease background. Chronic dry eye, or keratoconjunctivitis sicca, is an inflammatory disease that often affects the lacrimal (tear producing) glands of the eye. Over five million Americans suffer with this disorder, and many patients with chronic dry eye may also suffer with autoimmune conditions, including systemic lupus erythematosus and rheumatoid arthritis. Chronic dry eye is an irritating and painful disease that may be destructive to the cornea if not well controlled.

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Topical Ophthalmic JAK/SYK inhibitor program. Since both JAK and SYK are important components in the body's immune and inflammatory responses, R348's combined JAK/SYK inhibition is expected to offer relief directly to the eye. A recently completed Phase 1 study of R348 in patients with dry eye disease showed that the drug candidate is well tolerated. In July 2013, we initiated a Phase 2 study, called DROPS. This multi-center, randomized, double-masked study, evaluates two doses of R348 versus placebo administered twice a day over a three-month period in approximately 210 patients with dry eye disease. The efficacy endpoints will include change from baseline in corneal staining, tear production and dry eye symptom scores. Results of this Phase 2 study are expected in the second half of 2014.

R348 Dry Eye in Patients with Ocular Graft-Versus-Host Disease

Disease background. According to an article published by the American Academy of Ophthalmology, a significant number (22% to 80%) of patients with acute or chronic GvHD develop a secondary incidence of dry eye (keratoconjunctivitis sicca). In general, these patients are severely ill and have a great medical need for a topical therapy that may better manage their symptoms.

Topical Ophthalmic JAK/SYK inhibitor program. We expect to initiate a Phase 2 study of R348 in patients with dry eye as a result of primary GvHD in the second quarter of 2014.

R118 Intermittent Claudication

Disease background. Intermittent claudication (IC) refers to the muscle pain associated with peripheral artery disease (PAD) caused by either atherosclerosis or inflammation. Patients with IC have difficulty with simple activities, like walking, and current therapies do not provide sufficient relief. IC affects more than 5% of the population age 65 or older, but anyone with PAD may also suffer the effects of IC.

AMPK activator program. Preclinical evaluation of R118, an AMPK activator, has shown it to be a central regulator of lipid and metabolic activity and capable of increasing muscle endurance. We plan to initiate a Phase 1 trial of R118 in patients with IC in the first half of 2014.

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 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.

SITAR. In August 2013, we announced that R343, an inhaled SYK inhibitor being evaluated as a potential therapeutic for patients with allergic asthma, did not meet the primary or secondary endpoints in a recently completed Phase 2 clinical study. The primary endpoint was the change in pre-bronchodilator FEV1 (a measure of lung function) from baseline to dosing completion at Week 8, comparing active doses to placebo. R343 was shown to be relatively safe and well tolerated at both doses. The Phase 2 clinical study, called SITAR (SYK Inhibition for Treatment of Asthma with R343),

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was 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 was being delivered directly into the lungs via a dry powder inhalation device. In light of these overall findings, we have decided not to move forward with R343.

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 hair loss. The lesions most 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 Dermatological JAK/SYK inhibitor program. R333 is a topical dermatological JAK/SYK inhibitor, which may be useful in treating both the acute and chronic phases of DLE. We completed the Phase 1 clinical study of its topical agent to test its application in treating acute and chronic phases of DLE in the first half of 2012.

SKINDLE. In October 2013, we announced that R333, which was being evaluated as a potential therapeutic for active skin lesions in patients with DLE in a Phase 2 clinical study, called SKINDLE (SYK Kinase Inhibition for DLE), did not meet the primary endpoint in a recently completed Phase 2 clinical study. The primary endpoint was the proportion of patients who achieved at least a 50% decrease from baseline in the total combined Erythema and Scaling score of all treated lesions at Week 4. R333 was shown to be relatively safe and well tolerated. In light of these overall findings, we have decided not to pursue this indication further with R333.

Research/Preclinical Program

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.

We have active small molecule discovery programs 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.

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 (COPD), or diabetes, often experience a decrease in strength and increase in fatigue due to muscle myopathy.

Corporate Collaborations

We conduct research and development programs independently and in connection with our corporate collaborators. We currently do not have significant active collaborations.

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AstraZeneca

Fostamatinib

In February 2010, we entered into an exclusive worldwide license agreement with AZ for the 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 included a license of rights to fostamatinib, our late-stage investigational product candidate for the treatment of RA and other indications. AZ was responsible for conducting and funding all future development, regulatory filings, manufacturing and global commercialization of products containing most of our oral SYK inhibitors. The agreement became effective on March 26, 2010, and we received an upfront payment from AZ of $100.0 million in April 2010. In September 2010, we earned $25.0 million from AZ for completing the transfer of the fostamatinib long-term open label extension study to AZ and for their initiation of Phase 3 clinical trials in the fostamatinib program by AZ. Under the agreement, our deliverables were: (i) granting a license of rights to fostamatinib, (ii) transfer of technology (know-how) related to fostamatinib, and (iii) conducting, at our expense, the fostamatinib open label extension study until it was transferred to AZ on September 25, 2010. We concluded that these deliverables should be accounted for as one single unit of accounting, and we recognized the $100.0 million upfront payment received in April 2010 from AZ ratably over the performance period from March 26, 2010, the effective date of the agreement, through September 25, 2010, the completion date of the last deliverable, which was the transfer of the fostamatinib long-term open label extension study to AZ. We elected a straight-line method for recognition of this upfront payment as the effort to advance and transfer the study was consistent over the short transition period.

In June 2013, based on the totality of the results of the OSKIRA Phase 3 program in patients with RA, AZ informed us that it would not proceed with regulatory filings and, instead would return the rights to the compound to us. AZ was solely responsible for all costs and expenses incurred by both parties in connection with the transfer of responsibilities up to the effective termination of the agreement on December 4, 2013.

In September 2013, we announced that we would not continue further development of fostamatinib for the treatment of RA or lymphoma due to insufficient efficacy findings from recent clinical trials and the competitive landscape in those indications.

Other Agreements

We have several active collaborations with additional partners. Under these collaborations, which we enter into in the ordinary course of business, we received or may be entitled to receive upfront cash payments, progress dependent contingent payments on events achieved by such partners and royalties on any net sales of products sold by such partners under the agreements. Total future contingent payments to us under all of these current collaborations could exceed $152.3 million if all potential product candidates achieved all of the payment triggering events under all of our current collaborations (based on a single product candidate under each agreement). Of this amount, up to $61.2 million relates to the achievement of development events, up to $53.6 million relates to the achievement of regulatory events and up to $37.5 million relates to the achievement of certain commercial or launch events. This estimated future contingent amount does not include any estimated royalties that could be due to us if the partners successfully commercialize the licensed products.

Since we do not control the research, development or commercialization of the product candidates generated under these collaborations, we are not able to reasonably estimate when, if at all, any contingent payments would become payable to us. As such, the contingent payments we could receive thereunder involve a substantial degree of risk to achieve and may never be received. Accordingly, we do not expect, and investors should not assume, that we will receive all of the potential contingent

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payments provided for under these collaborations and it is possible that we may never receive any additional significant contingent payments or royalties under these collaborations.

In June 2012, we entered into an exclusive worldwide license agreement with AZ for the development and commercialization of our program, R256, an inhaled janus kinase (JAK) inhibitor shown to inhibit interleukin (IL)-13 and IL-4 signaling, which is being investigated as a treatment for moderate to severe chronic asthma. AZ is responsible for beginning the first-in-human clinical studies for R256, and for designing and conducting the clinical development of the compound. AZ also has exclusive rights to commercialize R256 around the world. AZ paid us an upfront payment of $1.0 million in July 2012. Under the agreement, we were obligated to provide the following deliverables: (i) granting a license of rights to our program, and (ii) delivery of a small batch of compound to AZ. We concluded that these deliverables should be accounted for as separate units of accounting. As our obligations with respect to the deliverables were achieved by June 30, 2012, we recognized revenue of $1.0 million in the second quarter of 2012. On December 31, 2013, we earned revenue associated with the time-based non-refundable payment of $5.8 million from AZ in consideration for AZ's decision to continue its development of R256 in asthma.

In June 2011, we entered into an exclusive license agreement with BerGenBio for the development and commercialization of an oncology program, which is currently in Phase 1 development. BerGenBio is responsible for all activities it wishes to perform under the license we granted to it. In July 2012, we received a time-based payment of $500,000 from BerGenBio due to us on June 29, 2012, pursuant to the terms of the agreement. We recognized the payment as revenue in the second quarter of 2012.

In August 2002, we entered into a collaboration agreement with Daiichi to pursue research related to a specific target from a novel class of drug targets called ligases that control cancer cell proliferation through protein degradation. In April 2013, we received a $1.4 million payment from Daiichi related to Daiichi's filing of an IND for an oncology compound, which is currently in Phase 1 development. In January 2012, we received a $750,000 payment from Daiichi. To date, we have earned payments under this arrangement totaling $7.9 million and may earn additional payments in connection with the achievement by Daiichi of certain clinical events. The research phase of this three-year collaboration expired in August 2005. Under the terms of the collaboration agreement, we retain the rights to co-develop and co-promote certain products resulting from this collaboration in North America, while Daiichi retains co-development and promotion rights in the remainder of the world. Future events that may trigger payments to us under the Daiichi agreement are based solely on Daiichi's future efforts and achievements of specified events.

Our Discovery Engine

The approaches that we use in connection with both our proprietary product development programs and our corporate collaborations are designed to identify protein targets for compound screening and validate the role of those targets in the disease process. Unlike genomics-based approaches, which begin by identifying genes and then searching for their functions, our approach identifies proteins that are demonstrated to have an important role in a specific disease pathway. By understanding the disease pathway, we attempt to avoid studying genes that will not make good drug targets and focus only on the subset of expressed proteins of genes that we believe are specifically implicated in the disease process.

We begin by developing assays that model the key events in a disease process at the cellular level. We then identify potential protein targets. In addition, we identify the proteins involved in the intracellular process and prepare a map of their interactions, thus giving us a comprehensive picture of the intracellular disease pathway. We believe that our approach has a number of advantages, including:

improved target identification: it focuses only on the subset of expressed proteins of genes believed to be specifically implicated in the disease process;

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rapid validation of protein targets: it produces validated protein targets quickly because it uses key events in the disease process as the basis to design the functional, disease-based screen;

improved disease pathway mapping: it produces a comprehensive map of the intracellular disease pathway, enabling the identification of a large number of potential protein targets;

informed target selection: it provides a variety of different types of targets and information concerning the role each plays in their endogenous state to better select targets more susceptible to pharmaceutical intervention;

efficient compound screening: it increases the probability and speed with which compound screening will identify "hits" because it provides detailed knowledge of the target that can be used to guide the design of the compound screen; and

risk reduction: it may reduce the risk of failure in the product development process due to serious side effects, including toxicity or other reasons, by selecting only targets that are specific to the disease in question and that have no apparent role in other cell types or signaling pathways.

Because of the very large numbers of screens employed, our technology is labor intensive. The complexity of our technology requires a high degree of skill and diligence to perform successfully. We believe we have been and will continue to be able to meet these challenges successfully and increase our ability to identify targets for drug discovery. Although other companies may utilize technologies similar to certain aspects of our technology, we are unaware of any other company that employs the same combination of technologies that we do.

Pharmacology and Preclinical Development

We believe that the rapid characterization and optimization of compounds identified in high-throughput screening (HTS) will generate high quality preclinical development candidates. Our pharmacology and preclinical development group facilitates lead optimization by characterizing lead compounds with respect to pharmacokinetics, potency, efficacy and selectivity. The generation of proof-of-principle data in animals and the establishment of standard pharmacological models with which to assess lead compounds represent integral components of lead optimization. As programs move through the lead optimization stage, our pharmacology and preclinical development groups support our chemists and biologists by performing the necessary studies, including toxicology, for investigational new drug (IND) application submissions.

Clinical Development

We have assembled a team of experts in drug development to design and implement clinical trials and to analyze the data derived from these trials. The clinical development group possesses expertise in project management and regulatory affairs. We work with external clinical research organizations with expertise in managing clinical trials, drug formulation, and the manufacture of clinical trial supplies to support our drug development efforts.

Intellectual Property

We are able to protect our technology from unauthorized use by third parties only to the extent that it is covered by valid and enforceable patents or is effectively maintained as a trade secret. Accordingly, patents and other proprietary rights are an essential element of our business. We have about 83 pending patent applications and over 260 issued and active patents in the United States, as well as corresponding pending foreign patent applications and issued foreign patents. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek U.S. and international patent

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protection for a variety of technologies, including new screening methodologies and other research tools, target molecules that are associated with disease states identified in our screens, and lead compounds that can affect disease pathways. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel drugs. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various license agreements that give us rights to use technologies in our research and development.

Our patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. Our material patents relate to compositions of matter covering specific drug candidates in clinical trials that target SYK. These patents will expire, excluding patent term extensions, in 2023, 2024 and 2026. Several of these patents will have patent term extensions, depending on the length of time required to conduct clinical trials.

We currently hold a number of issued patents in the United States, as well as corresponding applications that allow us to pursue patents in other countries, some of which have been allowed and/or granted and others of which we expect to be granted. Specifically, in most cases where we hold a U.S. issued patent, the subject matter is covered at least by an application filed under the Patent Cooperation Treaty (PCT), which is then used or has been used to pursue protection in certain countries that are members of the treaty. Our material patents relate to fostamatinib, an oral SYK inhibitor, and R406, the active metabolite of fostamatinib.

Fostamatinib. Fostamatinib is covered as a composition of matter in a U.S. issued patent that has an expiration date in September 2026, after taking into account a patent term adjustment, and may be granted further protection under the patent term extension rules related to conducting clinical trials. Fostamatinib is also covered under broader composition of matter claims in a U.S. issued patent that has an expiration date in March 2026, after taking into account a patent term adjustment. Methods of using fostamatinib to treat various indications, methods of making fostamatinib, and compositions of matter covering certain intermediates used to make fostamatinib are also covered, respectively, in three U.S. issued patents; the earliest expiration date of any of these patents is in April 2023 and the latest expiration date is in June 2026, after taking into account patent term adjustments. Corresponding applications have been filed in foreign jurisdictions under the PCT, and are at various stages of prosecution. Of note, a patent covering fostamatinib as a composition of matter and in compositions for use treating various diseases has been granted by the European Patent Office.

R406. R406 is covered as a composition of matter in a U.S. issued patent and, with a patent term adjustment, has an expiration date in February 2025. R406 is also covered under two broader composition of matter patents issued in the U.S. expiring in February 2023 and July 2024. Methods of using R406 to treat various indications and compositions of matter covering certain intermediates used to make R406 are also covered under patents described above. Corresponding applications have been filed in foreign jurisdictions under the PCT and are at various stages of prosecution.

Competition

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 ITP that may be alternative therapies to fostamatinib, if it is ultimately approved for commercialization. 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

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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 seek patent protection with respect to potentially competitive products or technologies and may establish exclusive collaborative or licensing relationships with our competitors.

We believe that our ability to compete is dependent, in part, upon our ability to create, maintain and license scientifically advanced technology and upon our and our collaborators' ability to develop and commercialize pharmaceutical products based on this technology, as well as our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary technology or processes and secure sufficient capital resources for the expected substantial time period between technological conception and commercial sales of products based upon our technology. The failure by any of our collaborators or us in any of those areas may prevent the successful commercialization of our potential drug targets.

Many of our competitors, either alone or together with their collaborative partners, have significantly greater experience than we do in:

- identifying and validating targets;
- screening compounds against targets; and
- undertaking preclinical testing and clinical trials.

Accordingly, our competitors may succeed in obtaining patent protection, identifying or validating new targets or discovering new drug compounds before we do.

Our competitors might develop technologies and drugs that are more effective or less costly than any that are being developed by us or that would render our technology and product candidates obsolete and noncompetitive. In addition, our competitors may succeed in obtaining the approval of the FDA or other regulatory agencies for product candidates more rapidly. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before us may achieve a significant competitive advantage, including certain patent and FDA marketing exclusivity rights that would delay or prevent our ability to market certain products. Any drugs resulting from our research and development efforts, or from our joint efforts with our existing

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or future collaborative partners, might not be able to compete successfully with competitors' existing or future products or obtain regulatory approval in the United States or elsewhere.

We face and will continue to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions and for licenses to additional technologies. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- identify and validate targets;
- discover candidate drug compounds that interact with the targets we identify;
- attract and retain scientific and product development personnel;
- obtain patent or other proprietary protection for our new drug compounds and technologies; and
- enter commercialization agreements for our new drug compounds.

Research and Development Expenses

A significant portion of our operating expenses is related to research and development and we intend to maintain our strong commitment to research and development. See "Item 8. Financial Statements and Supplementary Data" of this Annual Report on Form 10-K for costs and expenses related to research and development, and other financial information for each of the fiscal years 2013, 2012 and 2011.

Government Regulation

Our ongoing development activities are and will continue to be subject to extensive regulation by numerous governmental authorities in the United States and other countries, including the FDA under the Federal Food, Drug and Cosmetic Act. The regulatory review and approval process is expensive and uncertain. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each indication to establish a product candidate's safety and efficacy.

Preclinical studies generally are conducted in laboratory animals to evaluate the potential safety and the efficacy of a product. Drug developers submit the results of preclinical studies to the FDA as part of an IND application that must be approved before clinical trials can begin in humans. Typically, clinical evaluation involves a time consuming and costly three-phase process.

- Phase 1 Clinical trials are conducted with a small number of patients to determine the early safety profile, maximum tolerated dose and pharmacological properties of the product in human volunteers.
- Phase 2 Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.
- Phase 3 Large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product candidate for a specific disease.

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The approval process takes many years, requires the expenditure of substantial resources and may involve ongoing requirements for post-marketing studies. Clinical trials are subject to oversight by institutional review boards and the FDA. In addition, clinical trials:

- 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 oversight;
- may require large numbers of participants; 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.

Even if we are able to achieve success in our clinical testing, we, or our collaborative partners, must provide the FDA and foreign regulatory authorities with clinical data that demonstrates the safety and efficacy of our products in humans before they can be approved for commercial sale. We do not know whether any future clinical trials will demonstrate sufficient safety and efficacy necessary to obtain the requisite regulatory approvals or will result in marketable products. Our failure, or the failure of our strategic partners, to adequately demonstrate the safety and efficacy of our products under development will prevent receipt of FDA and similar foreign regulatory approval and, ultimately, commercialization of our products.

Any clinical trial may fail to produce results satisfactory to the FDA. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. Negative or inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be repeated or a program to be terminated. In addition, delays or rejections may be encountered based upon additional government regulation from future legislation or administrative action or changes in FDA policy or interpretation 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, as well as other regulatory action against our potential products, collaborative partners or us.

Outside the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the E.U., registration procedures are available to companies wishing to market a product in more than one E.U. member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization will be granted. This foreign regulatory approval process involves all of the risks associated with FDA clearance.

Manufacturing and Raw Materials

We currently rely on, and will continue to rely on, third party contract manufacturers to produce sufficient quantities of our product candidates for use in our preclinical and clinical trials.

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Employees

As of December 31, 2013, we had 129 employees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. Recruiting and retaining qualified scientific personnel to perform research and development work in the future will be critical to our success. We may not be able to attract and retain personnel on acceptable terms given the competition among pharmaceutical and biotechnology companies, academic and research institutions and government agencies for experienced scientists.

In September 2013, we announced that we reduced our workforce by 18%, which resulted in the elimination of 30 positions, mostly from the drug discovery area as a consequence of prioritizing projects and efforts to conserve our cash resources.

Scientific and Medical Advisors

We utilize scientists and physicians to advise us on scientific and medical matters as part of our ongoing research and product development efforts, including experts in clinical trial design, preclinical development work, chemistry, biology, infectious diseases, immunology, muscle wasting and metabolism, general metabolism and oncology. Certain of our scientific and medical advisors and consultants receive non-employee options to purchase our common stock and an honorarium for time spent assisting us.

Available Information

Our website is located at *www.rigel.com*. The information found on our website is not part of or incorporated by reference into this Annual Report on Form 10-K. We electronically file with the Securities and Exchange Commission (SEC) our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to the reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make available free of charge on or through our website copies of these reports as soon as reasonably practicable after we electronically file these reports with, or furnish them to, the SEC. Further, copies of these reports are available at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at *www.sec.gov*.

Item 1A. Risk Factors

In evaluating our business, you should carefully consider the following risks, as well as the other information contained in this Annual Report on Form 10-K. These risk factors could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. If any of the following risks actually occurs, our business, financial condition and operating results could be harmed. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business.

We will need additional capital in the future 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 April 2013, our partner, AZ announced the top-line results of OSKIRA-1, a Phase 3 study to assess the efficacy and safety of fostamatinib, the first oral SYK inhibitor in development for RA. In June 2013, AZ announced the topline results from OSKIRA-2 and OSKIRA-3, two pivotal Phase 3 clinical trials investigating fostamatinib. Based on the totality of the results of the OSKIRA Phase 3 program in patients with RA, in June 2013, AZ informed us that it would not proceed with regulatory filings and instead would

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return the rights to fostamatinib to us. As such, our collaboration agreement with AZ related to fostamatinib is no longer a potential source of future funds for us. We have decided not to continue development of fostamatinib for the treatment of RA or lymphoma due to insufficient efficacy findings from recent clinical trials and the competitive landscape in those indications. We plan to commence a Phase 3 clinical program to study fostamatinib in ITP in the first half of 2014 on our own, which may accelerate our need for additional capital. We may seek another collaborator or licensee in the future for further clinical development and commercialization of fostamatinib, as well as our other clinical programs, which we may not be able to obtain on commercially reasonable terms or at all. We believe that our existing capital resources will be sufficient to support our current and projected funding requirements through at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our product candidates and other research and development activities, including risks and uncertainties that could impact the rate of progress of our development activities, we are unable to estimate with certainty the amounts of increased capital outlays and operating expendit