ChemoCentryx, Inc.
Form 10-K
March 14, 2013
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2012

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 001-35420

ChemoCentryx, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**94-3254365**

(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
850 Maude Avenue Mountain View, California (Address of Principal Executive Offices)	94043 (Zip Code)

(650) 210-2900

(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 $0.001 per share	The NASDAQ Stock Market LLC

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 ¨ No x

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

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 x No ¨

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). x Yes ¨ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the 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. ¨

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

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ¨ No x

The aggregate market value of the registrant s common stock held by non-affiliates of the registrant as of the last business day of the registrant s most recently completed second fiscal quarter was approximately $201.5 million, based on the closing price of the registrant s common stock on the NASDAQ Global Select Market of $15.00 per share.

The number of outstanding shares of the registrant s common stock, par value $0.001 per share, as of March 7, 2013 was 36,767,734.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant s 2013 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant s fiscal year ended December 31, 2012.

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CHEMOCENTRYX, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2012

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PART I

Forward-Looking Statements and Market Data

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as may, could, will, would, should, expect, plan, aim, anticipate, believe, e predict, seek, contemplate, potential or continue or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- our collaborator s exercise of its option with respect to CCX168;
- the commercialization of our drug candidates;
- the implementation of our business model, strategic plans for our business, drug candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the timing or likelihood of regulatory filings and approvals;
- our ability to maintain and establish collaborations or obtain additional government grant funding;
- our financial performance; and
- developments relating to our competitors and our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Item 1A. Risk Factors and elsewhere in this Annual Report on Form 10-K.

Any forward-looking statement in this Annual Report on Form 10-K reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. Except as

required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates, the incidence of certain medical conditions, statements that certain drugs, classes of drugs or dosages are the most widely prescribed in the United States or other markets, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is

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inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In particular, unless otherwise specified, all prescription, prescriber and patient data in this Annual Report on Form 10-K is from Datamonitor or Global Data. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

ChemoCentryx®, the ChemoCentryx logo, Traficet and Traficet-EN are our trademarks in the United States, the European Community, Australia and Japan. EnabaLink® and RAM® are our trademarks in the United States. Each of the other trademarks, trade names or service marks appearing in this Annual Report on Form 10-K belongs to its respective holder.

Unless the context requires otherwise, in this Annual Report on Form 10-K the terms ChemoCentryx, we, us and our refer to ChemoCentryx, Inc., a Delaware corporation, and our subsidiary taken as a whole unless otherwise noted.

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Item 1. Business

Overview

ChemoCentryx is a biopharmaceutical company focused on discovering, developing and commercializing orally-administered therapeutics to treat autoimmune diseases, inflammatory disorders and cancer. Our approach has been to target the chemokine system, a network of molecules including chemokine ligands and their associated receptors, as well as related chemo-attractant receptors, all of which are known to drive inflammation. Chemokine ligands concentrate at the site of an inflammatory event, serving as signals that attract and guide inflammatory cells to the tissue, where, based on the chemokine ligand and receptor combination, a specific inflammatory response is initiated. In certain diseases, discrete chemokine receptors that play a specific role in the pathology of interest have been identified, and the therapeutic goal is to specifically inhibit that receptor to provide clinical benefit. Accordingly, each of our drug candidates is a small molecule designed to target a specific chemokine or chemo-attractant receptor, thereby blocking the inflammatory response driven by that particular chemokine while leaving the rest of the immune system unaffected. Using our pioneering insights and proprietary technologies designed to better understand the chemokine system, we believe that we have established the broadest pipeline of novel drugs targeting chemokine receptors. Our compounds are designed to be highly potent, selective to minimize the risk of off-target effects and generally orally-available for improved patient compliance. As small molecules, they are also easier and less costly to manufacture than protein therapeutics, or biologics.

We currently have six drug candidates in clinical development. Three of these drug candidates are wholly owned and are being developed independently by us while three are subject to our collaboration agreement with Glaxo Group Limited, or GSK, an affiliate of GlaxoSmithKline. Under this agreement, GSK has exercised its options to obtain exclusive licenses to further develop and commercialize vercirnon and CCX354 and each of their two respective defined back-up compounds and will have a similar option right to CCX168 if it meets the success criteria mutually agreed upon by the members of the joint steering committee, or JSC, established under our strategic alliance with GSK.

All of our drug candidates have been internally discovered and include:

Vercirnon (the FDA United States Adopted Name, or USAN designation; also known as Traficet-EN, CCX282 or GSK1605786) Our most advanced drug candidate targets the chemokine receptor known as CCR9 and is currently in four pivotal Phase III clinical trials being conducted by our partner GSK for the treatment of patients with moderate-to-severe Crohn s disease;

CCX140 Our lead independent drug candidate targets the chemokine receptor known as CCR2 and is currently in Phase II clinical trials in patients with diabetic nephropathy, a form of kidney disease;

CCX354 (GSK2941266) An inhibitor of the chemokine receptor known as CCR1, successfully completed a Phase II proof-of-concept clinical trial for the treatment of rheumatoid arthritis, or RA, and was subsequently exclusively licensed to GSK, now solely responsible for further clinical development;

CCX168 Targeting the chemoattractant receptor known as C5aR (which binds the complement fragment C5a), CCX168 is currently in a Phase II clinical trial for the treatment of anti-neutrophil cytoplasmic antibody, or ANCA, associated vasculitis, and subject to GSK s option in 2013 if it meets the success criteria established by the JSC;

CCX872 Our independent next generation of orally administered inhibitors targeting CCR2 for expanded indications of renal disease, is currently in Phase I clinical development; and

CCX507 Our *de novo* wholly-owned next generation CCR9 inhibitor for inflammatory bowel disease and related disorders, is currently in Phase I clinical development.

We are also advancing several additional independent drug candidates through preclinical development, the most advanced of which target chemokine receptors involved in atopic dermatitis, RA, liver inflammation, psoriasis, and cancer.

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Vercirnon, our most advanced drug candidate, is intended to control the inflammatory response underlying IBD by targeting the chemokine receptor known as CCR9. In adults, CCR9 is found primarily on a population of T cells, a subset of the body s inflammatory cells, which migrate selectively to the digestive tract. It is believed that when CCR9 s ligand, CCL25 (also known as TECK), is over-expressed, the migration of T cells to the small and large intestine causes persistent inflammation that may result in Crohn s disease or ulcerative colitis, the two forms of IBD. We have completed nine clinical trials with vercirnon in a total of 785 subjects, including five Phase I clinical trials (three in the United States and two in the United Kingdom), one Thorough QT study in the United States (an assessment of cardiovascular safety which is required for regulatory approval), and three Phase II clinical trials (one in the Netherlands, the United Kingdom, and the United States, one in Finland and one (PROTECT-1) in Australia, Austria, Belgium, Brazil, Bulgaria, Canada, the Czech Republic, Denmark, France, Germany, Hungary, Israel, the Netherlands, Poland, South Africa, Sweden and the United Kingdom). We completed our PROTECT-1 Phase II clinical trial in 436 patients with moderate-to-severe Crohn s disease in 2009. Results from this clinical trial indicated that vercirnon was effective in inducing a clinical response over a 12-week treatment period. The results also indicated that vercirnon was effective in maintaining clinical remission over an additional 36-week treatment period. Vercirnon was safe and well tolerated in all clinical trials completed to date. In December 2009, GSK exercised its option to obtain an exclusive license to further develop and commercialize vercirnon. To date, GSK has initiated four pivotal Phase III clinical trials with vercirnon in Crohn s disease. These studies are currently being conducted in Australia, Austria, Belgium, Canada, the Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Japan, Korea, New Zealand, Poland, the Netherlands, Norway, Slovakia, South Africa, Spain, Sweden, the United Kingdom and the United States. If approved, vercirnon would be the first orally administered agent with a novel mechanism of action introduced for the treatment of Crohn s disease since the introduction of corticosteroids and oral immunosuppressants.

CCX140, our lead independent drug candidate (by which we mean it is wholly owned by us and not subject to any partnership at this time), targets the chemokine receptor known as CCR2. CCX140 is a potent and selective antagonist of CCR2 that is found on subsets of monocytes and macrophages, which are cells of the immune system believed to play an important role in inflammatory processes. Blocking CCR2 is intended to reduce the abnormal monocyte and macrophage driven inflammatory response implicated in renal disease. In addition, it has been shown that levels of CCL2 (also known as MCP-1), the main ligand for CCR2, are elevated in the kidneys of patients with diabetic nephropathy, which is characterized by a persistent and usually progressive decline in renal function. New science has shown that renal cells themselves may express CCR2 under pathological conditions and that this may be responsible for some of the effects of diabetic nephropathy. Current treatments of patients with diabetic nephropathy primarily focus on treatment of the underlying type 2 diabetes and hypertension. Given that the current standard of care does not halt or reverse the progression of diabetic patients with impaired kidney function to end-stage renal disease, we believe that an unmet medical need persists for the treatment of diabetic nephropathy. As a precursor to our clinical trials in patients with diabetic nephropathy, in January 2011, we completed a 159-patient randomized Phase II clinical trial, conducted in Australia, the Czech Republic, Germany, Hungary and New Zealand, to assess the safety and tolerability of CCX140 in patients with type 2 diabetes, the most common cause of diabetic nephropathy. CCX140 was safe and well tolerated in this trial. In addition, CCX140 demonstrated biological activity through a dose-dependent decrease in fasting plasma glucose. The highest dose of 10mg CCX140 administered once-daily also lowered hemoglobin A1c, or HbA1c, with statistical significance compared to placebo over a four-week period. CCX140 is currently in two Phase II clinical trials in patients with diabetic nephropathy and we expect to have the first data from these clinical trials in the third quarter of 2013. One trial is being conducted in Belgium, the Czech Republic, Germany, Hungary, Poland and the United Kingdom, and the other is being conducted in the Netherlands.

CCX872 is our independent next generation CCR2 antagonist for the treatment of expanded indications of renal disease. We initiated a Phase I clinical trial in the fourth quarter of 2012, and anticipate completion of this Phase I trial in 2013. In addition to diabetic nephropathy and other renal diseases, CCR2-mediated effects are thought to drive the pathology of various metabolic diseases, such as atherosclerosis and cardiovascular disease. These effects may be mediated by a combination of direct activation of CCR2 in the cells of the target tissue and

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by inducing recruitment of circulating inflammatory cells into the tissue. Inhibition of CCR2 in various animal models has been shown to be beneficial in models of acute kidney injury, vascular endothelial injury and hepatosteatosis (fatty liver), among others.

CCX354 targets the chemokine receptor known as CCR1. Synovial fluid from the joints of RA patients contains high levels of activated CCR1 chemokine ligands. Blocking CCR1 is intended to reduce inflammation and prevent subsequent joint destruction by suppressing the infiltration of inflammatory cells into the arthritic joint. We successfully completed two Phase I clinical trials in a total of 84 healthy subjects, conducted in Switzerland followed by a Phase I/II clinical trial in 24 patients with stable RA, conducted in Belgium and Romania, and a Phase II proof-of-concept clinical trial in 160 patients with moderate-to-severe RA, conducted in Belgium, the Czech Republic, Germany, Hungary, Poland, Romania and the Ukraine. Results from the Phase II proof-of-concept clinical trial demonstrated that CCX354 was safe and well tolerated by patients with RA in this trial, and demonstrated clinical and biological activity at a dose of 200mg of CCX354 once-daily. This successful clinical trial triggered GSK s option rights under our collaboration agreement. GSK exercised its option to further develop and commercialize CCX354 in November 2011 and has an exclusive right to initiate a Phase IIb clinical trial for CCX354 in RA.

CCX168 targets the chemo-attractant C5a receptor, or C5aR, which binds to a biologically activated fragment of the complement protein known as C5. Chemo-attractant receptors are related to the chemokine receptor family and similarly regulate the migration of certain types of inflammatory cells. C5aR is thought to play a role in a range of inflammatory and autoimmune diseases such as ANCA-associated vasculitis, or AAV, lupus and RA. We completed a Phase I clinical trial for CCX168, conducted in Switzerland, which showed that CCX168 was well tolerated at doses up to 100mg. We initiated a Phase II clinical trial in AAV in the fourth quarter of 2011 and expect to have results from this clinical trial in 2013. This clinical trial is being conducted in Belgium, Czech Republic, Germany, Hungary, the Netherlands, Poland, Sweden and the United Kingdom. If CCX168 meets the success criteria mutually agreed upon by the members of the JSC, GSK may exercise its option to further develop and commercialize CCX168. An option decision is anticipated by the end of 2013.

CCX507 builds on our expertise in the area of CCR9 antagonists and IBD. Following the expiration of our target exclusivity obligations with respect to CCR9 under our collaboration agreement with GSK, we started a *de novo* discovery program under which we have designed a series of novel molecules that we believe represent the next generation of CCR9 inhibitors. CCX507 is our lead compound from this program and is selective for CCR9 relative to all other chemokine receptors, orally bioavailable, and has an excellent preclinical safety profile. Molecules such as CCX507 have been designed to interact with the CCR9 receptor in a unique way that produces molecules with greater potency towards CCR9 than other compounds reported to date. We initiated a Phase I clinical trial in the fourth quarter of 2012.

With the exception of PROTECT-1, our Crohn s disease trial for vercirnon, we have conducted the majority of our Phase I and Phase II clinical trials in Europe. Our planned future Phase III clinical trials for CCX140 will be conducted in the United States, Europe and possibly other countries outside of the United States and Europe.

GSK is solely responsible for all further clinical development and commercialization expenditures worldwide with respect to that drug candidate and its two designated back-up compounds under options that it exercised. These are, in their entirety, vercirnon, CCX354 and CCX168, if this final remaining option is exercised. Upon the exercise of any of these options, we would receive an option exercise fee and would become eligible to receive regulatory and commercial milestone payments, as earned under the terms of our agreement, and royalties on the net sales of licensed drugs. GSK has already exercised its option to vercirnon and CCX354. If GSK does not exercise its option to CCX168, we will evaluate our alternatives for further development of this drug candidate, which may entail internally developing it or identifying other collaboration partners for its development.

We have developed a suite of proprietary technologies, which we call the EnabaLink drug discovery engine, to better understand the chemokine system and to accelerate the identification of small molecule lead compounds

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that target and inhibit the function of specific chemokine receptors. We believe this platform provides us with an advantage in the rapid identification of highly specific drug candidates. An important element of this platform is our thorough map of the chemokine network, which allows us to better understand how a given chemokine-chemokine receptor interaction impacts the migration of cells in a given disease. With this understanding, we can apply our advanced screening methodologies, including a purpose-built high-throughput robotic screening technology, known as the Reverse Activation of Migration, or RAM, Assay, to identify small molecule antagonists for the chemokine receptor most closely associated with a specific disease. The RAM Assay is designed to markedly reduce or eliminate non-specific inhibitors and toxic inhibitors of cell migration, resulting in highly specific lead candidates. This technology allows us to screen against targets that are not easily accessible with traditional technologies, providing us with what we believe to be a competitive advantage in drug discovery. We have used our EnabaLink drug discovery engine in our drug candidate programs and continue to apply these powerful research tools in our early stage drug discovery efforts.

Focusing on the Chemokine System

Understanding Inflammation

The human immune system serves to protect the body against infections and injuries. It recognizes these threats and quickly mounts a defensive response. Inflammation is one component of the immune response and serves as a line of defense to infection, irritation or injury as immune system cells attempt to suppress and control an infectious agent, such as bacteria, or to break down and carry away damaged tissue, as in the case of injury. Specialized white blood cells, known as antigen presenting cells, and other cells such as macrophages and lymphocytes are mobilized to the affected tissue and work in concert to recognize, neutralize and eliminate the perceived threat. Macrophages and other antigen presenting cells pick up and ingest foreign materials and present the threatening antigens to lymphocytes, also known as T cells and B cells. T cells in turn destroy infected cells or coordinate other inflammatory cells, such as B cells, which produce antibodies, or proteins with the ability to neutralize antigens, to bind with the antigen leading to the destruction of the foreign agent. Macrophages then dispose of dead cells and debris.

Acute inflammation is characterized by the rapid onset of pain, heat, redness, swelling and loss of function. When inflammation is long-term, or chronic, and is directed at the body s own tissues, this can result in various forms of autoimmune disease. Different autoimmune diseases tend to affect different tissues or organs. For example, in Crohn s disease certain inflammatory cells attack tissues predominantly in the digestive tract, while in RA a different set of inflammatory cells is involved in attacking the tissues that make up the joints between bones. While the cause of autoimmune diseases is not known, we and others have demonstrated that the self-perpetuating, tissue-damaging inflammation associated with these conditions is in part characterized by dysregulation of the chemokine system.

IBD, RA, AAV, lupus and skin inflammatory diseases such as psoriasis and atopic dermatitis are all examples of chronic conditions in which an inappropriate inflammatory response underlies disease. In recent years, conditions that were not previously considered to be the result of inflammation, such as type 2 diabetes, chronic kidney disease and cancer, have joined the long list of human diseases thought to be the result, at least in part, of uncontrolled and chronic inflammation. Many autoimmune diseases are highly debilitating, creating a significant social and financial burden.

Role of Chemokines in Disease

Inflammation involves a complex series of cellular events that rely on chemical messengers known as chemokines, or ***chemo***-attractant cyto***kines***, which send out signals to attract inflammatory cells, or leukocytes, to the site of disease or injury. Chemokines bind to chemokine receptors found on the surface of leukocytes, and the specific combination of various chemokines and chemokine receptors serve to precisely coordinate the inflammatory response.

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The chemokine system, including chemokines and chemo-attractants, directs inflammatory responses, serving to precisely coordinate immune system cell movement. The human chemokine network is made up of more than 50 known chemokine ligands and approximately 25 identified chemokine receptors. Some chemokines are known to bind to more than one chemokine receptor. Certain receptors can bind to multiple chemokines, while other chemokine receptors only bind to a single ligand. Different chemokines are made in different tissues at different times and different chemokine receptors are expressed on the surface of different types of inflammatory cells. Those cells can only respond to a chemokine in a given organ or tissue if the cell possesses a receptor that specifically recognizes the chemokine that is present in the local environment. In this way, each chemokine-chemokine receptor combination may direct a different inflammatory response and this response can be tailored by the body based on the type of injury, irritation or other threat.

Inappropriate activity of the chemokine network is thought to be at the core of numerous autoimmune and inflammatory conditions. For example, in Crohn s disease dysregulation of either the chemokine CCL25 or the chemokine receptor to which it binds, CCR9, is thought to attract a certain population of inflammatory T cells to, and subsequently attack, tissues in the digestive tract. As drivers of the inflammatory response, chemokines and their receptors present opportunities for the development of new therapies. By selectively blocking a given chemokine-chemokine receptor combination, and largely leaving other chemokine-chemokine receptor interactions unaffected, we believe even aggressive forms of chronic inflammation and autoimmune diseases can potentially be brought under control in a safe, effective manner.

Chemokines are also involved in the causes of diseases that were not historically classified as inflammatory. For example, CCR2 is responsible for the recruitment of monocytes from blood into the adipose tissue and liver of obese, insulin-resistant individuals. The monocytes mature into inflammatory macrophages within these tissues and interfere with the biochemical signals involved in the regulation of glucose levels, often resulting in type 2 diabetes.

Research also indicates that chemokines may contribute to inflammatory damage by direct activation of non-inflammatory cells that are part of the affected tissue. For example, evidence indicates that certain cells within diabetic kidneys begin to express CCR2 on their surface and become impaired due to the resulting increased levels of the chemokine CCL2 found in such kidneys.

In addition to its central role in autoimmune and inflammatory conditions, the chemokine system plays an important role in other diseases, such as cancer. It is known that tumors induce the expression of chemokines that are involved in promoting the growth of blood vessels that feed tumors, providing a link to the chemokine system s role in the establishment and spread of cancer. In addition, certain chemokine ligands and their corresponding receptors have been implicated in the survival, growth and metastasis of human cancer. The chemokine system is likely a more recent evolutionary branch of other chemo-attractant systems in the body such as the complement system. The complement system includes the protein C5a, which under certain conditions has pro-inflammatory effects.

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Our Drug Candidates and Preclinical Programs

Vercirnon for Inflammatory Bowel Disease

Understanding Crohn s Disease

IBD refers to two diseases, Crohn s disease and ulcerative colitis, both characterized by inflammation of the gastrointestinal tract. Both Crohn s disease and ulcerative colitis are chronic and recurring autoimmune conditions. Researchers believe that these conditions occur when the body s inflammatory cells become over-reactive to microbes in the gastrointestinal tract(such as bacteria normally found in the intestines that aid digestion) resulting in a long lasting destructive inflammatory response.

According to the Crohn s and Colitis Foundation of America, or CCFA, in 2012 Crohn s disease was estimated to affect as many as 700,000 Americans. According to National Digestive Diseases Information Clearinghouse, men and women are affected equally by the disease. While patients may be of any age, Crohn s disease is primarily a disease that commences in adolescents and young adults, with onset between the ages of 15 and 35.

Crohn s disease is chronic; patients suffer periods of flare-ups or periods characterized by intense symptoms, interspersed with periods of remission where symptoms decrease or disappear. Symptoms may range from mild to severe and can include persistent diarrhea, abdominal pain, fever, and rectal bleeding, as well as loss of appetite and subsequent weight loss. Crohn s disease patients will experience ulcerations that penetrate deeply into the mucosal tissues that line the walls of the bowel. Crohn s disease may involve the entire length of the gastrointestinal tract from the mouth to the anus, but the most typical areas of involvement are in the small intestine and colon. Complications of Crohn s disease include obstruction or blockage of the intestine due to scar tissue build-up and nutritional deficiencies. Ulcerative lesions associated with the disease can, on occasion, completely penetrate the bowel wall, leading to painful fistula formation, or an abnormal break or opening in the bowel wall, which can cause infectious complications that require surgical intervention.

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Patients with Crohn s disease are typically referred to and treated by gastroenterologists. Prior to referral and accurate diagnosis, the condition may go undiagnosed or misdiagnosed as a variety of gastrointestinal ailments. Crohn s disease often mimics other conditions and symptoms may vary widely, presenting challenges for an accurate diagnosis. Crohn s disease is diagnosed through a colonoscopy, mucosal biopsy and small bowel x-ray to rule out other conditions such as ulcerative colitis and to ascertain which parts of the digestive tract are involved and establish a baseline for monitoring treatment and management. The primary goals for drug therapy are to induce and maintain significant clinical improvement or remission, resulting in improvement of active symptoms.

We believe that Crohn s disease represents a significant underserved clinical problem with high medical and economic costs and a large impact on quality of life. The disease is strongly linked to work disability and unemployment, as 48% of Crohn s disease patients were employed full-time at the time of diagnosis of their disease, and 39% of patients were unemployed, according to a 2005 publication in the Journal of Clinical Gastroenterology. Healthcare costs are significant, as patients typically require drug therapy over many years to control symptoms and maintain remissions, and a number of patients require multiple hospitalizations and, in some cases, surgeries over the course of their illness. In addition, currently available treatments for Crohn s disease are often associated with adverse reactions that may require frequent monitoring and impact patient compliance.

There is no known cure for Crohn s disease. Current treatments for Crohn s disease are directed toward bringing a patient s active disease, or acute flare-ups, under control or into remission. The initial induction therapy is often followed by chronic maintenance therapy to preserve the remission or to keep disease manifestations at a minimal level. If the disease continues to progress, patients continue on a given therapeutic regimen from the time of diagnosis forward, adding additional therapies as flare-ups recur or persist. Over their lifetimes, Crohn s disease patients will typically use a broad array of drugs, often in combination, to seek improvement of their symptoms. Many patients also often require one or more surgical procedures over the course of their lifetimes to treat the disease.

Vercirnon A Novel CCR9 Inhibitor

Vercirnon is being developed as a first-in-class oral anti-inflammatory agent for the treatment of IBD, including Crohn s disease and ulcerative colitis. Vercirnon is orally administered, which we believe would be an important improvement in patient convenience and potentially patient compliance as compared to existing intravenous and subcutaneous treatments with biologics. We believe that the combination of vercirnon s specificity and the convenience of oral administration may make this a treatment of choice for IBD patients. In addition, as a synthetic small molecule, the drug may have significant cost-of-goods advantages over protein therapeutics, or biologics, such as tumor necrosis factor-alpha, or TNF-a, inhibitors.

Vercirnon is designed to prevent the migration of inflammatory cells to the digestive tract by blocking the function of CCR9, which is found on a subset of inflammatory T cells that plays a key role in the development of both forms of IBD. T cell migration into the digestive tract is guided by a chemokine called CCL25 found in the intestines. CCL25-mediated activation of CCR9 draws T cells into the intestinal tissue, where they release inflammatory mediators that can ultimately lead to tissue damage. In adults, CCL25 only signals CCR9-expressing T cells to migrate to the gastrointestinal tract, and blocking CCR9 is not thought to interfere with cell migration elsewhere. Therefore, by blocking CCR9, vercirnon may be able to halt the inflammatory response underlying IBD without otherwise impacting the patient s immune system. In addition, by interrupting CCR9 signaling, we believe vercirnon may hasten the elimination of inflammatory T cells from the intestines, thus potentially speeding recovery by reducing the longevity of flare-ups associated with IBD. We believe this mechanism of action could allow vercirnon, if approved, to be a highly effective treatment with significantly fewer side effects than currently available immunosuppressive therapies, including TNF-a inhibitors.

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Vercirnon Drug Development Strategy and Clinical Trials

We have completed nine clinical trials with vercirnon in a total of 785 subjects, including five Phase I clinical trials in a total of 151 subjects, one Thorough QT study in 57 subjects demonstrating cardiovascular safety, two Phase II clinical trials in 510 patients with Crohn s disease and one Phase II clinical trial in 67 patients with celiac disease. The largest of these Phase II clinical trials, PROTECT-1, was conducted in 436 patients with moderate-to-severe Crohn s disease. Results from this clinical trial indicated that vercirnon was effective in inducing a clinical response over a 12-week treatment period in these patients. Furthermore, the results indicated that vercirnon was also effective in maintaining clinical remission over a 36-week treatment period. Vercirnon was safe and well tolerated in all clinical trials completed to date. In December 2009, GSK exercised its option to obtain an exclusive license to vercirnon and its two designated back-up compounds and is now solely responsible for all further clinical development and commercialization and the related expenditures associated with these activities worldwide.

To date, four pivotal Phase III clinical trials have been initiated by GSK with vercirnon in Crohn s disease. The pivotal Phase III clinical trials are designed to support the use of vercirnon to induce clinical response or remission of Crohn s disease, and to provide maintenance of remission for Crohn s disease.

Phase III Clinical Program

GSK has initiated four pivotal Phase III clinical trials intended to obtain the clinical results necessary to apply for marketing approval for vercirnon (GSK1605786) in Crohn s disease. In general, the development approach of the Phase III program is modeled after the design of our PROTECT-1 clinical trial. The following pivotal Phase III clinical trials are currently ongoing:

SHIELD-1 is a multi-national, randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of two doses, 500mg once-daily and 500mg twice-daily, of vercirnon over 12 weeks of treatment in approximately 600 adult patients with moderate-to-severe Crohn s disease. Patient recruitment was initiated in December 2010. Data from the induction phase of the SHIELD-1 trial are expected in the second half of 2013.

SHIELD-2 is a multi-national, randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of two doses, 500mg once-daily and 500mg twice-daily, of vercirnon in maintaining disease remission over 52 weeks in approximately 750 adult patients with Crohn s disease. Eligible patients will have achieved disease improvement and/or remission in SHIELD-1 or will be fed from SHIELD-4 as noted below. Patient recruitment was initiated in April 2011.

SHIELD-3 is a multi-national, open-label clinical trial to evaluate the safety and effectiveness of 500mg twice-daily of vercirnon over 108 weeks in approximately 800 adult patients with Crohn s disease. Patients completing previous clinical trials with the drug or patients who withdraw early from the SHIELD-2 maintenance clinical trial may be eligible to participate. Patient recruitment was initiated in April 2011.

SHIELD-4 is a multi-national, randomized, double-blind clinical trial with the primary objective to induce clinical response and/or remission with vercirnon in subjects with active Crohn s disease to qualify subjects for enrollment into SHIELD-2, the 52-week maintenance clinical trial. Patients receive either 500mg once-daily or 500mg twice-daily for 12 weeks in this clinical trial. Patient recruitment was initiated in November 2011.

Vercirnon Commercialization Strategy

Following the exercise of its option, GSK became solely responsible for all further clinical development and commercialization of vercirnon and its two designated back-up compounds worldwide. However, we have the option, which we can exercise at our sole discretion, to co-promote vercirnon to physician specialists in the United States, subject to our payment of 35% of GSK s development costs. Under the terms of the agreement,

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our promotional efforts could be as high as 50% of all promotional efforts to physician specialists in the United States. As consideration for our promotional efforts, GSK would be required to pay us an amount similar to what it would pay a third-party contract sales force.

Additional Indications for CCR9 Inhibitors

Ulcerative colitis is an additional indication for which CCR9 inhibitors could be developed. Preclinical studies showed that CCR9 inhibitors can prevent the onset of and treat large bowel inflammation in mice, and may have the potential to treat ulcerative colitis in humans. We have also recently demonstrated that, contrary to the prevailing assumption regarding the absence of CCL25 from the colon, increased levels of CCL25 are present in colonic tissue from human patients with IBD, which further supports our belief that CCR9 inhibitors have the potential for treating ulcerative colitis.

CCX140 for Diabetic Nephropathy and Other Renal Diseases

Understanding Diabetic Nephropathy

Diabetic nephropathy is a common disease among patients with diabetes and hypertension. It is characterized by a persistent and usually progressive decline in renal function, as measured by glomerular filtration rate, a measure of the rate of fluid filtration in the kidney, and/or albuminuria, a condition where elevated protein levels are present in the urine, which can be an indicator of kidney damage.

Given the rise in the incidence of obesity, type 2 diabetes and hypertension, the associated incidence of diabetic nephropathy has reached widespread proportions in industrialized nations. Current treatment options for patients with diabetic nephropathy mainly include drugs that treat the underlying conditions of diabetes and hypertension. Angiotensin receptor blockers, or ARBs, and angiotensin converting enzyme, or ACE, inhibitors are commonly prescribed to control hypertension and slow the progression of diabetic nephropathy. Even with these therapies, about 20% of patients with diabetic nephropathy will progress into a condition known as end-stage renal disease, the most severe stage of chronic kidney disease, at which point patients must rely on regular dialysis sessions or a kidney transplant in order to survive.

A number of experimental treatments for diabetic nephropathy are currently being evaluated in clinical trials, although none of them have yet demonstrated clear and convincing benefit in large long-term clinical trials, either in terms of slowing or reversing disease progression. Several of these treatments aim to interfere with the inflammatory or fibrotic processes that are now recognized as central to the disease.

CCX140 A Novel CCR2 Inhibitor

CCX140 is our lead independent drug candidate which successfully completed a Phase II clinical trial in type 2 diabetics and is currently in two Phase II clinical trials in patients with diabetic nephropathy, a form of kidney disease. While historically diabetic nephropathy was not considered an inflammatory disease, there is now clear evidence of the role of macrophages in this disease. Kidney biopsies from patients with diabetic nephropathy show elevated numbers of macrophages in the glomeruli, which are the basic filtering elements in the kidney. It has also been shown that the extent of tissue damage in the interstitial areas surrounding the proximal tubules, which are the second component of the filtering apparatus in the kidney, is strongly correlated with the numbers of macrophages present. Experimental studies in preclinical diabetic models have clarified that monocyte and macrophage infiltration begins at early stages of disease and that this infiltration correlates with renal injury.

In recent years, CCR2 has been identified as a main driver of monocyte and macrophage recruitment into diseased kidneys. Various cell types in glomeruli also appear to express CCR2, which drives some of the renal impairment in diabetic nephropathy. Levels of CCL2, the main ligand for CCR2, are elevated in the kidneys of patients with diabetic nephropathy. CCL2 is produced by kidney cells in response to such factors as high blood glucose levels and physical stresses, such that levels of CCL2 in the urine are strong indicators of renal damage and correlate well with albuminuria and interstitial macrophage numbers.

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We have utilized various animal models to study the relationship between CCR2 inhibition and renal function. Data generated from these models have confirmed and expanded observations made by other independent investigators in preclinical models of diabetic nephropathy indicating that CCR2 inhibition leads to pronounced reduction in albuminuria, as well as improvement in markers of renal function. We have also demonstrated that CCR2 inhibition provides benefit in several models of non-diabetic nephropathy. The following table summarizes the key findings from each of these animal models:

Summary of Findings From CCR2 Inhibition in Animal Models of Nephropathy

Biological Parameter	Effect of CCR2 Inhibition
Albuminuria	Reduced
Hyperglycemia	Reduced
Glomerular Filtration Rate	Decreased hyperfiltration
Serum Markers of Renal Function	Reduced serum creatinine and blood urea nitrogen levels
Histological Improvements	Reduced number of renal interstitial macrophages
	Reduced percentage of glomeruli with mesangiolysis
	Increased podocyte density

Data from preclinical studies indicate that CCX140 is a potent and selective antagonist of CCR2 which is required for monocytes to infiltrate the inflamed kidney, where they differentiate into macrophages. While CCX140 is not the first CCR2 antagonist to advance into clinical trials, we believe that it is unique in a number of ways, including its high selectivity for CCR2 relative to other chemokine receptors such as CCR5. We believe that CCX140 also distinguishes itself from other CCR2 antagonists in that it has been shown preclinically to be free of the cardiovascular safety signals associated with other CCR2 antagonists. CCX140 has been shown in a number of preclinical toxicology studies to be suitable for evaluation in humans for chronic use in diabetic nephropathy.

CCX140 Drug Development Strategy and Clinical Trials

Our clinical development strategy was to assess the safety and tolerability of CCX140 first in healthy subjects, then in patients with type 2 diabetes and normal renal function, then finally in patients with diabetic nephropathy. As a precursor to our clinical trials in patients with diabetic nephropathy, in January 2011, we completed a 159-patient randomized Phase II clinical trial to assess the safety and tolerability of CCX140 in patients with type 2 diabetes, the most common cause of diabetic nephropathy. CCX140 is currently in two Phase II clinical trials in diabetic nephropathy and we expect to have the first results from these clinical trials in the third quarter of 2013.

CCX140 Phase I Clinical Trials

We completed four Phase I clinical trials in 118 healthy volunteers. A CCX140 dose range of 0.05 to 15mg was studied. CCX140 was generally well tolerated and no serious adverse events, or SAEs, were observed in these Phase I clinical trials. The pharmacokinetic, or PK, profile was supportive of once daily oral dosing of CCX140.

CCX140 Phase II Clinical Trial in Type 2 Diabetes

Our Phase II clinical trial was designed to demonstrate safety of CCX140 in patients with type 2 diabetes and normal renal function and to examine the effect of CCX140 on glycemic indices. We conducted a randomized, double-blind, placebo and active controlled clinical trial in 159 patients with type 2 diabetes on a

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stable dose of metformin for at least eight weeks, with 32 patients receiving placebo, 32 receiving pioglitazone hydrochloride (an approved therapeutic for type 2 diabetes serving as the active control), 63 receiving 5mg of CCX140 and 32 receiving 10mg of CCX140 orally once-daily for 28 days.

The clinical trial met its primary objective by demonstrating the safety and tolerability of CCX140 in these patients. In addition, CCX140 showed encouraging signs of biological activity based on a statistically significant decrease in HbA1c, a marker of glycemic control, for the 10 mg dose group.

Patients receiving CCX140 experienced a dose-dependent decrease in fasting plasma glucose, or FPG, from baseline to day 29 of the trial period, or Day 29. The least squares mean change from baseline to Day 29 in FPG was -4.3mg/dL for 5mg CCX140, -16.1mg/dL for 10mg CCX140, -10.7mg/dL for placebo, and -21.4mg/dL for 30mg pioglitazone hydrochloride. The decrease in FPG observed in the active control group receiving 30mg pioglitazone hydrochloride was in line with the anticipated decrease of 25mg/dL as reported in published literature. Decreases in FPG from baseline to Day 29 for the pioglitazone hydrochloride and CCX140 groups were not statistically different when compared to placebo. However, the decrease in FPG in the 10mg CCX140 group was comparable to the 30mg pioglitazone hydrochloride response observed over four weeks of treatment.

Patients in the 10mg CCX140 group also showed a statistically significant (p=0.045 vs. placebo) decrease from baseline in HbA1c, one of the most important glycemic indices, indicating an improvement in glycemic control which may be an added benefit when treating patients with diabetic nephropathy. The least squares mean change from baseline in HbA1c was -0.09% for 5mg CCX140, -0.23% for 10mg CCX140, -0.09% for placebo, and -0.13% for 30mg pioglitazone hydrochloride. In addition, the fructosamine levels, another index of glycemic control, trended lower in the CCX140 and pioglitazone hydrochloride groups, but did not reach statistical significance compared to placebo. Plasma CCL2 and circulating monocyte levels were unchanged by CCX140 treatment.

No SAEs were observed in patients receiving CCX140 treatment. The incidence of SAEs across treatment groups was similar. Two patients discontinued the clinical trial due to an adverse event. One patient, in the 5mg CCX140 group, experienced an adverse event of dyspepsia, which led to discontinuation of clinical trial medication. The adverse event was considered by the clinical investigator to be moderate in severity and possibly related to clinical trial medication. A second patient, in the 10mg CCX140 group, experienced an adverse event of gouty arthritis, which led to discontinuation of clinical trial medication. This patient had a medical history of gout and this adverse event was considered by the clinical investigator to be severe in intensity and probably not related to CCX140. Adverse events of hypertension were reported in three patients in the 5mg CCX140 group. However, no such events were reported in patients in the 10mg CCX140 group. Review of the blood pressure data from the subjects with SAEs of hypertension, as well as the overall group blood pressure data, did not reveal any significant worsening trend in blood pressure with CCX140 treatment compared to placebo. CCX140 treatment did not negatively affect the patients serum lipid profiles (total cholesterol, HDL and LDL cholesterol, triglycerides, and non-esterified fatty acids) over the four-week treatment period. Changes in ECG were not clinically meaningful and there was no detrimental effect on renal function observed.

Current and Future CCX140 Clinical Development in Diabetic Nephropathy

CCX140 is currently in two Phase II clinical trials in patients with diabetic nephropathy. The first randomized, double-blind, placebo-controlled Phase II clinical trial will enroll up to 270 patients. The primary safety objective of this clinical trial is to evaluate the safety and tolerability of CCX140 in patients with diabetic nephropathy. The primary efficacy objective is evaluation of the effect of CCX140 on albuminuria. Secondary efficacy objectives are evaluation of the effect of CCX140 on HbA1c and estimated glomerular filtration rate, or eGFR. The three treatment groups consist of placebo, 5mg and 10mg of CCX140 and the treatment duration will be up to 52 weeks, with a four-week follow-up period. Patients with residual albuminuria, despite being on a stable therapeutic dose of an ACE inhibitor or ARB are included in this clinical trial. The key efficacy endpoint is change from baseline in first morning urinary albumin:creatinine ratio, a major indicator of renal function. The sample size of the trial was increased from 135 to 270 patients in 2012 and the dosing duration was extended

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from 12 weeks to 52 weeks, following completion of long-term toxicology studies that allowed extension of dosing beyond 12 weeks. We expect to have 12-week data from this study in the third quarter of 2013 and 52-week data in 2014.

A second randomized, double-blind, placebo-controlled Phase II clinical trial we have conducted is in 20 patients with diabetic nephropathy. The primary objective of this clinical trial is to evaluate the effect of CCX140 on 24-hour urinary albumin excretion which was collected in a controlled clinical setting. The two treatment groups consist of placebo and 10mg of CCX140. The treatment duration is 12 weeks, with a four-week follow-up period. Patients with residual albuminuria, despite being on a stable therapeutic dose of an ACE inhibitor or ARB are included in this clinical trial. We expect to have data from this clinical trial in 2013.

If the Phase II clinical program indicates that CCX140 is safe and efficacious in treating patients with diabetic nephropathy, we plan to conduct end-of-Phase II meetings with the FDA and European Medicines Agency, at which time the clinical results from the CCX140 program will be reviewed and a Phase III clinical program will be discussed. It is anticipated that the Phase III program will include at least 1,500 patients.

CCX140 Commercialization Strategy

We plan to retain commercial rights to CCX140 in North America and intend to build a specialty sales force to call on nephrologists who treat diabetic nephropathy patients. There are approximately 8,300 nephrologists in the United States. We believe that a moderately sized sales force will be sufficient to call on all key prescribing nephrologists in this market. In addition, we plan to seek partners for co-development and commercialization of CCX140 outside North America.

CCX872 Next Generation CCR2 Inhibitor for Other Renal Indications

Building on our expertise in the field of CCR2 therapeutics, we advanced CCX872 as our next-generation CCR2 inhibitor drug candidate. Like CCX140, our leading independent drug candidate, CCX872 is a potent and selective inhibitor of human CCR2. CCX872 has demonstrated excellent safety and efficacy in various preclinical models of metabolic disease. In addition to diabetic nephropathy, CCR2-mediated effects are thought to drive the pathology of various metabolic diseases, such as atherosclerosis and cardiovascular disease, as well as additional kidney diseases such as acute kidney injury. These effects may be mediated by a combination of direct activation of CCR2 in the cells of the target tissue and by inducing recruitment of circulating inflammatory cells into the tissue. Inhibition of CCR2 in various animal models has been shown to be beneficial in models of acute kidney injury, vascular endothelial injury and hepatosteatosis (fatty liver), among others.

We initiated a Phase I clinical trial in the fourth quarter of 2012 and expect to complete this trial in 2013.

CCX354 for Rheumatoid Arthritis

Understanding Rheumatoid Arthritis

Rheumatoid Arthritis, a chronic inflammatory disease, is among the most debilitating of all forms of arthritis, causing pain, stiffness, swelling and limitation in the motion and function of multiple joints which may eventually become deformed. Sometimes these symptoms make even the simplest activities, such as walking, difficult to manage. The exact cause of RA is unknown, but it is believed to result from the body s immune system attacking the synovium, which is the tissue that lines a patient s joints. Although therapy for patients with RA has improved dramatically over the last 25 years, there is still no cure and no single therapy which is effective for all patients. Many patients will need to change treatment strategies during the course of their disease due to lack of efficacy and adverse side effects. People with RA, particularly those whose disease is not well controlled, may have a higher risk of other diseases such as osteoporosis, or thinning of bone resulting in fracture.

As of 2006, more than two million Americans suffered from RA, according to a report by Data Monitor. RA is two to three times more common in women than in men and generally strikes between the ages of 20 and 50, but it can also affect young children and adults older than age 50.

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CCX354 A Novel CCR1 Inhibitor

There is strong evidence implicating CCR1 in the pathology of RA; first, CCR1-expressing monocytes, macrophages and T cells are consistently found at high levels in the synovium of RA patients, and second, the C6 superagonists of CCR1, which are activated highly potent forms of certain CCR1 ligands, are consistently detected at high levels in synovial fluids from RA patients. Blocking CCR1 is intended to reduce the inflammation and prevent subsequent joint destruction by suppressing the infiltration of inflammatory cells into the arthritic joint.

CCX354 is in a new class of proprietary small molecule CCR1 inhibitors. CCX354 was designed by optimization of a chemical lead that was discovered using our EnabaLink drug discovery engine and is chemically distinct from all known inhibitors of this receptor. Our preclinical data suggest that the compound selectively inhibits CCR1-mediated migration of monocytes and does not inhibit migration of inflammatory cells mediated by other chemokine receptors, even when the compound is given at high doses. We believe that this high degree of target specificity is an important safety feature that may allow CCX354 to be effective while avoiding unwanted side effects associated with existing injectable biologics and other immunosuppressive agents currently used to treat RA.

CCX354 Drug Development Strategy and Clinical Trials

We have completed two Phase I clinical trials with CCX354 in 84 healthy subjects, also a Phase I/II clinical trial in 24 patients with RA, and lastly a Phase II proof-of-concept clinical trial in 160 patients with moderate-to-severe RA partially responsive to methotrexate. In November 2011, GSK exercised its option to obtain an exclusive license to CCX354 and its two designated back-up compounds and is now solely responsible for all further clinical development and commercialization expenditures worldwide.

CCX354 Phase II Clinical Trial in Rheumatoid Arthritis

We have successfully completed a randomized, double-blind, placebo-controlled Phase II proof-of-concept clinical trial in 160 patients with RA on a stable dose of methotrexate for at least eight weeks. Patients received either placebo, 100mg of CCX354 twice-daily or 200mg of CCX354 once-daily for 84 days, followed by 28 days without treatment. The primary objective of the clinical trial was to evaluate the safety and tolerability of CCX354 in patients with moderate-to-severe RA. Key secondary objectives included assessment of the effect of CCX354 on RA disease activity measured by the ACR response criteria, Disease Activity Score 28-CRP, the ACR components and bone resorption markers. ACR20, ACR50 and ACR70 responses refer to patients who achieve a 20%, 50% and 70% improvement, respectively, according to criteria set by the American College of Rheumatology, or ACR. Patients who met inclusion criteria at the start of dosing demonstrated an ACR20 response at Week 12 of 56% in subjects receiving 200mg of CCX354 once-daily compared to 44% in subjects receiving 100mg of CCX354 twice daily, and 30% in subjects receiving placebo. The ACR20 response difference between the 200mg CCX354 once-daily and placebo groups was statistically significant (p=0.014). Patients who met inclusion criteria at the start of dosing and who did not previously receive biologic agents, such as anti-TNF drugs, demonstrated an ACR20 response at Week 12 of 62% in subjects receiving 200mg of CCX354 once-daily compared to 41% in subjects receiving 100mg of CCX354 twice-daily and 26% in subjects receiving placebo. The ACR20 response difference between the 200mg CCX354 once-daily and placebo groups was statistically significant (p=0.002). The decrease in CRP was statistically significant in the 200mg CCX354 once-daily group compared to placebo at Week 12 (p=0.023). There was a median CRP decrease from baseline to Week 12 of 33% in the 200mg CCX354 once-daily group, 30% in the 100mg twice-daily group and 11% in the placebo group in subjects eligible at the start of dosing. Similarly, there was a median CRP decrease from baseline to Week 12 of 38% in the 200mg CCX354 once-daily group, 30% in the 100mg twice-daily group and 10% in the placebo group in subjects eligible at the start of dosing who also did not previously receive biologic agents. ACR50, ACR70, Disease Activity Score 28-CRP, and ACR component results indicated greatest efficacy in the 200mg CCX354 once-daily group. Decreases in bone turnover markers were more pronounced in the CCX354 groups compared to placebo and reached statistical significance at several time points during the study.

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Clinical responders had higher plasma CCX354 concentrations than non-responders. CCX354 was safe and well tolerated by study subjects. No SAEs were observed in the 200mg CCX354 once-daily or placebo groups. Four SAEs were reported in the 100mg CCX354 twice-daily group, none considered related to CCX354 use by the study investigators. These were vasovagal reaction, or fainting, following blood draw, non-cardiac related chest pain, myocardial infarction, or heart attack, and psychomotor epilepsy, which was observed one week after stopping study medication. No significant safety issues were observed regarding safety laboratory parameters including hepatic, renal, metabolic and hematologic data.

Future CCX354 Clinical Development in Rheumatoid Arthritis

CCX354 is subject to our collaboration agreement with GSK and in November 2011 it exercised its option to obtain a license to further develop and commercialize CCX354 and its two defined back-up compounds for all indications, including RA. Upon exercising its option, GSK became solely responsible for all further clinical development and commercialization expenditures worldwide with respect to CCX354 and its two designated back-up compounds.

CCX168 for ANCA-Associated Vasculitis

Understanding ANCA-Associated Vasculitis

ANCAs are autoantibodies that attack a certain type of white blood cells called neutrophils. AAV is a type of autoimmune disease caused by autoantibodies, which are abnormal antibodies that attack one s own cells and tissues resulting in blood vessel damage. In AAV, activation of the complement cascade, an escalating group of inflammatory responses, leads to production of the very potent chemo-attractant factor known as C5a. This in turn leads to the attraction and activation of neutrophils and other white blood cells, which play a key role in the disease.

AAV currently is treated with high-dose corticosteroids and cyclophosphamide, azathioprine, mycophenolate mofetil, rituximab, and plasma exchange in severe cases. Even though these approaches may induce a treatment response in 70% to 90% of patients, corticosteroids and cyclophosphamide are associated with substantial morbidity and mortality, particularly as a result of serious infections.

CCX168 A Novel C5a Receptor Inhibitor

CCX168 is a potent and highly specific antagonist of the human C5a receptor. The compound displays oral bioavailability in various species and has demonstrated an excellent preclinical safety profile, consistent with its intended chronic use in patients. The efficacy of CCX168 was demonstrated in a mouse model of ANCA-associated glomerulonephritis which recapitulates many of the histological features of the human disease. In these studies, oral doses of CCX168 completely blocked the glomerulonephritis induced by intravenous injection of anti-myeloperoxidase antibodies (a form of anti-neutrophil cytoplasmic antibody). Levels of CCX168 in the blood of these mice were comparable to those expected in the blood of patients participating in our ongoing Phase II proof-of-concept clinical trial with CCX168.

CCX168 Drug Development Strategy and Clinical Trials

CCX168 Phase I Clinical Trial

We have completed a Phase I clinical trial with CCX168 in 31 healthy subjects. This was a randomized, double-blind, placebo-controlled, two-period clinical trial in which subjects received either CCX168 or placebo, as a single dose in the first period and as multiple once-daily or twice-daily oral doses in the second period. Single oral doses of 1mg, 3mg, 10mg, 30mg, and 100mg of CCX168 were studied. In period two, CCX168 doses of 1mg, 3mg, and 10mg once-daily for seven days, and 30mg and 50mg twice-daily for seven days, were studied. CCX168 appeared to be well tolerated by clinical trial subjects in this clinical trial and no SAEs or withdrawals due to adverse events have been observed. The most commonly reported adverse events in subjects receiving CCX168 in the multi-dose period were headache, diarrhea, dizziness, lower abdominal pain, nausea, and oropharyngeal pain.

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CCX168 Phase II Clinical Trial

We have initiated a Phase II clinical trial for CCX168. This is a randomized, double-blind, placebo-controlled clinical trial in patients with AAV with mild-to-moderate renal involvement, the aim of which is to optimize the treatment to induce remission for patients with non-life-threatening AAV with mild-to-moderate renal involvement. The intent is to reduce the toxicity of induction therapy by reducing the overall exposure to or eliminating entirely the use of systemic corticosteroids during the induction period with an inhibitor of the complement C5a receptor plus cyclophosphamide. The primary objective of this clinical trial is to evaluate the safety and tolerability of CCX168 in patients with AAV on background cyclophosphamide treatment. The secondary objectives of this clinical trial include assessment of the feasibility of reducing or eliminating the use of corticosteroids in the treatment of patients with AAV without the need for rescue corticosteroid measures; evaluation of the PK profile of CCX168 in patients with AAV and assessment of changes in renal function based on estimated glomerular filtration rate, hematuria, and proteinuria with CCX168 compared to placebo. The clinical trial is being conducted in sequential steps. Step 1 involves partial corticosteroid withdrawal and Step 2 involves full corticosteroid withdrawal. 30mg of CCX168 twice-daily given orally will be compared to placebo twice-daily for 84 days, followed by an 84-day follow-up period. We expect to complete enrollment of Step 2 in the second quarter of 2013. If this clinical trial meets the success criteria mutually agreed upon by the members of the JSC, GSK may exercise an option to further develop CCX168. Assuming that this clinical trial establishes clinical proof of concept, GSK s decision regarding the option is anticipated by the end of 2013. If GSK does not exercise its option, we will evaluate our options for further development of CCX168, which may entail internally developing this drug candidate or identifying another collaboration partner for its development.

CCX507 Next Generation CCR9 Inhibitor for IBD

Building on our expertise in the area of CCR9 antagonists and IBD, we started a *de novo* discovery program under which we have designed a series of novel molecules that we believe represent the next generation of CCR9 inhibitors. This followed the expiration of our target exclusivity obligations with respect to CCR9 under our collaboration agreement with GSK. The development candidate from this *de novo* series, CCX507, is selective for CCR9 relative to all other chemokine receptors, orally bioavailable, and has an excellent preclinical safety profile. Molecules such as CCX507 have been designed to interact with the CCR9 receptor in a unique way that produces molecules with greater potency towards CCR9 than other compounds reported to date. CCX507 is in Phase I clinical development and several related molecules from this program are currently in preclinical development.

CCX507 Phase I Clinical Trial

We have initiated a Phase I clinical trial with CCX507 in 40 healthy subjects. This is a randomized, double-blind, placebo-controlled clinical trial in which subjects receive either CCX507 as a single oral dose of 3mg, 10mg, or 30mg, or placebo. The primary study objective is assessment of safety and tolerability of CCX507. The PK profile of CCX507 will also be characterized.

CCX650 CXCR7 Inhibitor for Glioblastoma Multiforme (GBM)

Understanding Glioblastoma Multiforme

GBM is the most common and most aggressive of the primary brain tumors, accounting for 50%-60% of primary brain tumors in adults and it is slightly more common in men than in women. GBM is the most severe grade of brain tumors and is highly malignant, infiltrates the brain extensively and at times may become quite large before turning symptomatic. Median life expectancy of GBM patients receiving radiation post-surgery is only 12 months. Current treatments for GBM are still limited. The overall prognosis for GBM has changed little in the past two decades, despite major improvements in neuroimaging, neurosurgery, radiation treatment techniques, adjuvant chemotherapy, and supportive care. There are considerable unmet needs in GBM, most notably the relatively low survival benefit offered by the existing standard of care.

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CCX650 A Novel CXCR7 Inhibitor

We are developing drugs that target CXCR7 and combine an anti-angiogenic approach to stopping the blood supply to cancerous cells with anti-tumor activity via direct attack of tumor cells. Our most recent data support the notion that CXCR7 could be causally connected to tumor growth regulation. This is coupled with clear evidence from immunohistochemistry staining of primary human tumor tissues which revealed clear evidence of CXCR7 expression. In contrast to standard chemotherapies which can be highly toxic, our compounds are designed to selectively target CXCR7 in an effort to halt cancer progression while minimizing detrimental effects, such as generalized immunosuppression or cytotoxicity.

We believe we were the first to provide clear evidence that CXCR7 expression can directly control tumor growth *in vivo*. We and others have shown that CXCR7 regulates several important biological processes including tumor cell survival, cell adhesion, trans-endothelial migration, tumor development and metastatic growth in secondary organs, in a variety of *in vivo* and *in vitro* models. CXCR7 is expressed on many human tumor cells but not on most healthy cells. In our tumor model systems we found that reduction or inhibition of CXCR7 by genetic and pharmacological means reduces or abolishes tumor formation *in vivo*, and that the introduction of CXCR7 into a naïve background is both necessary and sufficient for that tumor to grow aggressively *in vivo*. CXCR7 is highly expressed in human GBM and in GBM-associated blood vessels.

We and others have demonstrated, using various aggressive GBM models in rodents, that CXCR7 inhibition is effective at preventing tumor growth, particularly when utilized in combination with radiation. Recent discoveries support a role for CXCR7 in preventing apoptosis, or programmed cell death, of human GBM cells. Separate observations indicate that recruitment of bone-marrow derived cells from blood into irradiated mouse GBM/brain is critical for tumor re-vascularization after irradiation and is dependent on CXCL12, the main chemokine ligand for CXCR7.

We have discovered several highly potent and selective small molecule compounds for CXCR7. An earlier compound CCX662, had excellent properties but was not suitable for oral administration. More recently, we developed CCX650, an orally active drug, as a potential clinical candidate and it is currently in preclinical development. Due to scientific and medical need reasons, our current efforts are primarily focused on the development of CCX650 for the treatment of GBM. A CXCR7 antagonist for the treatment of GBM may qualify for orphan drug status, which may provide a faster path to regulatory approval.

We believe that CCX650 represents a promising novel therapeutic for the treatment of GBM and other cancers. Preclinical studies support not only the anti-tumor efficacy of this drug but also an excellent safety profile, a reflection of its highly targeted and specific activity profile, which is fundamentally different from many other cytotoxic drugs in development or on the market.

Other Preclinical Programs

CCR4 Inhibitor for Atopic Dermatitis

CCR4 is expressed primarily on T helper-2, or Th2, cells, which are key drivers of allergic conditions, such as atopic dermatitis, asthma, and allergic rhinitis. Multiple investigators have demonstrated increased levels of CCR4-activating chemokines in skin and lung tissues in connection with atopic dermatitis and asthma, respectively. During the past few years, a number of pharmaceutical companies have tried to develop small molecule CCR4 antagonists but have consistently failed to advance a molecule into clinical trials, primarily due to the inability to identify molecules with sufficient potency and PK properties and with an adequate safety profile, particularly in regards to cardiovascular safety.

CCX6239, a novel, orally administered CCR4 antagonist with potential utility in the treatment of atopic dermatitis, an inflammatory disease of the skin that affects as many as 3% of adults in the United States. In its most severe form, it can be an absolutely debilitating disease.

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We have shown in preclinical models that CCX6239 effectively blocks the mobilization of white blood cells mediated by CCR4.

CCR6 Inhibitor for Autoimmune Diseases

One of the most intriguing areas of current research in immunology involves the study of a newly discovered type of helper T cells known as Th17 cells. While Th17 cells most likely play a role in the protection against extracellular pathogens, there is a large amount of preclinical and clinical data that implicate these cells, as well as IL-17, in the development of a large number of autoimmune diseases, including RA, psoriasis, asthma, and multiple sclerosis. Activated Th17 cells isolated from chronically inflamed human tissues produce high levels of TNF-a and other cytokines. A hallmark of Th17 cells is that they express high levels of CCR6, which is not found on Th1 and Th2 cells. High levels of the CCR6 chemokine CCL20 have been found in RA joint biopsies, psoriatic skin, and asthmatic lungs. We believe that these are potential therapeutic opportunities for a CCR6 antagonist. Our RAM screening technique has produced several suitable CCR6 antagonist leads, which are now being optimized via medicinal chemistry approaches.

CXCR6 Inhibitor for Chronic Hepatitis

Clearance of viral infections is associated with a vigorous T cell response. However, the immune system is often unable to clear hepatic infections. In fact, inflammation, chronic hepatitis and liver damage often result from persistent attempts by the immune system to deal with the underlying infection. The chemokine receptor known as CXCR6 is expressed on a subset of specialized inflammatory cells and is accepted, based on preclinical work with CXCR6-deficient mice, as a liver homing receptor for those cells. Under inflammatory conditions, various cell types in the liver produce the chemokine ligand that attracts CXCR6-expressing inflammatory cells. We believe that these effects may be blocked by our CXCR6 antagonists without the adverse side effects associated with the current methods of treatment.

Our Proprietary Drug Discovery Platform, EnabaLink

Since the founding of our company, we have developed a set of proprietary drug discovery tools, known collectively as the EnabaLink technology suite, specifically designed to unlock the chemokine system s complexity and to accelerate a productive drug discovery program. Our proprietary EnabaLink drug discovery technologies allow our scientists to accurately predict the specific chemokine receptors implicated in a given condition and to identify and optimize small molecule compounds best suited for treatment of the disease. One of the initial tools that we developed is a thorough functional genomic map of the chemokine system which assists us in our understanding of the role of a given chemokine receptor in the system as well as its likely effect on the migration of inflammatory cells in a given inflammatory disease state.

As part of this platform, we have also developed a proprietary high throughput cell migration-based assay, known as the RAM Assay, capable of identifying chemokine receptor inhibitors while eliminating non-specific inhibitors and cytotoxic inhibitors of cell migration. Our proprietary RAM Assay typically uses cells expressing a given chemokine receptor in its natural environment and enables the screening of small molecule libraries against chemokine receptor targets which are not amenable to traditional screening technologies. This produces additional novel chemical hits with structural diversity, allowing us to expand the number of chemical structures, which serve as starting points for subsequent optimization into drug candidates.

We have used our EnabaLink drug discovery engine to create a broad pipeline of promising chemokine-based drug candidates. The combination of proprietary in-house technologies and internally discovered drug candidates has resulted in an extensive intellectual property estate covering composition of matter and associated method of treatments for our compounds, novel biology-related discoveries, such as unique targets and new drug discovery technologies. We have generated more than six clinical or preclinical-stage programs, each targeting distinct chemokine receptors with different small molecule compounds. Drug candidates emerging from these programs act with high affinity and selectivity *in vitro* by binding to the precise chemokine receptor associated

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with the essential inflammatory processes underlying a given condition. Our compounds are designed to be highly potent and selective to minimize the risk of off-target effects and orally-available for improved patient compliance. As small molecules, they are also easier and less costly to manufacture than biologics.

Strategic Alliance with GSK

In August 2006, we entered into our strategic alliance with GSK. Through February 2013, we have received over $250 million from GSK, consisting of up-front and milestone payments, equity investments, research funding and option exercise fees. Under the terms of our agreement with GSK, we are responsible for the discovery and development of small molecule antagonists targeting four defined chemokine and chemo-attractant receptor targets (CCR9, CCR1, C5aR and ChemR23) and for advancing them through clinical proof-of-concept or to such other success criteria as are established by the JSC. After we demonstrate the satisfaction of the applicable success criteria, GSK is entitled to options to exclusively license drug candidates that are subject to the collaboration and two defined back-up compounds for each drug candidate for further development and commercialization on a worldwide basis. Upon exercising any of its options to drug candidates under the collaboration, GSK is solely responsible for all further clinical development and commercialization expenditures worldwide with respect to that drug candidate and its two designated back-up compounds. In exchange for the rights granted to GSK upon the exercise of its options, we are also entitled to receive regulatory and commercial milestone payments, as earned under the terms of our agreement, and royalties on the net sales of licensed drugs.

In December 2009, GSK exercised its option to obtain an exclusive license to further develop and commercialize vercirnon (CCR9) following our completion of the PROTECT-1 clinical trial. We received an option exercise fee of $35.0 million in January 2010 after GSK obtained Hart-Scott-Rodino clearance. After exercising the option, GSK became solely responsible for all further clinical development and commercialization expenditures for vercirnon and its two designated back-up compounds (CCX025 and CCX807) worldwide.

In November 2011, GSK exercised its option to obtain an exclusive license to further develop and commercialize CCX354 (CCR1) following our completion of the proof-of-concept clinical trial for this drug candidate. After exercising this option, GSK became solely responsible for all further clinical development and commercialization expenditures for CCX354 and its two designated back-up compounds (CCX721 and CCX956) worldwide. We received an option exercise fee of $25.0 million in December 2011.

In February 2012, based on unblinded data from a Phase I clinical trial of CCX832 (ChemR23), we and GSK determined not to further advance the development of CCX832 or its two designated back-up compounds. Thus, GSK s only remaining option is to CCX168 (C5aR) and its associated back-up compounds (CCX1378 and CCX1641).

With respect to CCX168, the remaining drug candidate subject to the agreement, GSK has an option exercisable with respect to such drug candidate and its two designated back-up compounds upon our demonstration that CCX168 successfully met the success criteria established by the JSC and, if GSK elects to exercise its option, we will be entitled to an option exercise fee of $25.0 million upon the exercise of such option by GSK.

GSK does not have exclusive rights to a given clinical indication or substitution rights with respect to a given collaboration target. Specifically, our proprietary programs around CCR2, CCR4, CCR6, CXCR7, CXCR6, or de novo efforts in CCR9 or CCR1 inhibitors, or any other receptors are not part of the GSK collaboration.

For each of our drug candidates subject to the agreement, we would be entitled to receive regulatory filing milestones of up to $47.0 million in the aggregate for the filing of an NDA in the United States and comparable filings in other territories, up to $75.0 million in the aggregate for the regulatory approval of products for commercial sale in the United States and other territories and up to $250.0 million in sales milestones for vercirnon and $125.0 million for each of CCX354 and CCX168.

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The collaboration agreement requires GSK to use commercially reasonable efforts to further develop and commercialize all licensed drug candidates, including conducting all further clinical trials, developing additional formulations if necessary, preparing and filing all regulatory filings, manufacturing the drug product and marketing the licensed drug worldwide. However, GSK has the right to discontinue the development and commercialization of any licensed drug candidate based on factors or considerations consistent with its diligence efforts. In the event that GSK exercises an option with respect to a drug candidate and later determines in good faith to cease the development and commercialization of the licensed drug, either in its entirety, or on a country-by-country basis, we can elect to further develop and commercialize such licensed drug under a non-exclusive license grant from GSK. If we so elect, we will be solely responsible for satisfying all obligations to third parties with respect to the development, manufacture or commercialization of such licensed drug including any ongoing obligations of GSK under any third party manufacturing, licensing or other agreements, and we will be obligated to pay GSK 3% to 5% of annual worldwide net sales of such licensed drug depending on the licensed drug s stage of development at the time at which we make such election.

In addition, we are entitled to receive base royalties on net sales of the licensed drugs. The base royalties for each program differ, but are set at levels commensurate with the development stage of each program at the time we entered into the agreement. With respect to vercirnon and its two designated back-up compounds, GSK is obligated to pay us different base royalties on net sales in the United States and outside the United States. Tiered base percentage royalties on net sales in IBD indications in the United States range from the mid-teens to the low twenties while tiered percentage royalties on net sales in IBD indications outside the United States range from the low to high teens. If we decide to exercise our co-development option for vercirnon, base royalty rates will increase by up to 5%, depending on the sales tier, the region and the indication for which the co-development option is exercised. With respect to CCX354 and CCX168, or any of their designated back-up compounds, GSK is obligated to pay us double-digit tiered percentage royalties with the potential to reach the mid-teens on annual worldwide net sales. We are also entitled to receive sales milestones on a per drug basis.

This agreement will expire with respect to each licensed drug and country upon the expiration of the payment obligations of GSK for that licensed drug in that country and would expire in its entirety upon the expiration of the last payment obligation of GSK for the last licensed drug in the last country. Following GSK s exercise of its options, GSK is obligated to pay us royalties on net sales of products that include a compound from such collaboration program in a given country for so long as a valid claim of our independently owned patents or a jointly owned patent covers or claims the composition of matter or a relevant method of use of a licensed drug candidate subject to the collaboration agreement. In the absence of such a valid claim on a country-by-country basis, GSK is obligated to pay a reduced royalty rate for a period of 12 years from the date of the first commercial sale of a licensed drug candidate as long as we own or control a pending patent application which covers the composition of matter or a relevant method of use of a licensed drug candidate. In the event that a particular licensed drug candidate is sold in a country in which a generic pharmaceutical product approved in reliance on the prior approval of such licensed drug candidate is also sold, then GSK is no longer obligated to pay us royalties on such licensed products after the end of the first 180-day period in which one or more third parties sell a number of units of the generic product worldwide equal to 25% or more of the aggregate number of units of the licensed drug candidate sold in such country during that same 180-day period. Consequently, it is not possible at this time to determine when GSK s payment obligations under the collaboration agreement will expire.

GSK may terminate the collaboration agreement for any reason upon 90 days prior written notice to us. The agreement and each program under the agreement may also be terminated under certain circumstances, including by either party for material breach or insolvency of the other party. The rights and obligations of the parties that survive termination of the agreement vary depending on the basis of the termination.

Under the terms of the agreement, with respect to each collaboration target, we are obligated to not, either alone or with a third party, conduct any research or development activities or grant any license or other rights with respect to the identification or optimization of small molecule inhibitors or agonists, as applicable, for such collaboration target unless and until either (i) GSK exercises its option to a drug candidate and its two back-up compounds with respect to such collaboration target or (ii) GSK terminates the collaboration program with

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respect to such collaboration target. Once the target exclusivity with respect to a collaboration target expires, we are free to initiate our own *de novo* proprietary drug discovery effort with respect to such target free of the exclusivity restrictions of our strategic alliance with GSK. There are no contractual restrictions that would preclude GSK from developing or investing in drug candidates that would compete with drug candidates that are subject to our collaboration with GSK.

Under the terms of the agreement, GSK has the right, but not the obligation, to defend against third party patent infringement claims for licensed drugs. If GSK elects to defend against any such claims, it has the sole right to direct the defense of such claims and settle such claims at its own cost and expense. If GSK elects not to defend against such claims, we have the right, but not the obligation, to defend against such claims. If the development or commercialization of licensed drugs requires use of third party intellectual property, we and GSK will share all license fees, provided however, that in the event that Millennium has valid patents relating to CCR9 and we are required to take a license from Millennium, we will be solely responsible for all fees required to be paid to Millennium in connection with such license. See Intellectual Property.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, novel biological discoveries, screening and drug development technology and other know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

As for the pharmaceutical products we develop and commercialize, as a normal course of business, we intend to pursue composition-of-matter patents, where possible, and dosage and formulation patents, as well as method of use patents on novel indications for known compounds. We also seek patent protection with respect to novel biological discoveries, including new targets and applications as well as adjuvant and vaccine candidates. We have also pursued patents with respect to our proprietary screening and drug development processes and technology. We have sought patent protection, either alone or jointly with our collaborators, as our collaboration agreements may dictate.

Our patent estate, on a worldwide basis, includes approximately 490 issued or allowed patents and approximately 255 pending patent applications, with claims relating to all of our current clinical stage drug candidates. With respect to our lead drug candidates in the CCR1, CCR2 and CCR9 programs, we have approximately 280 issued or allowed patents worldwide relating to their chemical composition or use thereof. There are also patent applications pending for our other clinical stage compounds in the C5aR program. We have approximately 70 issued patents relating to other small molecule compounds and approximately 90 issued patents relating to our novel biological discoveries. We also have approximately 50 issued patents relating to our proprietary screening and drug development technologies.

Our issued patents will expire on dates ranging from 2020 to 2029. However, the actual protection afforded by a patent varies on a product by product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the pate.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention

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assignment agreements with our commercial partners and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party.

Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drugs may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office to determine priority of invention.

Millennium Pharmaceuticals, Inc., or Millennium, has obtained certain United States patents which include claims to small molecules that modulate CCR9, compositions thereof, and methods of using them to treat conditions such as IBD. Millennium may contend that the claims of these patents cover our patented vercirnon drug candidate. We believe that our activities related to vercirnon are currently exempt from patent infringement liability because these activities are strictly limited to obtaining information for regulatory approval. However, if and when our vercirnon related activities extend beyond those related to seeking regulatory approval, such as, for example, if and when we commercialize vercirnon, Millennium might then commence an infringement action against us based on these patents and/or other related patents that it may be granted in the future. If Millennium elects to sue us, we believe that we may have viable defenses to any such infringement suit. However, we cannot assure you that the relevant court would find in our favor with respect to such defenses.

Competition

We compete in the pharmaceutical, biotechnology and other related markets that address IBD, chronic kidney disease and diabetic nephropathy, rheumatoid arthritis, other autoimmune diseases and inflammatory disorders, and cancer. We face significant competition from many pharmaceutical and biotechnology companies that are also researching and selling products designed to address these markets. Many of our competitors have materially greater financial, manufacturing, marketing, research and drug development resources than we do. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. 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. These organizations may also establish exclusive collaborative or licensing relationships with our competitors.

It is possible that our competitors will develop and market drugs that are less expensive and more effective than our drug candidates, or that will render our drug candidates obsolete. It is also possible that our competitors will commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates. If approved for marketing by the FDA, vercirnon, our lead drug candidate for the treatment of IBD, would compete against existing IBD treatments such as Remicade, Humira, and other TNF-a inhibitors, immunomodulatory drugs and corticosteroids and potentially against other novel IBD drug candidates that are currently in development. Remicade is a humanized monoclonal antibody targeted to TNF-a, indicated for the treatment of Crohn s disease, ulcerative colitis, rheumatoid arthritis, psoriasis, psoriatic arthritis and ankylosing spondylitis. Annual sales for Remicade totaled at least $7.5 billion in 2012. Humira, a similar drug, is also a human monoclonal antibody that acts as a TNF-a inhibitor. Marketed by Abbott Laboratories in the United States and Europe, Humira is approved for the treatment of Crohn s disease, rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. Annual worldwide sales for Humira totaled $9.5 billion in 2012.

We believe that vercirnon offers three distinct potential advantages as compared to currently used biologic therapies such as Remicade and Humira. First, unlike Remicade and Humira which are given by infusion or injection, vercirnon would be administered orally as a capsule or a tablet. We expect that oral administration of vercirnon will have a positive effect on patient compliance. Second, given that vercirnon is a small molecule

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which can be synthesized using standard chemistry processes, the molecule will be cheaper to manufacture than biologic agents which require complex and expensive cell based systems to produce a given biologic agent. The lower cost of goods for vercirnon could result in a more favorable pricing structure which, in turn, could lead to pharmaco-economic benefits for patients and healthcare providers. Third, vercirnon s mode of action may not lead to the broad suppression of the patient s immune system which is often seen with TNF-a inhibitors.

Our lead independent drug candidate, CCX140, a CCR2 antagonist, if approved for marketing by the FDA for diabetic nephropathy, would compete with treatments commonly used for type 2 diabetes and hypertension patients. ARBs and ACE inhibitors, are commonly prescribed treatments used to reduce blood pressure and preserve kidney function, reducing the progression of diabetic nephropathy. Many patients eventually progress to end-stage renal disease and require hemodialysis, peritoneal dialysis, or renal transplant.

CCX354 is our lead CCR1 antagonist candidate in RA. Current treatment options for RA consist of corticosteroids such as prednisone, immunosuppressants such as methotrexate (Rheumatrex and Trexall), azathioprine (such as Imuran), sulfasalazine (Azulfidine), hydroxychloroquine (Plaquenil) and 6-mercaptopurine (Purinethol), leflunomide (Arava), biologic agents including TNF-a inhibitors (etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), certolizumab (Cimzia), and golimumab (Simponi)), anakinra (Kineret), rituximab (Rituxan), abatacept (Orencia), and tocilizumab (Actemra), and a JAK inhibitor, tofacitinib (Xeljanz). There are also several novel, oral kinase inhibitors in Phase III development for RA including AstraZeneca / Rigel s fostamatinib.

Many of these currently approved treatments have notable and common adverse events including liver and bone marrow toxicity, renal toxicity, pneumonitis, immunosuppression, allergic reactions, autoimmune diseases and infections.

We expect that competition among any of our drugs approved for sale will be based on various factors, including drug safety and efficacy, prevalence of negative side effects, reliability, ease of administration, availability, price, insurance coverage and reimbursement status and patent position. We believe that our ability to compete depends largely upon our ability to research, develop and commercialize our existing and future drug candidates. Further, we need to continue to attract and retain qualified personnel, obtain patent protection, develop proprietary technology or processes and secure sufficient capital resources for the substantial time period between technological conception and commercial sales of drugs. Our ability to compete will also be affected by the speed at which we are able to identify and develop, conduct clinical testing and obtain regulatory approvals of our drug candidates. Potential competitors may develop treatments that are more effective and/or safer than our drug candidates or that would make our technology and drug candidates obsolete or non-competitive.

Established pharmaceutical companies that currently sell or are developing drugs in our markets of interest include AbbVie, Amgen, AstraZeneca, Biogen Idec, Bayer, Bristol-Myers Squibb, Elan, GSK, Johnson & Johnson, Merck, Merck Serono, Takeda, Novartis, Pfizer, Sanofi and Teva. Many or all of these established competitors are also heavily involved in research and drug development regarding various chemokine receptors. Pharmaceutical and biotechnology companies which are known to be involved in chemokine research and related drug development include Pfizer, GSK, Bristol-Myers Squibb, Merck, AstraZeneca, Boehringer-Ingelheim, Takeda, Sanofi, Incyte, and UCB Pharma among others. These companies and others also compete with us in recruiting and retaining qualified scientific and management personnel, and in acquiring technologies complementary to, or necessary for, our programs.

Manufacturing

Our current drug candidates are manufactured using common chemical engineering and synthetic processes from readily available raw materials. Following GSK s exercise of its options for the further development of vercirnon and CCX354, it assumed sole manufacturing responsibility for these drug candidates and each of their two respective designated back-up compounds. We rely on contract manufacturing organizations to produce our

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other drug candidates in accordance with the FDA s current good manufacturing practices, or cGMP, regulations for use in our clinical trials. However, we currently rely on a single source supplier for our requirements of the API of each of these other drug candidates. The manufacture of pharmaceuticals is subject to extensive cGMP regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel and quality control. We expect to rely on contract manufacturers for the manufacture of clinical and commercial supplies of our compounds other than those drug candidates for which GSK has exercised its option.

We purchase quantities of our drug candidates from our contract manufacturers pursuant to purchase orders that we place from time to time. If we were unable to obtain sufficient quantities of drug candidates or receive raw materials in a timely manner, we could be required to delay our ongoing clinical trials and seek alternative manufacturers, which would be costly and time-consuming. We believe we have multiple potential sources for our contract manufacturing.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, export and import of our drug candidates.

In the United States, the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act and the FDA s implementing regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA s refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. The process required by the FDA before our drug candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies all performed in accordance with the FDA s current good laboratory practices, or cGLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application which must become effective before human clinical trials in the United States may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP regulations; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our drug candidates will be granted on a timely basis, if at all.

Once a pharmaceutical drug candidate is identified for development, it enters the preclinical testing stage. Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. The IND automatically

becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or

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questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing the clinical trials to commence or not allowing the clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial conducted during drug development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. An independent institutional review board, or IRB, for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, requirements, including the requirements for informed consent.

All clinical research performed in the United States in support of an NDA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to FDA in support of an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial. We conducted our PROTECT-1 clinical trial solely at foreign clinical research sites, and we did not have authorization from the FDA under an IND to conduct that clinical trial in the United States. We designed the clinical trial to comply with FDA regulatory requirements for the use of foreign clinical data in support of an NDA, and the data were submitted from the PROTECT-1 clinical trial in support of future U.S. marketing application for vercirnon. We are pursuing a similar development strategy for CCX140 for which we are currently conducting two Phase II clinical trials in patients with diabetic nephropathy in certain European countries. These clinical trials are also designed to comply with FDA regulatory requirements so that the data from these trials can be used to support a regulatory filing in the United States. We plan to include the United States and Europe in our later-stage clinical development program for CCX140 and for other drug candidates we develop independently prior to filing for an NDA with the FDA and the EMA.

Clinical Trials

For purposes of NDA submission and approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

Phase I clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.

Phase II clinical trials are generally conducted in a limited patient population to:

evaluate dosage tolerance and appropriate dosage;

identify possible adverse effects and safety risks; and

evaluate preliminarily the efficacy of the drug for specific targeted indications in patients with the disease or condition under study.

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Phase III clinical trials, commonly referred to as pivotal studies, are typically conducted when Phase II clinical trials demonstrate that a dose range of the drug candidate is effective and has an acceptable safety profile. Phase III clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.

In some cases, the FDA may condition approval of an NDA on the sponsor s agreement to conduct additional clinical trials to further assess the drug s safety and effectiveness after NDA approval. Such post-approval clinical trials are typically referred to as Phase IV clinical trials.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

New Drug Applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Once an NDA has been accepted for filing, by law the FDA has 180 days for a priority review to examine the application and respond to the applicant. However, the review process is often significantly extended by FDA requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to NDAs within ten months of the filing date for standard review, but this timeframe is also often extended. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of an NDA if the applicable statutory and regulatory criteria are not satisfied, or it may require additional clinical data or an additional Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. Once the FDA approves an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the drug reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such drug or require a recall of any drug already on the market. In addition, the FDA may require testing, including Phase IV clinical trials and surveillance programs to monitor the effect of approved drugs which have been commercialized. The FDA has the authority to prevent or limit further marketing of a drug based on the results of these post-marketing programs.

A sponsor may also seek approval of its drug candidates under programs designed to accelerate FDA s review and approval of NDAs. For instance, a sponsor may seek FDA designation of a drug candidate as a fast track product. Fast track products are those products intended for the treatment of a serious or life-threatening disease or condition and which demonstrate the potential to address unmet medical needs for such disease or condition. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the remaining information. In some cases, a fast track product may be approved on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on

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irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Approvals of this kind typically include requirements for appropriate post-approval Phase IV clinical trials to validate the surrogate endpoint or otherwise confirm the effect of the clinical endpoint. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established a new category of drugs referred to as breakthrough therapies that may be subject to accelerated approval. A sponsor may seek FDA designation of a drug candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. FDA is required to issue guidance to implement this provision and, if deemed necessary, is required to amend its regulations by 2014. Drug candidates may also be eligible for priority review, or review within a six month timeframe from the date a complete NDA is accepted for filing, if a sponsor shows that its drug candidate provides a significant improvement compared to marketed drugs. When appropriate, we intend to seek fast track designation and/or accelerated approval for our drugs. We cannot predict whether any of our drug candidates will obtain a fast track and/or accelerated approval designation, or the ultimate impact, if any, of the fast track or the accelerated approval process on the timing or likelihood of FDA approval of any of our proposed drugs.

Drugs may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving an application, the FDA will inspect the facility or the facilities at which the finished drug product, and sometimes the active drug ingredient, is manufactured, and will not approve the drug unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the drug unless compliance with GCP requirements is satisfactory.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our drug candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Preclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the drugs. After approval, certain changes to the approved drug, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Depending on the nature of the change proposed, an NDA supplement must be filed and approved before the change may be implemented. For many proposed post-approval changes to an NDA, the FDA has up to 180 days to review the application. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

Other Regulatory Requirements

Any drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or

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possible civil penalties. We cannot be certain that we or our present or future third party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution or withdraw approval of the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product s labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers communications regarding off-label use.

Healthcare Reform

In March 2010, the President signed one of the most significant healthcare reform measures in decades. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The comprehensive $940 billion dollar overhaul is expected to extend coverage to approximately 32 million previously uninsured Americans. The Affordable Care Act contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Additionally, the Affordable Care Act:

- mandates a further shift in the burden of Medicaid payments to the states;
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D, beginning January 2011; and
- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell branded prescription drugs to specified federal government programs.

The Affordable Care Act also establishes an Independent Payment Advisory Board, or IPAB, to reduce the per capita rate of growth in Medicare spending. Beginning in 2014, IPAB is mandated to propose changes in Medicare payments if it is determined that the rate of growth of Medicare expenditures exceeds target growth rates. The IPAB has broad discretion to propose policies to reduce expenditures, which may have a negative impact on payment rates for services, including imaging services. A proposal made by the IPAB is required to be implemented by the U.S. government s Centers for Medicare & Medicaid Services unless Congress adopts a proposal with savings greater than those proposed by the IPAB. IPAB proposals may impact payments for physician and free-standing services beginning in 2015 and for hospital services beginning in 2020.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. Most recently, on August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other

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things, creates the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. In the event that the Joint Select Committee is unable to achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, or Congress does not act on the committee s recommendation, without amendment, by December 23, 2011, an automatic reduction is triggered. These automatic cuts would be made to several government programs and, with respect to Medicare, would include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. The ATRA also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The full impact on our business of the Affordable Care Act and other new laws is uncertain. Nor is it clear whether other legislative changes will be adopted, if any, or how such changes would affect the demand for our drugs once commercialized.

Third-Party Payor Coverage and Reimbursement

Although none of our drug candidates has been commercialized for any indication, if they are approved for marketing, commercial success of our drug candidates will depend, in part, upon the availability of coverage and reimbursement from third-party payors at the federal, state, and private levels. Government payor programs, including Medicare and Medicaid, private health care insurance companies, and managed-care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The U.S. Congress and state legislatures from time to time propose and adopt initiatives aimed at cost-containment. Ongoing federal and state government initiatives directed at lowering the total cost of health care will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid payment systems. Examples of how limits on drug coverage and reimbursement in the United States may cause reduced payments for drugs in the future include:

- changing Medicare reimbursement methodologies;
- fluctuating decisions on which drugs to include in formularies;
- revising drug rebate calculations under the Medicaid program; and
- reforming drug importation laws.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers who use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our drug candidates and operate profitably.

Other Healthcare Laws and Regulations

We are also subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. The laws that may affect our ability to operate include:

- the federal healthcare programs Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

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- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and impact our financial results.

International Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future drugs. Whether or not we obtain FDA approval for a drug, we must obtain approval of a drug by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the drug in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marking authorization that is valid for all European Union member states. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marking authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of our future drugs.

Employees

As of December 31, 2012, we had 61 full-time employees, 29 of whom hold Ph.D.s, M.D.s or both. Of our total workforce, 50 employees are engaged in research and development, and 11 employees are engaged in business development, finance, legal, human resources, facilities, information technology administration and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We believe that our relations with our employees are good.

Research and Development

We invested $34.6 million, $28.4 million and $33.5 million in research and development in the years 2012, 2011 and 2010, respectively.

About ChemoCentryx

We commenced operations in 1997. Our principal offices are located at 850 Maude Avenue, Mountain View, California 94043, and our telephone number is (650) 210-2900. Our website address is www.chemocentryx.com. The information contained in, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. We have a wholly owned subsidiary, ChemoCentryx Limited, organized under the laws of the United Kingdom that is currently inactive.

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Financial Information about Segments

We operate only in one business segment, which is the commercialization and development of pharmaceutical products. See note 1 to our consolidated financial statements included in this Annual Report on Form 10-K. For financial information regarding our business, see Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and related notes.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at www.chemocentryx.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov. The information in or accessible through the SEC and our website are not incorporated into, and are not considered part of, this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

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Item 1A. Risk Factors

The following section includes the most significant factors that may adversely affect our business and operations. You should carefully consider the risks and uncertainties described below and all information contained in this Annual Report on Form 10-K before deciding to invest in our common stock. If any of the following risks actually occur, our business, financial condition, results of operations and growth prospects would likely be materially and adversely affected. In that event, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risks Related to Our Business

We anticipate that we will continue to incur significant losses for the foreseeable future, and if we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

We are a clinical-stage biopharmaceutical company. We do not currently have any products approved for sale, and we continue to incur significant research and development and general and administrative expenses related to our operations. Our net loss for the years ended December 31, 2012, 2011 and 2010 was $39.9 million, $4.6 million and $3.1 million, respectively. As of December 31, 2012, we had an accumulated deficit of $134.2 million. We expect to continue to incur significant losses for the foreseeable future. We expect these losses and our cash utilization to increase in the near term as we continue to conduct clinical trials for CCX140, CCX168, CCX872 and CCX507 and conduct research and development of our other drug candidates. Glaxo Group Limited, or GSK, an affiliate of GlaxoSmithKline, has assumed all funding obligations for the further clinical development and commercialization of vercirnon and CCX354. If GSK exercises its option for further development and commercialization of CCX168, our remaining drug candidate subject to the agreement, it will assume all funding obligations with respect to further clinical development of such drug candidate, but if it does not exercise such option, we will be responsible for such funding obligations. All of our products are in development and none has been approved for sale. To date, we have derived all of our revenues from up-front fees and milestone payments, other payments pursuant to our collaboration agreements and government grants and contracts for research and development. We do not anticipate that we will generate revenue from the sale of our products for the foreseeable future. In addition, if approved, we expect to incur significant costs to commercialize our drug candidates and our drugs may never gain market acceptance. If our drug candidates fail to demonstrate safety and efficacy in clinical trials, do not gain regulatory approval, or do not achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or whether we will become profitable.

The commercial success of vercirnon depends, in large part, on the development and marketing efforts of GSK, and if GSK is unable to perform in accordance with the terms of our agreement, or is unable to obtain the required regulatory approvals for vercirnon, our potential to generate future revenue from this drug candidate would be significantly reduced and our business would be materially and adversely harmed.

Since inception, we have invested a significant portion of our time and financial resources in the development of our most advanced drug candidate, vercirnon. We currently have five other drug candidates in clinical trials, but we anticipate that our ability to generate significant product revenues in the near term will depend primarily on the successful development, regulatory approval, marketing and commercialization of vercirnon by us or by GSK, which is subject to significant uncertainty. In particular, we rely on GSK to fund and conduct the current pivotal Phase III trials with respect to vercirnon. Any of the following events or factors could have a material adverse effect on our ability to generate revenue from the commercialization of vercirnon:

- GSK may be unable to successfully complete the clinical development of vercirnon;
- GSK must comply with additional requests and recommendations from the FDA, including additional clinical trials;

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GSK may not obtain all necessary approvals from the FDA and similar foreign regulatory agencies;

GSK may not commit sufficient resources to the development, regulatory approval, marketing and distribution of vercirnon;

Vercirnon must be manufactured in compliance with requirements of the FDA and similar foreign regulatory agencies and in commercial quantities sufficient to meet market demand;

Vercirnon may not achieve market acceptance by physicians, patients and third party payors;

Vercirnon may not compete successfully against alternative products and therapies; and

We, GSK or any other pharmaceutical organization may independently develop products that compete with vercirnon.

In order to obtain approval from the FDA of a new drug application, or NDA, for vercirnon, GSK will need to demonstrate through evidence from adequate and well-controlled clinical trials that vercirnon is safe and effective for each proposed indication. However, vercirnon may not be approved even though it achieved its specified endpoints in the current and/or future pivotal Phase III clinical trials intended to support an NDA which may be conducted by GSK. The FDA may disagree with the trial design and the interpretation of data from clinical trials, may ask GSK to conduct additional costly and time consuming clinical trials in order to obtain marketing approval or approval to enter into an advanced phase of development, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. The FDA may also approve vercirnon for fewer or more limited indications than GSK may request, or may grant approval contingent on the performance of costly post-approval clinical trials. In addition, the FDA may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of vercirnon.

If GSK or any of our future collaboration partners does not perform in the manner we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, regulatory approval, and commercialization efforts related to vercirnon could be delayed or terminated. It may be necessary for us to assume the responsibility at our own expense for the development of vercirnon. In that event, we would likely be required to limit the size and scope of one or more of our programs or increase our expenditures and seek additional funding and our potential to generate future revenue from vercirnon would be significantly reduced and our business would be materially and adversely harmed.

If GSK does not exercise its option thereunder, if the further development and commercialization efforts of GSK are not successful with respect to drug candidates for which it does exercise its options thereunder, or if GSK terminates the alliance or a particular program thereunder, we will not receive any additional revenue under the alliance with respect to such programs and our results of operations and financial condition will be materially adversely affected.

In August 2006, we entered into our strategic alliance with GSK. Under the terms of our agreement, we are responsible for the discovery and development of small molecule antagonists targeting four defined chemokine and chemo-attractant receptor targets (CCR9, CCR1, C5aR and ChemR23) and taking them through clinical proof-of-concept, or to such other success criteria as are established by the JSC. If we demonstrate the satisfaction of the applicable success criteria, GSK is entitled to options to exclusively license drug candidates that are subject to the collaboration and two defined back-up compounds for each drug candidate for further development and commercialization on a worldwide basis.

In December 2009, GSK exercised its option under the agreement to obtain an exclusive license for the further development and commercialization of vercirnon, our CCR9 drug candidate, and two identified back-up compounds (CCX025 and CCX807). As a result of GSK s exercise of this option, we are entitled to receive (x) up to $82.0 million, in the aggregate, consisting of (1) a non-refundable option exercise fee of $35.0 million and (2) up to $47.0 million in the aggregate for the filing of an NDA in the United States and comparable filings in other territories, (y) up to $75.0 million in the aggregate for the regulatory approval of products for

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commercial sale in the United States and other territories and (z) up to $250.0 million in sales milestones. In January 2010, after GSK obtained Hart-Scott-Rodino clearance for its option exercise, it paid us the option exercise fee of $35.0 million and assumed sole responsibility for the further development and commercialization of vercirnon and its two designated back-up compounds, at its expense, subject to our specified co-development and commercial participation rights.

In November 2011, GSK exercised its option under the agreement to obtain an exclusive license for the further development and commercialization of CCX354, our CCR1 drug candidate, and two identified back-up compounds (CCX721 and CCX956). As a result of GSK s exercise of this option, we are entitled to receive (x) up to $72.0 million, in the aggregate, consisting of (1) a non-refundable option exercise fee of $25.0 million and (2) up to $47.0 million in the aggregate for the filing of an NDA in the United States and comparable filings in other territories, (y) up to $75.0 million in the aggregate for the regulatory approval of products for commercial sale in the United States and other territories and (z) up to $125.0 million in sales milestones. In December 2011, GSK paid us the option exercise fee of $25.0 million and assumed sole responsibility for the further development and commercialization of CCX354 and its two designated back-up compounds, at its expense. There is no assurance that GSK will be successful in its further development and commercialization of CCX354 or that the relevant regulatory filing or approval or sales milestones can be achieved such that we will receive the related milestone payments.

In February 2012, we and GSK determined not to further advance the development of CCX832 (ChemR23) or its two designated back-up compounds. Thus, GSK s only remaining option is to CCX168 (C5aR) and its associated back-up compounds (CCX1378 and CCX1641).

If GSK elects to exercise its option to CCX168, we would be entitled to receive, as with CCX354, (x) up to $72.0 million, in the aggregate, consisting of (1) an option exercise fee of $25.0 million and (2) up to $47.0 million in the aggregate for the filing of an NDA in the United States and comparable filings in other territories, (y) up to $75.0 million in the aggregate for the regulatory approval of products for commercial sale in the United States and other territories and (z) up to $125.0 million in sales milestones. We cannot assure you that we will be able to satisfy the success criteria established by the JSC under this strategic alliance with respect to CCX168 or that the relevant regulatory filing or approval milestones can be achieved for any our programs so that we will receive the related option exercise fees and milestone payments. In addition, even if CCX168 results does satisfy the agreed upon success criteria, GSK is under no obligation to exercise its remaining option with respect to CCX168 and we cannot assure you that GSK will exercise such option, or that GSK will obtain Hart-Scott-Rodino clearance with respect to such option, to the extent that such approval is required.

GSK may terminate the entire collaboration agreement or any collaboration program on a program-by-program basis for any reason upon 90 days prior written notice to us. The agreement or any program under the agreement may also be terminated for cause under certain circumstances, including material breach and insolvency. In addition, GSK may terminate its rights with respect to the licensed product if it determines in good faith, for any reason, to cease the development and commercialization of such product and provides us with a written notice of such intent.

If GSK does not exercise its option with respect to CCX168, terminates its rights with respect to a licensed product, or terminates the agreement:

- we would not be entitled to receive the relevant option exercise fee or milestone payments;
- we would owe GSK up to 5% royalties with respect to drug candidates covered by the agreement which we elected to subsequently commercialize, depending upon the stage of development at which such product commercialization rights reverted back to us;
- the development of our drug candidates subject to the agreement may be terminated or significantly delayed;

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- we may be required to hire additional employees and allocate scarce resources to the development and commercialization of drug candidates that were previously the subject of the GSK agreement and as a result our cash expenditures could increase significantly;

- we would bear all of the risks and costs related to the further development and commercialization of drug candidates that were previously the subject of the GSK agreement, including the reimbursement of third parties; and

- we may need to establish alternative collaboration arrangements, and we may not be able to do so, or may not be able to do so on terms which are acceptable to us, in which case we would likely be required to limit the size or scope of one or more of our programs or increase our expenditures and seek substantial additional funding.

Any of these events would have a material adverse effect on our results of operations and financial condition.

The development of new drugs is a highly risky undertaking which involves a lengthy process, and our drug discovery and development activities therefore may not result in products that are approved by the applicable regulatory authorities on the time schedule we have planned, or at all.

Our drug candidates are in the early stages of drug discovery or clinical trials and are prone to the risks of failure inherent in drug development. As of the date of this Annual Report on Form 10-K, only six of our current drug candidates, vercirnon, CCX140, CCX354, CCX168, CCX872 and CCX507 have been tested in human beings. We will need to conduct significant additional preclinical studies and clinical trials before we can demonstrate that any of our drug candidates is safe and effective to the satisfaction of the FDA and other regulatory authorities. Preclinical studies and clinical trials are expensive and uncertain processes that take years to complete. For example, we incurred significant expenses related to the IND filing and the completed single ascending dose Phase I clinical trial for CCX915, our first generation CCR2 drug candidate, which did not advance into Phase II clinical trials because its pharmacokinetic properties in humans did not meet our expectations. Failure can occur at any stage of the process, and we cannot assure you that any of our drug candidates will result in commercially successful products.

We cannot assure you that our ongoing clinical trials or any future clinical trial of any of our other drug candidates, will be completed on schedule, or at all, or whether our planned clinical trials will start in a timely manner. The commencement of our planned clinical trials could be substantially delayed or prevented by a number of factors, including:

- delays or failures in obtaining sufficient quantities of the active pharmaceutical ingredient, or API, and/or drug product;

- delays or failures in reaching agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites;

- delays or failures in obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;

- the need to successfully complete, on a timely basis, preclinical safety pharmacology studies;

- the limited number of, and competition for, suitable sites to conduct the clinical trials;

- the limited number of, and competition for, suitable patients for enrollment in the clinical trials; and

- delays or failures in obtaining regulatory approval to commence a clinical trial.

The completion of our clinical trials could also be substantially delayed or prevented by a number of factors, including:

slower than expected rates of patient recruitment and enrollment;

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failure of patients to complete the clinical trials;

failure of our third party vendors to timely or adequately perform their contractual obligations relating to the clinical trials;

inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;

inability to monitor patients adequately during or after treatment;

termination of the clinical trials by one or more clinical trial sites;

unforeseen safety issues;

lack of efficacy demonstrated during clinical trials;

lack of adequate funding to continue the clinical trials;

the need for unexpected discussions with the FDA or other foreign regulatory agencies regarding the scope or design of our clinical trials or the need to conduct additional trials;

unforeseen delays by the FDA or other foreign regulatory agencies after submission of our results;

an unfavorable FDA inspection of our contract manufacturers of API or drug product; and

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold.

Any failure or significant delay in completing clinical trials for our drug candidates would harm the commercial prospects for our drug candidates and adversely affect our financial results.

Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to regulatory agencies and ethics committees for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for our drug candidates may be harmed and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a drug candidate.

If we are required to suspend or discontinue clinical trials due to side effects or other safety risks, or if we are required to conduct studies on the long-term effects associated with the use of our drug candidates, our efforts to commercialize our products could be delayed or halted.

Our clinical trials may be suspended or terminated at any time for a number of safety-related reasons. For example, we may voluntarily suspend or terminate our clinical trials if at any time we believe that our drug candidates present an unacceptable safety risk to the clinical trial patients. In addition, IRBs or regulatory agencies may order the temporary discontinuation or termination of our clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, including if they present an unacceptable

safety risk to patients. Administering any drug candidate to humans may produce undesirable side effects. The existence of undesirable side effects resulting from our drug candidates could cause us or regulatory authorities, such as the FDA, to interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory agencies denying further development or approval of our drug candidates for any or all targeted indications. This, in turn, could affect whether GSK exercises its remaining option with respect to CCX168 under our strategic alliance and could prevent us from commercializing our drug candidates.

Further, chemokine receptors and chemo-attractant receptors are a novel class of targets. As a result, we may experience unforeseen adverse side effects with our existing and future drug candidates, including vercirnon

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and CCX140. As of the date of this Annual Report on Form 10-K, six of our current drug candidates have been tested in human beings. Although we have not observed significant harmful side effects in prior studies of vercirnon, CCX140 or our other drug candidates, later trials could reveal such side effects. The pharmacokinetic profile of preclinical studies may not be indicative of results in any clinical trial. For example, prior to commencing our preclinical studies of our CCX140 drug candidate, we studied another drug candidate that targeted CCR2, which we abandoned after pharmacokinetic results were not as favorable in humans as in earlier preclinical animal studies. We have not conducted studies on the long-term effects associated with the use of our drug candidates. Studies of these long-term effects may be required for regulatory approval and would delay our introduction of vercirnon, CCX140 or our other drug candidates into the market. These studies could also be required at any time after regulatory approval of any of our drug candidates. Absence of long-term data may also limit the approved uses of our products, if any, to short-term use. Some or all of our drug candidates may prove to be unsafe for human use.

Even if our drug candidates do obtain regulatory approval they may never achieve market acceptance or commercial success.

Even if we obtain FDA or other regulatory approvals, our drug candidates may not achieve market acceptance among physicians, patients and third party payors and, ultimately, may not be commercially successful. Market acceptance of our drug candidates for which we receive approval depends on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the clinical indications for which the drug is approved;
- acceptance by physicians, major operators of clinics and patients of the drug as a safe and effective treatment;
- the potential and perceived advantages of our drug candidates over alternative treatments;
- the safety of drug candidates seen in a broader patient group, including its use outside the approved indications;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third parties and government authorities;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of our sales and marketing efforts.

Any failure by our drug candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our financial results.

The commercial success of CCX140 depends, in part, on our ability to develop and market the drug in North America and to find partners to co-develop and commercialize the drug outside North America, and if we fail in these initiatives, our ability to generate future revenue could be significantly reduced.

If we successfully complete the Phase II program for our lead independent drug candidate, CCX140, we plan to initiate Phase III clinical trials either alone or together with a co-development partner. We plan to retain commercial rights to CCX140 in North America and find partners for co-development and commercialization outside North America. We have invested a significant amount of our time and financial resources in the development of CCX140 and our ability to generate future revenue will depend, in part, on our ability to identify a co-development partner and the development, regulatory approval, marketing and commercialization of CCX140 by us and any future partners. Any of the following events or factors could have a material adverse effect on our ability to generate revenue from the commercialization of CCX140:

We may be unable to successfully complete the clinical development of CCX140;

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Our lack of experience in commercializing and marketing drug products;

We may not have or be able to obtain sufficient financial resources to develop and commercialize CCX140;

We may not be able to identify a suitable co-development partner;

We or any of our future partners may fail to fulfill our responsibilities in a timely manner or fail to commit sufficient resources to the development, regulatory approval, and commercialization efforts related to CCX140;

We or any of our future partners must comply with additional requests and recommendations from the FDA, including additional clinical trials;

We or any of our future partners may not obtain all necessary approvals from the FDA and similar foreign regulatory agencies;

CCX140 must be manufactured in compliance with requirements of FDA and similar foreign regulatory agencies and in commercial quantities sufficient to meet market demand;

CCX140 may not achieve market acceptance by physicians, patients and third party payors;

CCX140 may not compete successfully against alternative products and therapies; and

We or any pharmaceutical company may independently develop products that compete with CCX140.

We rely on third parties to conduct all our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize any of our drug candidates.

We currently do not have the ability to independently conduct preclinical studies or clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, collaborative partners and other third parties, such as clinical research organizations, or CROs, to conduct clinical trials on our drug candidates. The third parties with which we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. These third parties are not our employees, and except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our programs. In particular, we rely on GSK to fund and conduct the current pivotal Phase III trials with respect to vercirnon. Although we rely on these third parties to conduct our preclinical studies and clinical trials, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol. Moreover, the FDA and foreign regulatory authorities require us to comply with regulations and standards, commonly referred to as current good clinical practices, or cGCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials.

In addition, the execution of preclinical studies and clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. Moreover, these third parties may also have relationships with other commercial entities, some of which may compete with us. In most cases, these third parties may terminate their agreements with us upon 30 days prior written notice of a material breach by us that is not cured within 30 days. Many of these agreements may also be terminated by such third parties under certain other circumstances, including our insolvency or our failure to comply with applicable laws. In general, these agreements require such third parties to reasonably cooperate with us at our expense for an orderly winding down of services of such third parties under the agreements. If the

third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial

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protocols or cGCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties, which could be costly, and our clinical trials may be extended, delayed or terminated or may need to be repeated, and we may not be able to obtain regulatory approval for or commercialize the drug candidate being tested in such trials.

If any of our drug candidates receives marketing approval and we or others later identify undesirable side effects caused by the drug candidate, our ability to market and derive revenue from the drugs could be compromised.

If we or others identify undesirable side effects caused by one of our drugs, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we may be required to recall the drug or change the way the drug is administered;
- additional restrictions may be imposed on the marketing of the particular drug or the manufacturing processes;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these could result in the loss of significant revenues, which would materially and adversely affect our results of operations and business.

We will need additional financing and may be unable to raise capital on acceptable terms, or at all, when needed, which would force us to delay, reduce or eliminate our research and development programs and other operations or commercialization efforts.

We are advancing multiple drug candidates through discovery and development and will require substantial funds to conduct development, including preclinical studies and clinical trials, of our drug candidates. Commercialization of any drug candidate will also require substantial expenditures. While we currently expect GSK to assist us in our development and commercialization efforts with respect to those of our drug candidates for which GSK exercises an option under our agreement, we may also need additional financing to the extent that we are required to hire additional employees to co-promote drug candidates or to commercialize drug candidates that may not be covered by our collaboration agreement.

As of December 31, 2012, we had approximately $119.0 million in cash, cash equivalents and investments. We believe that our available cash, cash equivalents and investments will be sufficient to fund our anticipated level of operations for at least the next 12 months. Our future financing requirements will depend on many factors, some of which are beyond our control, including:

the rate of progress and cost of our clinical trials, preclinical studies and other discovery and research and development activities;

the timing of, and costs involved in, seeking and obtaining FDA and other regulatory approvals;

the continuation and success of our strategic alliance with GSK and future collaboration partners;

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the exercise of the remaining option with respect to CCX168 under the GSK agreement;

the costs of preparing, filing, prosecuting, maintaining and enforcing any patent claims and other intellectual property rights, including litigation costs and the results of such litigation;

our ability to enter into additional collaboration, licensing, government or other arrangements and the terms and timing of such arrangements;

potential acquisition or in-licensing of other products or technologies; and

the emergence of competing technologies or other adverse market developments.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. We currently have no understandings, commitments or agreements relating to any of these types of transactions.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to finance future cash needs primarily through public or private equity offerings, debt financings, government grants and contracts and/or strategic collaborations. Additional financing may not be available to us when we need it or it may not be available on favorable terms, if at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or our commercialization efforts. We may be required to enter into collaborative partnerships for one or more of our drug candidate programs at an earlier stage of development or on less favorable terms, which may require us to relinquish rights to some of our drug candidates that we would otherwise have pursued on our own.

We may form additional strategic alliances in the future with respect to our independent programs, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties with respect to our independent programs that we believe will complement or augment our existing business. For example, we plan to find a partner for co-development and commercialization of CCX140 outside North America upon completion of clinical development of CCX140 for the treatment of patients with diabetic nephropathy. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction. Any delays in entering into new strategic partnership agreements related to our product candidates could also delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Key elements of our proprietary suite of drug discovery technologies, known as EnabaLink, including our RAM screening technology, are new approaches to the discovery and development of new drug candidates and may not result in the discovery of any small molecule compounds of commercial value.

We must continue to identify and develop compounds that target the chemokine network and expand our portfolio of drug candidates. Research programs to identify new disease targets and drug candidates require substantial technical, financial and human resources. We have limited resources to study the more than 50 known chemokine ligands, as described in a February 2006 article in the New England Journal of Medicine , and approximately 25 identified chemokine receptors. EnabaLink represents a new approach to the development of new drug candidates (see Item 1. Business Our Proprietary Drug Discovery Platform, EnabaLink) and we cannot assure you that EnabaLink will result in the discovery of new drug candidates. EnabaLink has only

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resulted in a limited number of clinical and preclinical stage programs to date, and we may not identify any therapeutic small molecule compounds of commercial value using EnabaLink or other commercially available drug discovery technologies.

If our Reverse Activation of Migration, or RAM, screening technology or any other screening technologies fail to identify highly specific hits that lead to the development of new drug candidates, our business may be materially and adversely affected. Our scientists may be unable to optimize the chemical hits identified by our RAM screening technology and develop the identified starting material into a candidate for further development that meets the desired product criteria. Our research and development programs may initially show promise in identifying chemokine receptors and their impact on the body s immune system, yet fail to yield drug candidates that are suitable for preclinical and clinical development. We cannot assure you that our current efforts will be successful or that we will not abandon any of our efforts in the future related to a particular chemokine receptor or small molecule program.

We rely on third party contract manufacturing organizations to manufacture and supply our drug candidates for us, other than vercirnon and CCX354 for which GSK has manufacturing responsibility. If one of our suppliers or manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts to find new suppliers or manufacturers. We may also face delays in the development and commercialization of our drug candidates.

Following GSK s exercise of its options for the further development of vercirnon and CCX354, it assumed sole manufacturing responsibility for those drug candidates and each of their two respective back-up compounds and we are no longer involved in their manufacture. We currently have limited experience in, and we do not own facilities for, manufacturing our other drug candidates. We rely upon third party contract manufacturing organizations to manufacture and supply larger quantities of these other drug candidates. The manufacture of pharmaceutical products in compliance with current good manufacturing practices, or cGMP, requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the drug candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced FDA cGMP requirements, other federal and state regulatory requirements, and foreign regulations. Raw materials for the synthesis of our API are sourced globally. If the manufacturers of our raw materials and pharmaceutical products were to encounter any difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide study drugs in our preclinical studies and clinical trials would be jeopardized. Any delay or interruption in the supply of preclinical study or clinical trial materials could delay the completion of our preclinical studies and clinical trials, increase the costs associated with maintaining our preclinical study and clinical trial programs and, depending upon the period of delay, require us to commence new trials at significant additional expense or terminate the studies and trials completely.

All manufacturers of our drug candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our component materials may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies at any time may also implement new standards, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of our drug candidates or entail higher costs or impair our reputation.

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We currently rely on a single source supplier for API for each of our drug candidates, other than vercirnon and CCX354 for which the responsibility for supplying the API and drug product has been assumed by GSK. IRIX Pharmaceuticals, Inc., currently manufactures the API for CCX140 and CCX168 for our Phase II clinical trials and CCX507 for our Phase I clinical trial. Cambridge Major Laboratories has been contracted to manufacture CCX140 API for our Phase III clinical trials. Carbogen Amcis produces the API for CCX872. Our current agreements with our suppliers do not provide for the entire supply of the API necessary for additional clinical trials or for full-scale commercialization. We have agreements with the University of Iowa Pharmaceuticals to manufacture the drug product for CCX140 for our Phase II clinical trials and GSK to manufacture the drug product for CCX168. Patheon has been contracted to manufacture CCX140 drug product for our Phase III clinical trials. In the event that we and our suppliers cannot agree to the terms and conditions for them to provide some or all of our API clinical and commercial supply needs, or if any single source supplier terminates the agreement in response to a breach by us, we would not be able to manufacture the API on a commercial scale until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, drug candidates.

Although alternative sources of supply exist, the number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New suppliers of any API would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing such ingredients. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs which may be passed on to us.

We currently have no sales and marketing staff or distribution organization. If we are unable to develop a sales and marketing and distribution capability on our own or through collaborations with GSK or other marketing partners, we will not be successful in commercializing our future products.

We currently have no sales, marketing or distribution capabilities or experience. If our products are approved for sale, we intend to rely on GSK to assist us in the marketing and distribution of our products for which GSK has exercised an option under our agreement, but there can be no assurance it will elect to market and distribute our products or that it will not terminate our collaboration arrangement. If GSK does not exercise its remaining option with respect to CCX168, we may need to enter into distribution or co-marketing arrangements with other third parties. To the extent we rely on third parties for marketing and distributing our approved products, any revenue we receive will depend upon the efforts of third parties, which may not be successful and are only partially within our control and our product revenue is likely to be lower than if we directly marketed or sold our products. GSK or other future collaborators may fail to develop or effectively commercialize our drug candidates because they cannot obtain necessary regulatory approvals, development or commercialization is not commercially reasonable, they elect to pursue competitive products outside of the collaboration; or for other reasons. If we are unable to enter into arrangements with third parties to commercialize the approved products on acceptable terms or at all, we may not be able to successfully commercialize our future products or we will have to market these products ourselves, which will be expensive and require us to build our own sales force, which we do not have experience doing. For example, we plan to retain commercial rights to CCX140 in North America and intend to build a small specialty sales force calling on nephrologists in North America. In addition, under our collaboration agreement with GSK, we have co-promotion rights with respect to certain drugs, but we do not have experience managing a sales force, selling drugs or marketing drugs. We cannot assure you we will be successful in any of these initiatives. If we are not successful in commercializing our future products, either on our own or through collaborations with GSK or one or more third parties, or co-promoting drugs with GSK, any future product revenue will be materially adversely affected.

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We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of December 31, 2012, we had 61 full-time employees. We will need to continue to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize our drug candidates. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- manage our clinical trials effectively, including our Phase II clinical trials for CCX140 and CCX168, which are being conducted at numerous trial sites throughout the world;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators, government agencies and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- identify, recruit, maintain, motivate and integrate additional employees.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The biotechnology and pharmaceutical industries are highly competitive, and we face significant competition from companies in the pharmaceutical, biotechnology and other related markets that are researching and marketing products designed to address IBD, chronic kidney disease, including diabetic nephropathy, rheumatoid arthritis, other autoimmune diseases and inflammatory disorders, and cancer. Established pharmaceutical companies that currently sell or are developing drugs in our markets of interest include, for example, AbbVie, Amgen, AstraZeneca, Biogen Idec, Bayer, Elan, GSK, Johnson & Johnson, Merck, Merck Serono, Takeda, Novartis, Pfizer, Sanofi and Teva. Many or all of these established competitors are also involved in research and drug development regarding various chemokine receptors. Pharmaceutical and biotechnology companies which are known to be involved in chemokine research and related drug development include Pfizer, GSK, Bristol-Myers Squibb, Merck, Takeda, Sanofi, Incyte, and UCB Pharma among others.

We are developing small molecule therapeutics that will compete with other drugs and alternative therapies that are currently marketed or are being developed to treat IBD, chronic kidney disease and diabetic nephropathy, rheumatoid arthritis, other autoimmune diseases, metabolic diseases, inflammatory disorders, and cancer. If approved for marketing by the FDA, vercirnon, our lead IBD drug candidate, would compete against existing IBD treatments such as Remicade, Humira, and other TNF-a inhibitors, Tysabri, and immunomodulatory drugs and corticosteroids and potentially against other novel IBD drug candidates that are currently in development. Similarly, other future drug candidates we are pursuing would compete against numerous existing and established drugs and potentially against other novel drugs and therapies that are currently in development. See Item 1. Business - Competition. We also anticipate that we will face increased competition in the future as new companies enter into our target markets and scientific developments surrounding the chemokine system continue to develop.

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. 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. These organizations may also establish exclusive collaborative or licensing relationships with our competitors.

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We may be subject to costly product liability claims related to our clinical trials and drug candidates and, if we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage, a material liability claim could adversely affect our financial condition.

Because we conduct clinical trials with human patients, we face the risk that the use of our drug candidates may result in adverse side effects to patients and to otherwise healthy volunteers in our clinical trials. We face even greater risks upon any commercialization of our drug candidates. Although we have product liability insurance for clinical trials for up to $10.0 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer, and we will be required to increase our product liability insurance coverage for our advanced clinical trials that we plan to initiate. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage on acceptable terms, or at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. There is also a risk that third parties that we have agreed to indemnify could incur liability. An individual may bring a product liability claim against us if one of our drug candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

withdrawal of clinical trial volunteers, investigators, patients or trial sites;

the inability to commercialize our drug candidates;

decreased demand for our drug candidates;

regulatory investigations that could require costly recalls or product modifications;

loss of revenues;

substantial costs of litigation;

liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;

an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;

the diversion of management s attention from our business; and

damage to our reputation and the reputation of our products.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which may be expensive and restrict how we do business.

Our third-party manufacturers activities and our own activities involve the controlled storage, use and disposal of hazardous materials, including the components of our pharmaceutical products, test samples and reagents, biological materials and other hazardous compounds. We and our manufacturers are subject to federal, state and local and foreign laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these hazardous materials. We currently carry no insurance specifically covering environmental claims relating to the use of hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials and waste products

comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of hazardous materials. In the event of an accident, state or federal or other applicable authorities may curtail our use of these materials and/or interrupt our business operations. In addition, if an accident or environmental discharge occurs, or if we discover contamination caused by prior operations, including by prior owners and operators of properties we acquire, we could be liable for cleanup obligations, damages and fines. The substantial unexpected costs we may incur could significantly harm our financial condition and results of operations.

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Future financings may adversely affect our stockholders or impose restrictions on our assets or operations, which may harm our business.

If we raise additional capital by issuing equity securities or convertible debt securities, then our existing stockholders ownership will be diluted and the terms of any new equity securities may have preferences over our common stock. If we raise additional capital through the issuance of debt securities, the debt will have rights senior to the holders of our common stock and may contain covenants that restrict our operational flexibility or impose liens or other restrictions on our assets. In addition, the terms of future financings may restrict our ability to raise additional capital, which would delay or prevent the further development or commercialization of our drug candidates. If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our current drug candidates, potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. If adequate funds are not available, our ability to achieve profitability or to respond to competitive pressures would be significantly limited and we may be required to delay, significantly curtail or eliminate the development of one or more of our drug candidates.

We are highly dependent on the services of our founder, President and Chief Executive Officer, Dr. Thomas J. Schall, and if we are not able to retain Dr. Schall or other members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.

We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We are highly dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. The competition for qualified personnel in the pharmaceutical industry is intense. Due to our limited resources, we may not be able to effectively attract and recruit additional qualified personnel. If we are not able to retain our management, particularly our founder, President and Chief Executive Officer, Dr. Schall, and attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Schall, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. In addition to the competition for personnel, the San Francisco Bay area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

In addition, we have scientific and clinical advisors who assist us in formulating our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

Requirements associated with being a public company increase our costs significantly, as well as divert significant company resources and management attention.

Prior to our initial public offering in February 2012, we were not subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or the other rules and regulations of the SEC or any securities exchange relating to public companies. We are continuing to work with our legal, independent

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accounting and financial advisors to identify those areas in which changes should be made to our financial and management control systems to manage our growth and our obligations as a public company. These areas include corporate governance, corporate control, internal audit, disclosure controls and procedures and financial reporting and accounting systems. We have made, and will continue to make, changes in these and other areas. However, the expenses that will be required in order to continue as a public company could be material. Compliance with the various reporting and other requirements applicable to public companies also require considerable time and attention of management. In addition, the changes we make may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis.

In addition, being a public company may make it more difficult or more costly for us to obtain certain types of insurance, including directors and officers liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

We are an emerging growth company and our election to delay adoption of new or revised accounting standards applicable to public companies may result in our financial statements not being comparable to those of other public companies and we also are entitled to utilize other reduced disclosure and governance requirements applicable to emerging growth companies.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act), and we intend to utilize certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to provide the auditor attestation report otherwise required by Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In addition, Section 107 of the JOBS Act also provides that an emerging growth company can utilize the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for implementing new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are electing to delay such adoption of new or revised accounting standards, and as a result, we may not implement new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. As a result of such election, our financial statements may not be comparable to the financial statements of other public companies. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may utilize these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company for up to five years, although if the market value of our common stock that is held by nonaffiliates exceeds $700 million as of any June 30 before that time, we would cease to be an emerging growth company as of the following December 31.

We are required to maintain compliance with Section 404 of the Sarbanes-Oxley Act of 2002 or we may be subject to sanctions by regulatory authorities.

Section 404(a) of the Sarbanes-Oxley Act of 2002 requires that we evaluate and determine the effectiveness of our internal controls over financial reporting and beginning with this Annual Report on Form 10-K provide a management report on the internal control over financial reporting. We have performed the system and process evaluation and testing required to comply with the management certification. Once we are no longer an emerging growth company as defined in the JOBS Act, we will also need to comply with auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002. If we do not properly implement the requirements of Section 404 in a timely manner or with adequate compliance, we may be subject to sanctions or investigation by regulatory authorities, such as the Securities and Exchange Commission, or SEC, or The NASDAQ Stock Market

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LLC, or NASDAQ. Any such action could adversely affect our financial results or investors confidence in us and could cause our stock price to fall. If we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. If we or our independent registered public accounting firm identifies deficiencies in our internal controls that are deemed to be material weaknesses, we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources and could materially adversely affect our stock price.

We may be adversely affected by the current economic environment.

Our ability to attract and retain collaboration partners or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States and inflationary pressures. We cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaboration partners or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to reduce their support of our programs or financing activities. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. This, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the United States result in widespread and prolonged unemployment, either regionally or on a national basis, prior to the effectiveness of certain provisions of the Affordable Care Act, a substantial number of people may become uninsured or underinsured. To the extent economic challenges result in fewer individuals pursuing or being able to afford our products once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our drug candidates could be delayed.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular,

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sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code, if a corporation undergoes an ownership change (generally defined as a greater than 50% change, by value, in its equity ownership over a three year period), the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income and taxes may be limited. We previously determined that we had ownership changes that occurred in July 1999 and June 2004, which limit our ability to use our then existing tax attributes. Future changes in our stock ownership, many of the causes of which are outside our control, could result in additional ownership changes. Any such ownership changes could further limit our ability to use net operating loss carryforwards and other pre-change tax attributes.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our corporate headquarters is located in California and certain clinical sites for our drug candidates, operations of our existing and future partners and suppliers are or will be located in California near major earthquake faults and fire zones. The ultimate impact on us, our significant partners, suppliers and our general infrastructure of being located near major earthquake faults and fire zones and being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural or manmade disaster.

Risks Related to Intellectual Property

We may have to license rights from Millennium Pharmaceuticals, Inc. or engage in patent litigation in order to secure the rights necessary to commercialize vercirnon. Patent litigation could absorb significant management time and financial resources, and, if we do not prevail, could have a material adverse effect on our ability to derive revenues from our agreement with GSK.

Millennium Pharmaceuticals, Inc., or Millennium, has obtained certain U.S. patents which include claims to small molecules that modulate CCR9, compositions thereof, and methods of using them to treat conditions such as IBD. We became aware of Millennium s CCR9-related patent applications during our own routine patent and patent literature review. Millennium, which was acquired by Takeda Pharmaceutical Company Limited, or Takeda, in May 2008 and is currently a wholly owned subsidiary of Takeda, may contend that the claims of these patents cover our patented vercirnon drug candidate. We believe that our activities related to vercirnon are currently exempt from patent infringement liability because these activities are strictly limited to obtaining information for regulatory approval. However, if and when our vercirnon related activities extend beyond those related to seeking regulatory approval, such as, for example, if and when we commercialize vercirnon, Millennium might then commence an infringement action against us based on these patents and/or other related

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patents that it may be granted in the future. If Millennium elects to sue us, we believe that we may have viable defenses to any such infringement suit. However, we cannot assure you that the relevant court would find in our favor with respect to such defenses. Intellectual property litigation and patent litigation in particular, is expensive, complex and lengthy and its outcome is difficult to predict. A court could enter orders that temporarily, preliminarily or permanently enjoin us or our strategic partners from using, selling, offering to sell or importing out current or future drug candidates or could enter an order mandating that we undertake certain remedial activities. During 2005, we did engage in preliminary discussions with Millennium regarding potentially collaborating with respect to CCR9, given that both we and Millennium have patents relating to CCR9. However, these discussions were general in nature and did not progress beyond the preliminary stage. Other than these preliminary discussions, we have not had any conversations or contacts with Millennium relating to CCR9. In addition, in April 2012, an opposition was filed with the European Patent Office by Millennium with respect to one of our patents relating to broad genus claims describing small molecules that target CCR9, the scope of which also relates to vercirnon. The opposition filed by Millennium alleges that the subject matter of such patent is not novel; such patent does not involve an inventive step; such patent does not sufficiently disclose the invention and the subject matter of such patent extends beyond the content of its patent application. The European Patent Office is currently evaluating our response to the opposition. We disagree with the points alleged in the opposition and will defend our issued European patent in question vigorously. Furthermore, we hold patents in Europe on CCR9 inhibitors including a selection patent on vercirnon that are not subject to the opposition filed. Under our agreement with GSK, GSK has the right, but not the obligation, to defend against third party patent infringement claims for licensed drugs. If GSK elects to defend against any such claims, it has the sole right to direct the defense of such claims and settle such claims at its own cost and expense. If GSK elects not to defend against such claims, we have the right, but not the obligation, to defend against such claims.

We may also be subject to negative publicity due to litigation. Pending or future patent litigation against us or any strategic partners by Millennium or anyone else may force us or any strategic partners to stop or delay developing, manufacturing or selling potential drug candidates that are claimed to infringe a third party s intellectual property, unless that party grants us or any strategic partners rights to use its intellectual property. If Millennium is able to obtain an injunction and neither we nor our strategic partners are able to obtain a license, both we and our strategic partners would be precluded from the manufacture and sale of vercirnon. U.S. patents are entitled to a presumption of validity and the burden of proving invalidity would be heavily weighted against us. Specifically, we would be required to show by clear and convincing evidence that Millennium s patents are invalid. Such decisions on patent validity often favor the patent owner because of the presumption of validity. If we or our strategic partners are unable to show that Millennium s patent is invalid and neither we nor our strategic partners are able to obtain a license from Millennium for the use of their intellectual property at all or on commercially acceptable terms, this would preclude both us and our strategic partners from the manufacture and sale of vercirnon or related candidate compounds found to be covered by Millennium s patent claims. If we are able to obtain a license from Millennium, we will be solely responsible for all fees required to be paid to Millennium in connection with such license and GSK will bear no responsibility for such license fees. See Item 1. Business - Intellectual Property.

The cost to us of any patent litigation or other proceedings, such as interference proceedings, which are meant to determine who first invented any of the claims covered by the patent even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Discovery proceedings in the United States might lead to the disclosure of some of our proprietary confidential information. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management and technical staff s time which may materially and adversely impact our financial position and results of operations.

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Our proprietary rights may not adequately protect our technologies and drug candidates. If we are unable to protect our drug candidates and our intellectual property rights, it may materially adversely affect our position in the market.

Our commercial success will depend on our ability to obtain patents and maintain adequate protection for our technologies, intellectual property and drug candidates in the United States and other countries. Our patent estate, on a worldwide basis, includes approximately 490 issued or allowed patents and approximately 255 pending patent applications, with claims relating to all of our current clinical stage drug candidates. With respect to our lead drug candidates in the CCR1, CCR2 and CCR9 programs, we have approximately 280 issued or allowed patents worldwide relating to their chemical composition or use thereof. There are also patent applications pending for our other clinical stage compounds in the C5aR, CXCR7 and CCR4 programs. We have approximately 70 issued patents relating to other small molecule compounds and approximately 90 issued patents relating to our novel biological discoveries. We also have approximately 50 issued patents relating to our proprietary screening and drug development technologies. We cannot assure you that any of our patent applications will result in issued patents. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies and future products are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

We apply for patents covering both our technologies and drug candidates, as we deem appropriate. However, we may fail to apply for patents on important technologies or drug candidates in a timely fashion, or at all. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies. Moreover, the patent positions of numerous biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. As a result, the validity and enforceability of our patents cannot be predicted with certainty. In addition, we cannot assure you that:

- we were the first to make the inventions covered by each of our issued patents and 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 by inventing around our claims;
- any of our pending patent applications will result in issued patents;
- a third party will not challenge our proprietary rights or that a court will hold that our patents are valid and enforceable;
- any patents issued to us or our collaboration partners 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 an adverse effect on our business.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the U.S. Patent and Trademark Office, or USPTO, which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, on September 16, 2011, President Obama signed the America Invents Act which codifies several significant changes to the U.S. patent laws, including, among other things, changing from a first to invent to a first inventor to file system, limiting where a patentee may file a patent suit, requiring the apportionment of patent damages, replacing interference proceedings with derivation actions, and creating a post-grant opposition process to challenge patents after they have issued. The effects of these changes are currently unclear as the USPTO must still implement

various regulations, the courts have yet to address any of these provisions, and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed.

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We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. However, it is possible that techno